

Search: Kent Opioids

PubMed, Embase, Scopus

Database: PubMed

Set		Results
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2	("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR "general surgery"[MeSH Terms] OR surgical[tiab] OR operation[tiab])	4473262
3	(Chronic[tiab] OR "long term"[tiab] OR persistent[tiab] OR longitudinal[tiab] OR prolonged[tiab])	2166790
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5	#1 AND #2 AND #3 AND #4	1875
6	#5 AND English[lang] NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])	1423
7	#5 AND ("2007/01/01"[PDAT] : "3000/12/31"[PDAT])	926

Database: Embase

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	'discectomy':ab,ti OR 'arthrodesis'/exp OR 'arthrodesis':ab,ti OR 'laparoscopy'/exp OR 'laparoscopy':ab,ti OR 'laparoscopic':ab,ti OR 'laparotomy'/exp OR 'laparotomy':ab,ti OR 'cesarean section'/exp OR cesarean:ab,ti OR caesarean:ab,ti OR 'hysterectomy'/exp OR hysterectomy:ab,ti OR robotic:ab,ti)	
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3	(Chronic:ab,ti OR 'long term':ab,ti OR persistent:ab,ti OR longitudinal:ab,ti OR prolonged:ab,ti)	3,030,299
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5	#1 AND #2 AND #3 AND #4	6667
6	#5 AND AND ([article]/lim OR [article in press]/lim OR [review]/lim OR [short survey]/lim) AND [humans]/lim AND [english]/lim	3692
7	#6 AND [2007-2018]/py	2566

Database: Scopus

Set		Results
1	TITLE-ABS(abdomen OR abdominal OR "Pelvis" OR pelvic OR "mastectomy" OR "breast" OR chest OR Thoracotomy OR Thoracoscopic OR thoracic OR lung OR Knee OR "knee replacement" OR "hip" OR "hip replacement" OR "spine" OR "lumbosacral" OR Lumbar OR "neck" OR "cervical" OR "discectomy" OR "discectomy" OR "arthrodesis" OR "laparoscopy" OR "laparoscopic" OR "laparotomy" OR cesarean OR caesarean OR hysterectomy OR robotic)	2950471
2	TITLE-ABS("surgery" OR surgical OR operation)	3,517,250
3	TITLE-ABS(Chronic OR "long term" OR persistent OR longitudinal OR prolonged)	3,256,075
4	TITLE-ABS("opioid-related disorders" OR "opioid" OR "opioids" OR Opioid OR "narcotics" OR "narcotic" OR "oxycodone" OR "tramadol" OR "hydrocodone" OR "tapentadol")	106685
5	#1 AND #2 AND #3 AND #4	1176
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Supplemental Table 1: GRADE Assessment of Included Studies : Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3-Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

Author/Yr	Surgery	Sample Size	Univariate	Multivariate	Study Limitations	Indirect	Imprecise	Pub Bias	Overall Quality	NOTES
<u>Arthroplasty</u>										
Franklin 2010 ⁴¹	TKA	6364	Yes	Yes	2	2	2	2	+	Methods unclear, unclear measure of opioid use at 12 months.
Carroll 2012 ¹³	Mixed	109	Yes	Yes	2	3	3	2	+	Pilot Study. Small N=19 TKA 26 THA.
Singh 2010 ⁴⁶	THA	5707	Yes	Yes	2	1	2	2	+	Drug use from self report via survey, 57% response rate, only age and comorbidities, including depression were significant predictors
Singh 2012 ⁴⁷	TKA	7,139	Yes	Yes	XX	X	XX	XX	++	Self report survey
Namba 2018 ³⁸	THA	12,859	Yes	Yes	2	1	2	2	++	Many non-significant results, single hospital system, very low number of revisions (~1%) which was the primary outcome.
Goesling 2016 ³⁴	TKA/THA	574	Yes	Yes	2	1	2	2	+++	Small sample size, single hospital, opioid use came from medical records of what was ordered and not verified by prescription fills, postoperative use largely self reported by patients
Sun 2016 ⁹	TKA/THA	62,746	Yes	Yes	1	1	2	2	+++	TKA N= 40 672, THA N=22 074.
Zarling 2016 ⁴⁰	TKA/THA	315	Yes	No	2	2	2	2	+	Majority of scripts written by primary care provider, small sample size, single

										hospital, lacked a comparable control group
Bedard 2017 ³¹	TKA	73959	Yes	No	2	2	1	2	+	Only univariate analysis.
Bedard 2018 ³²	UKA	4205	Yes	No	2	2	1	2	++	Only univariate analyses. No adjustment based on covariates.
Cancienne 2018 ³³	TKA	113,337	Yes	Yes	1	2	1	2	+++	Liberal definition of opioid use. Post was ≥ 1 Rx in 3-6 months post. Pre operative opioid use was 1 prescription 1-4 months pre.
Hadlandsmyth 2018 ³⁵	TKA	6653	Yes	Yes	1	2	1	2	+++	VA Study with good methods, stats, and results reporting. Very conservative definition of postoperative opioid use requiring continuous use for 12 months.
Hernandez 2017 ⁴⁸	TKA	105			2	1	1	2	+	Single institution. Small sample size. Incidence only reported.
Kim 2017 ³⁷	TKA/THA	57545	Yes	Yes	1	2	1	2	+++	Large N, sophisticated analysis, looked at important risk factors

Namba 2018 ³⁸	TKA	24,105	Yes	Yes	2	1	2	2 ++	Incidence only study. PPOU secondary measure and not pre-defined.
Politzer 2018 ⁴⁹	TKA	66,950	Yes	Yes	2	1	1	2 +++	Lack of psychosocial variables.
Sun 2017 ³⁹	TKA	120,080	Yes	Yes	2	1	1	2 +++	
Kim 2018 ³⁶	TKA	338	Yes	Yes	3	2	3	2 +	Single institution, small sample, large CI, most results non-significant, results were described as different with p values >.05

Abdominopelvic

Darnall 2011 ⁵⁰	Hysterec tomy	323	Yes	Yes	3	3	3	2 +	Very small sample size. One clinic.
Alam 2012 ¹⁵	Mixed	391,13 9	Yes	Yes	3	2	2	3 +	Methods not clearly described, Canadian sample with 90% use of codeine, definition was 1 Rx within 60 days of anniversary date
Raebel 2013 ²⁸	Bariatric	11,719	Yes	Yes	1	1	2	2 +++	Chronic pre-op opioid users excluded
Clark 2014 ⁸	Mixed	39,140	Yes	Yes	2	2	2	2 ++	Same patient population as Soneji. Looked at first 180 days. Complete description of methods. Only patients 66 and older and in Canada. Some results appear different than in Soneji 2016, but not sufficient detail to tell.
Kulshrestha 2014 ²⁶	Kidney Txp	1045	Yes	Yes	2	3	3	2 ++	Single center, relied on prescription orders, not fills.
Raebel 2014 ²⁹	Bariatric	10,643	Yes	Yes	2	2	2	2 ++	Good description of methods
Soneji 2016 ³⁰	Mixed	39,140	Yes	No	3	2	2	2 +	Very limited description of methods, only patients 66 and older, Canadian study with

											different health care system and opioid use patterns.
Sun 2016 ⁹	Mixed	641,941	Yes	Yes	1	2	1	2	+++		Large sample, reports incidence by surgery, strong observational study
Ladha 2016 ⁴⁵	Open Abd Surgery	11,537	Yes	Yes	3	1	2	2	+		Eliminated 30% of pts with a preoperative opioid prescription, no significant differences
Brummett 2017 ³	Mixed	36,177	Yes	Yes	2	2	1	2	+++		Optum Insight national data. 1 Rx qualified as persistent use. Surgery condition reported with incidence.
King 2017 ⁵¹	Bariatric	2218	Yes	Yes	1	2	1	2	+++		Prospective. Excellent methods.
Lee 2017 ¹²	Mixed	68463	Yes	Yes	1	2	2	2	++		Eliminated patients with no opioid fills post discharge. Would increase rate by lowering denominator
Moran 2017 ⁵²	Pancreatotomy	46	Yes	Yes	2	3	2	2	++		Very small sample size. No statistically significant results related to opioids. Power not discussed.
Shah 2017 ⁴²	Urology	675,527	Yes	Yes	2	2	2	2	++		Didn't report chronic opioid use but rather opioid dependence and overdose. Significant chance of under reporting opioid use.

Spine

Lawrence 2008 ⁴⁴	ACDF	91	No	No	3	2	3	2 +	Single institution with very small sample size. Opioid use assessed by self report.
Nguyen 2011 ⁴³	Spine (Mixed)	725	Yes	Yes	2	2	3	2 +	Not representative of broader group of patients. Workers compensation in Ohio.
Zigler 2013 ⁵³	Lumbar Fusion	75	No	No	3	2	3	2 +	Very small sample size of surgical patients who failed non-surgical treatment. Lack of appropriate statistical analysis
Mirza 2013 ⁵⁴	Mixed/Spine	86 (Surgical)	Yes	Yes	2	2	3	2 +	Very large number of excluded patients. Very small sample size of surgical patients. Opioid use not well described.
Armaghani 2014 ²⁴	Mixed/Spine	583	Yes	Yes	1	1	2	2 +++	Excellent methodology. Limited to one center. Relatively small sample size - 583.
Mayer 2014 ⁵⁵	Fusion and Non Fusion	546	Yes	Yes	3	2	2	2 +	Workers compensation patients. Opioids not a focus of the study
Anderson 2015 ⁵⁶	Lumbar Fusion	1002	Yes	Yes	2	2	3	2 +	Not representative of broader group of patients. Workers compensation in Ohio.
Mino 2017 ⁵⁹	Lumbar fusion	850	Yes	No	3	2	3	2 +	Purely descriptive. Lack of appropriate statistical analysis.
De la Garza-Ramos 2016 ⁵⁷	ACDF	97	No	No	3	2	3	2 +	Very small sample size. One institution. Generally no difference in pre and post opioid use.

Connolly 2017 ⁵⁸	Lumbar Fusion	8377	Yes	Yes	1	2	1	2	+++	National data source. Good methodology. Methods say analysis limited to patient >=65 but data reported on <65.
Schoenfeld 2017 ²⁵	Spine (Mixed)	9991	Yes	No	3	2	1	2	++	Active military population. Young.
O'Connell 2018 ⁶¹	Lumbar Fusion	60,597	Yes	Yes	1	1	1	2	+++	Strong methodology. Focus on preoperative depression and opioid use.
Butterman 2018 ⁶⁰	ACDF	159	No	No	3	2	3	2	+	Very small sample size. Limited statistical evaluation re opioids
<u>Thoracic</u>										
Carroll 2012 ¹³	Mixed	109	Yes	Yes	2	3	3	2	+	Pilot Study. Very small sample size. 27 Thoracotomy patients
Clark 2014 ⁸	Mixed	39,140	Yes	Yes	2	2	2	2	++	Same patient population as Soneji. Looked at first 180 days. Complete description of methods. Only patients 66 and older and in Canada. Some results appear different than in Soneji, but not sufficient detail to tell
Soneji 2016 ³⁰	Mixed	39,140	Yes	No	3	2	2	2	+	Very limited description of methods, only patients 66 and older, Canadian study with different health care system and opioid use patterns.

Lee 2017 ¹²	Mixed	68463	Yes	Yes	1	2	2	2	++	Eliminated patients with no opioid fills post discharge. Would increase rate by lowering denominator
<u>Mastectomy</u>										
Carroll 2012 ¹³	Mixed	109	Yes	Yes	2	3	3	2	+	Pilot Study. Very small N. 25 Mastectomy patients
Lee 2017 ¹²	Mixed	68463	Yes	Yes	1	2	2	2	++	Eliminated patients with no opioid fills post discharge. Would increase rate by lowering denominator
Marcusa 2017 ¹⁰	Mastectomy with Recon	4113	Yes	Yes	2	1	1	2	+++	National data.

Supplemental Table 2: Patient Characteristics Associated with PPOU in Total Joint Arthroplasty: Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3-Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

<u>Risk Variable</u>	<u>Study Limitations</u>	<u>Indirectness</u>	<u>Imprecision</u>	<u>Inconsistency</u>	<u>Level of Evidence</u>
Preoperative Opioid Use	1	1	1	2	++++
Depression	2	1	1	2	+++
Substance Abuse	2	2	1	1	+++
Preoperative Painful Condition	2	3	1	1	+++
Smoking	2	1	2	2	+++
Psychotropic Drug Use (Antidepressant, Benzodiazepine)	2	2	2	2	+++
Anxiety	2	2	2	2	++
Gender	2	2	3	3	++
Age	2	1	3	3	++
BMI	2	2	3	3	++
Catastrophization	3	3	3	3	++
Low physical function based off validated scales (i.e. WOMAC, SF - 12)	3	3	3	3	++

Supplemental Table 3: Studied reviewed pertaining to knee and hip arthroplasty.

Arthroplasty								
<i>Study (Author, Yr)</i>	<i>Study Design</i>	<i>Data Source</i>	<i>Setting</i>	<i>Sample Size</i>	<i>Definition or Measure of Opioid Use or Prescription</i>	<i>Incidence</i>	<i>Risk Factors</i>	<i>Notes</i>
Franklin et al. 2010 ⁴¹	Retrospective Cohort	National TKA registry sponsored by Zimmer, Inc. Warsaw, Ind. (2000-2004)	TKA-USA	6364	Opioid prescription at 12 months postoperatively	<p><u>Overall:</u> 5.5% at 1 year</p> <p><u>Opioid Naïve:</u> 2.6% at one year</p> <p><u>Preoperative Opioid Prescription:</u> 14% at one year</p>	<p>Preoperative opioid</p> <p>Age (Young)</p> <p>Gender (F>M)</p> <p>Obese</p> <p>Lower Knee Society Score</p> <p>Lower SF-12 Mean Physical Function Score</p>	
Singh, 2010 ⁴⁶	Observational Cohort	Mayo Total Joint Registry (1993-2005) Patient self report	THA-USA	5,707 at 2 years 3,289 at 5 years	2 & 5 year reported use	<p><u>Overall:</u> 2.3% at 2 years</p> <p>2.8% at 5 years</p>	<p><u>Overall at 2 years:</u> Women</p> <p>Depression</p> <p><u>Overall at 5 years</u> Women</p> <p>Higher BMI</p>	

Singh, 2012 ⁴⁷	Prospective Observational Cohort	Mayo Total Joint Registry (1993-2005)	TKA – USA	7139 at 2 years 4234 at 5 years	Percentage of patients at 2 & 5 year reporting use for pain in operative knee	<u>Overall:</u> 1.4% at 2 & 5 years	Anxiety	Male & Age > 70 yrs served as protective factors
Carroll, 2012 ¹³	Prospective, longitudinal inception cohort	Single site, Patient Report	USA- Mastectomy, lumpectomy, thoracotomy, TKR, THR.	109 total enrolled (19 TKA/ 26 THA)	Time until opioid cessation.- The time from surgery until the first of 5 consecutive days of zero opioid use was defined as postoperative “time to opioid cessation,” and this was the primary end point.	<u>Overall:</u> TKA – 26% at 713 days THA -- 23% AT 644 days	<u>Overall Sample:</u> Legitimate preoperative opioid use Self perceived susceptibility to addiction Depressive Symptoms	
Goesling, 2016 ³⁴	Secondary analysis of prospective outcome study	Patient Report	USA – THA + TKA	574	Patient reported opioid use at 6 months post surgery	<u>Overall:</u> 14.8 % reported use <u>Opioid naive:</u>	Worse pain a surgical site Greater functional impairment More stiffness	

						8.2% TKA/ 4.3% <u>Preoperative opioid users:</u> 53.3% TKA/ 34.7% THA	Increase body pain More depression Catastrophizing Preop opioid use (>60 OME) Overall change in body pain Knee > hip in opioid naive	
Zarling, 2016 ⁴⁰	Retrospective Chart and Database review	Single site, State prescription database (2010-2011)	TKA/THA – USA	315 (158 TKA/157 THA)	Number of prescriptions followed until 12 months post surgery	<u>Opioid Naïve:</u> 22% filling at one year <u>Chronic Preoperative Users:</u> 64% filling at one year	Chronic preoperative opioid use Female TKA	
Sun, 2016 ⁹	Retrospective Cohort	Health Claims (MarketScan) (2001-2013)	USA – 11 Surgical Procedures	641,941 (all surgeries) TKA 40,672 THA 22,074	Having filled 10 or more prescriptions or more than 120 days' supply within the first year after surgery, excluding	<u>Opioid Naïve</u> 1.41% for TKA 0.59% for THA	<u>Overall</u> (all surgeries considered) Male Older than 50 years Drug abuse	

					the first 90 postoperative days.		Alcohol abuse Depression Benzodiazepine use Anti-depressant use	
Bedard, 2017 ³¹	Retrospective Cohort	Humana Inc administrative claims database (2007-2015)	TKA- USA	73,959	Opioid refill rates per month until 1 year post surgery	<u>Overall:</u> 11.9% Filling opioid prescription at 1 year post surgery <u>Opioid Naïve:</u> 3.3% filling at one year <u>Chronic Preoperative Users:</u> 33.2% filling at one year	Preop opioid use Younger (<50) Female Anxiety Depression Low back pain Myalgia Drug/Alcohol Dependence Tobacco use	
Hernandez, 2017 ⁴⁸	Retrospective institutional registry review	Mayo Total Joint Registry	TKA- USA (2012)	105	Patient tracked until 2.4 +/- 0.5 years	<u>Overall:</u> 4.8 % at 2.4 years	Not measured	

Kim, 2017 ³⁷	Retrospective Cohort	United Health Care/Optum Clinformatics® Data Mart Database (2004-2013)	TKA/THA – USA	39,401 TKA 18,144 THA	Persistent use was defined as having any use of opioid prescriptions in each of the 12 months continuously based on a group-based trajectory modeling	<u>Overall:</u> 5.5% incidence (combined TKA/THA)	Younger Female Tobacco use Preoperative opioid use More painful comorbidities (fibromyalgia, lower back pain, migraine, RA) More prescription drug use (i.e. benzodiazepine) Longer length of stay Total knee arthroplasty Discharged to acute rehabilitation center	
Namba, 2018 ³⁸	Retrospective Registry	Kaiser Permanente Total Joint Replacement Registry (2008-2011)	TKA – USA	24,105	90 day exposure periods	<u>Overall:</u> 29.8% Days 270-360	- Not measured	

Kim, 2017 ³⁷	Retrospective Chart Review	Single institution chart review with state prescription registry. (2016)	TKA – USA	338	Continued use at 6 months	<p><u>Overall :</u> 10.9%</p> <p><u>Opioid Naïve group:</u> 4.9% incidence</p> <p><u>Opioid tolerant group:</u> 43.4% incidence</p>	<p>Male</p> <p>Prior injury/surgery to knee</p> <p>Tobacco use</p> <p>Preoperative opioid use</p> <p>Psychiatric Dg (anxiety, depression, bipolar)</p> <p>MSO4 > 12 mg/d</p>	
Politzer, 2018 ⁴⁹	Retrospective Cohort	Humana Health Insurance (2007-2015)	TKA- USA	66,950	Chronic opioid users were defined as those patients who were prescribed any opioids for over 6 contiguous months postoperatively in each cohort.	<p><u>Overall :</u> 21.3%</p> <p><u>Opioid Naïve group:</u> 2.2% incidence</p> <p><u>Opioid tolerant group:</u> 34.8% incidence</p>	<p>Preoperative opioid use</p> <p>Female</p> <p>Younger</p> <p>Greater length of stay</p> <p>Charlson Comorbidity Index > 3</p>	
Sun, 2017 ³⁹	Retrospective Cohort	Marketscan - administrative health claims (2001-2013)	USA-TKA	120,080	Having filled 10 or more prescriptions or >120	<p><u>Overall :</u> 21.3%</p>	Not Measured	

					days' supply within a 1-year period.	<u>Opioid Naïve group:</u> 1.8 % incidence <u>Opioid tolerant group:</u> 68% incidence		
Cancienne, 2018 ³³	Retrospective Cohort	PearlDiver patient record database (2007-2016)	USA- TKA	113,337	Prolonged postoperative narcotic use was defined as a patient filling a prescription for a narcotic pain medicate between 3 and 6 months postoperatively	<u>Overall:</u> 31.6 % combined	Preoperative prescription (higher number filled) Filling other prescriptions preoperatively (Anxiolytics, muscle relaxants, methadone) - Substance use/abuse(tobacco, alcohol, marijuana) Age <50 Back pain Morbid obesity Depression	
Hadlandsmyth, 2018 ³⁵	Retrospective Cohort (2013-2015)	VHA dataset	TKA-VA Sample	6653	6 and 12 month receipt of opioid	<u>Overall:</u> 14.6% at one year	<u>Preoperative opioid users</u> Opioid tolerant	

						<p><u>Opioid Naïve:</u> 2% at 1 year</p> <p><u>Opioid Tolerant:</u> 57% at 12 months</p>	<p>Antidepressant use</p> <p>Antiepileptic use</p> <p>Unknown racial identification</p> <p>Obese</p> <p>Muscle relaxant use</p> <p><u>Opioid naïve:</u> Substance abuse</p> <p>Muscle relaxant use</p>	
Bedard, 2018 ³²	Retrospective cohort	Humana Inc. database (2007-2015)	Unicompartmental Knee Arthroplasty TKA/THA comparator groups	4205	Number of repeat opioid prescriptions tracked per month for the first postoperative year.	<p><u>Overall sample at 12 months:</u></p> <p>UKA: 9.8%</p> <p>TKA: 14.6%</p> <p>THA: 13.7%</p> <p><u>Opioid Naïve at 12 months:</u></p> <p>UKA: 3.75%</p> <p>TKA: 3.3%</p> <p>THA: 2.9%</p>	<p>Anxiety</p> <p>Depression</p> <p>Substance Abuse</p> <p>Smoking</p> <p>Preoperative Opioid Use</p> <p>Low Back Pain</p> <p>Myalgia</p>	

						<u>Opioid Tolerant at 12 months:</u> UKA: 25.62% TKA/THA: Not reported		
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Table 4: Patient Characteristics Associated with PPOU in Abdominopelvic Surgery: Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3-Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

<u>Risk Variable</u>	<u>Study Limitations</u>	<u>Indirectness</u>	<u>Imprecision</u>	<u>Inconsistency</u>	<u>Level of Evidence</u>
Preoperative Opioid Use	1	3	1	1	++++
Depression	3	2	1	1	+++
Substance Abuse	2	3	2	2	+++
Preoperative Pain Conditions	2	2	1	1	+++
Smoking	1	2	2	2	+++
Anxiety	3	2	3	3	++
Gender	2	2	3	3	+
Age	2	2	2	2	++
Psychotropic Drug (Antidepressant, Benzodiazepine)	1	2	2	2	+++
BMI	-	-	-	-	4 studies - No association

Supplemental Table 5: Studies reviewed pertaining to Abdominopelvic Surgery

Abdominopelvic								
<i>Study (Author, Yr)</i>	<i>Study Design</i>	<i>Data Source</i>	<i>Setting</i>	<i>Sample Size</i>	<i>Definition or Measure of Opioid use OR prescription</i>	<i>Incidence</i>	<i>Risk Factors</i>	<i>Notes</i>
Darnall, 2011 ⁵⁰	Retrospective cross sectional	Chart review	New female chronic pain clinic evaluation	323	None	33.6% opioid at remote time following hysterectomy patients Rx opioid	Not measured	
Alam, 2012 ¹⁵	Retrospective cohort - Opioid Naive	Canada – Ontario health administrative databases (1997-2008)	Short Stay surgery (cataract, lap. Chole, TURP, varicose vein)	391,139	Prescription for an opioid within 60 days of the 1-year anniversary of the surgery.	<u>Opioid Naive</u> - 0.2% Lap Chole	Receipt of opioid prescription within 7 days of surgery	
Morgan, 2012 ²⁷	Prospective Database	Patient Report	Pancreatectomy with Islet Autotransplantation for Chronic Pancreatitis	33	None	77% using opioids at 1 year postoperatively	Not Measured	
Raebel, 2013 ²⁸	Retrospective Cohort	10 sites of the Scalable Partnering Network	Bariatric Surgery	11,719	10 or more opioid dispensings over 90 or more days or at least a 120-day supply of opioids dispensed sometime in	<u>Chronic Preoperative Opioid</u> - 77% incidence 1 year post		

					the year before bariatric surgery.			
Kulshrestha, 2014 ²⁶	Prospective observational	Single center-Chart documentation of opioid prescription (2004-2008)	Kidney Transplant	1045	Chronic opioid usage (COU) was defined as active use of opioid analgesics at all the three time intervals or first two time intervals if the patient had an event (death and/or graft loss) between three and 12 months.	Overall: 11.4% by authors definition 14.6% at 10-12 months.	Pre transplant opioid use Prior Psychiatric Diagnosis Chronic Pain before transplant Illicit drug use Use of induction therapy with rATG Smoking history Length of inpatient stay	
Clarke, 2014 ⁸	Retrospective Cohort-Opioid Naive	Canada – Population based administrative databases (2003-2010)	9 Major surgeries	39,140	Prolonged opioid use after hospital discharge was defined as one or more opioid prescriptions within 1 to 90 days after surgery along with one or more prescriptions for opioids within 91 to 180 days after surgery	<u>Pelvic:</u> Radical Prostate: 2.8% <u>Abdominal:</u> Minimally Invasive Colorectal- 3.2% Open Colorectal- 2.8%	Younger Lower 5 th of neighborhood income Comorbidities (Diabetes/HF/Pulmonary disease) Benzodiazepine use ACE Inhibitor use SSRI use.	

						Gynecologic : Minimally Invasive Hysterectomy-1.5% Open Hyst 2.5%		
Raebel, 2014 ²⁹	Retrospective Cohort	9 health systems in Scalable Partnering Network	Bariatric Surgery	10,643	Chronic opioid use was defined as ≥ 10 opioid dispensings over ≥ 90 days or ≥ 120 total days' supply dispensed.	<u>Overall</u> : 4% <u>Opioid Naïve</u> : 1.3% <u>Preoperative opioid use</u> : 8.1%	Increasing total days' supply the year prior At least two dispensing of non opioid analgesic/anti- anxiety - Tobacco	Increased Age and Lap Band Procedure associated with significant decreased risk.
Ladha, 2016 ⁴⁵	Retrospective Cohort	InVision for Data Mart (2004- 2013)	Open abdominal surgery	6432	Time until 30 day without filling opioid prescription	<u>Opioid Naïve</u> : 11.5 % filled single opioid prescription 90-180 days postoperatively	Not Measured	
Sun, 2016 ⁹	Retrospective Cohort - Opioid Naïve	MarketScan Health Claims Database (2001- 2013)	11 Surgical Procedures	641,941	Having filled 10 or more prescriptions or more than 120 days' supply within the first year	C sxn- 0.119% Open Appy ~0.2--0.3%	Male Older than 50 years Drug abuse Alcohol abuse	

					after surgery, excluding the first 90 postoperative days.	Lap Appy- ~0.2% Open Chole ~1.2% Lap Chole ~0.3-0.4%	Depression Benzodiazepine use Anti-depressant use	
Bateman , 2016 ¹¹	Retrospective Cohort	Clininformatics Data Mart (2003-2011)	Caesarean Section	80,127	Opioid prescriptions followed 12 consecutive 30 day periods post caesarean section.	<u>Overall:</u> 0.36% persistent use rate at 1 year overall <u>Opioid Naive:</u> 0.23% persistent use rate at 1 year	Younger Illicit subst use Tobacco Pain conditions (back pain, fibromyalgia, migraines) Psychotropic medications (anti-depressant, benzodiazepine)	
Soneji, 2016 ³⁰	Retrospective Cohort	- Canada-Opioid Naïve		39,140	- Cessation defined by the absence of any opioid prescription within the preceding 90 days	- 53% received an opioid prescription - 0.4% continued to receive prescriptions at 1 year - Open Abd/Gyn:	- Open and minimally invasive lung resection	

						~<0.1% at 1 year - MI Abd/Gyn: ~<0.1% at 1 year		
Shah, 2017 ⁴²	Retrospective Cohort	Healthcare Cost and Utilization Project (2007-2011)	Variety of Urologic Surgeries	675,527	Patients were assessed for a new diagnosis of opioid dependence and/or opioid overdose within 1 year post-operatively.	<u>Opioid Naïve</u> - 0.09% Highest for stone procedures - 0.15% Lowest for major pelvic surgery - 0.12%	Younger Less likely to have undergone ambulatory procedure Depression Tobacco user Less likely to carry malignancy diagnosis Caucasian Non private insurance Peptic Ulcer Disease Liver Disease Chronic Obstructive Pulmonary Disease	
Lee, 2017 ¹²	Retrospective Insurance Claim-	Truven Health Marketscan Research	Curative intent procedures for melanoma, breast,	68,463 Colorectal - 6082	Filling opioid prescriptions 90 to 180 days after surgery	<u>Opioid Naïve</u>	Adjuvant Chemotherapy	

	(Opioid Naive Patients)	Databases (2010-2014)	colorectal, lung, esophageal, and hepatopancreatobiliary/gastric cancer.	Hepatobiliary/Gastric - 1508		Colorectal: 7.5% Hepato-Bil-Gast: 12.4%	Preoperative opioid prescription	
Brummett, 2017 ³	Retrospective Cohort - Opioid Naive Patients	Clinformatics Data Mart (2013-2014)	Minor (varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral prostate surgery, parathyroidectomy, and carpal tunnel) Major (ventral incisional hernia repair, colectomy, reflux surgery, bariatric surgery, and hysterectomy)	36,177	New persistent opioid use, which was defined as an opioid prescription fulfillment between 90 and 180 days after the surgical procedure	Laparoscopy ~6% Laparoscopy Appendectomy ~ 4-5% Venralt Hernia Repair~8% Colectomy ~ 10% Reflux ~ 7% Bariatric ~8% Hysterectomy ~ 5-6%	<u>Overall Sample</u> Preoperative opioid prescription in the 30 days before surgery Preoperative tobacco use Alcohol/Substance Abuse Mood disorders (Anxiety/Depression) Preoperative Pain Disorders (Back pain, neck pain, arthritis, centralized pain)	

King, 2017 ⁵¹	Prospective Observational	Multisite-Patient report	Bariatric Surgery	2258		<p><u>Overall:</u> 13.8% at 1 year 20.3% at 7 years</p> <p><u>Opioid Naive:</u> 5.8% at 1 year 14.2% at 7 years</p> <p><u>Preoperative Opioid Use:</u> 58.8% at 1 year 56.3% at 7 years</p>	<p>More baseline pain</p> <p>Worsening pain after surgery</p> <p>Starting/Continuing nonopioid analgesic use</p> <p>Benzodiazepine use</p> <p>Public insurance</p> <p>Back/hip/knee/ankle surgery</p> <p>Subsequent bariatric procedure</p> <p>More improvement in mental health after surgery</p>	
Moran, 2017 ⁵²	Prospective Observational Cohort	Single site - Patient report (2011-2015)	Total pancreatectomy with islet autotransplantation	46	Opioid independence at last follow up	46% opioid independence at 66 weeks post surgery		

Supplemental Table 6: Patient Characteristics Associated with PPOU in Spine Surgery: Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3- Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

<u>Risk Variable</u>	<u>Study Limitations</u>	<u>Indirectness</u>	<u>Imprecision</u>	<u>Inconsistency</u>	<u>Level of Evidence</u>
Preoperative Opioid Use	2	2	1	1	++++
Depression	2	2	1	1	++++
Anxiety	3	3	3	2	++
Preoperative Pain	3	3	3	2	++
Lumbar Fusion	2	2	3	2	++
Revision Surgery	2	3	3	2	++
Legal representation	3	3	3	3	+
Out of work greater than 12 weeks	3	3	3	3	+
Substance Abuse	-	-	-	-	1 study - No association
Gender	-	-	-	-	2 studies - No association
Age	-	-	-	-	4 studies - No association
Smoking	-	-	-	-	2 studies - No association
BMI	-	-	-	-	2 studies - No association
Psychotropic Drug Use (Antidepressant, Benzodiazepine)	-	-	-	-	N/A

Supplemental Table 7: Studies reviewed pertaining to Spine Surgery

Spine								
<i>Study (Author, Yr)</i>	<i>Design</i>	<i>Data source</i>	<i>Setting</i>	<i>Sample Size</i>	<i>Definition PPOU</i>	<i>Incidence</i>	<i>Risk Factors</i>	<i>Notes</i>
Lawrence, 2008 ⁴⁴	Retrospective Chart Review	Single site, single surgeon	Anterior cervical discectomy and fusion	91	Opioid use documented in medical chart	<p><u>Overall:</u> 20.8% > 3 months post surgery</p> <p><u>Preoperative Opioid Use:</u> 34% > 3 months post surgery</p> <p><u>Opioid naive:</u> 7% > 3 months post surgery</p>		
Nguyen, 2011 ⁴³	Retrospective Cohort Study	Ohio Bureau of Workers' Compensation database. (1999-2001)	Lumbar fusion	725	Patient using opioids throughout the duration of the study (2 years)	Overall: 85% of patients used opioid medication throughout entire study with a 41% increase from baseline	Not Measured	
Zigler, 2013 ⁵³	RCT	Patient report	Total disc replacement versus circumferential fusion	75	"Narcotic" use at 2 and 5 years	<p>2 years - 42.5%</p> <p>5 years - 40%</p> <p>*Significant decrease from baseline 76% preoperative "narcotic" use</p>		
Mirza, 2013 ⁵⁴	Prospective Observational cohort	Patient report	Instrumented fusion Artificial disc replacement Laminectomy	495 (409 non surgical controls + 86 surgical)	Medication use at defined timepoints (no a priori definition)	<p>Baseline: 80% Non Surgical use</p> <p>88% Surgical candidate use</p> <p>53% of patient use of opioids 1 year after enrollment</p>	Not measured	
Armaghani, 2014 ²⁴	Prospective Cohort	Prospective spine registry (patient report)	Cervical/Thoracic/Lumbar Surgeries	583	12 months opioid use	<u>Overall:</u>	More invasive surgery	

						56% opioid independence at 12 months <u>Opioid Naive:</u> 74% of opioid naïve patients were opioid free where 41% of patients on pre-opioid were “free”	Higher MSPQ Revision Greater preoperative opioid use Anxiety Depression	
Mayer 2014 ⁵⁵	Prospective		331 Fusion 233 Non Fusion Surgery	564 surgical patients 349 matched comparison	Opioid dependence diagnosis at 1 year post functional rehabilitation program (Secondary Outcome)	31.3 % Fusion group 19.4 Non Fusion group	Lumbar Fusion	
Anderson, 2015 ⁵⁶	Retrospective Cohort	Ohio Bureau of Workers' Compensation. (1993-2013)	Lumbar Fusion	1002	Postoperative chronic opioid therapy defined as being supplied opioid analgesics for more than 1 year after the immediate 6-week postoperative period.	Overall: 57% > 1 year use	Preoperative opioids (Days/Rx) Out of Work greater than 12 weeks Depression Psychotherapy Additional Lumbar Surgery Failed Back Syn before fusion Discography Legal representation Spondylosis	

De la Garza-Ramos 2016 ⁵⁷	Retrospective Chart Review	Single academic institution	Anterior cervical discectomy and fusion	71	Opioid prescription (secondary outcome)	32.% Median follow up time 7.6 year (1-22 years)	Not measured	
Connolly, 2017 ⁵⁸	Population Based Retrospective Cohort Study	Clinformatics Data Mart (2009-2012)	Lumbar Fusion	8377	Long-term opioid use was measured as a binary greater than 365 days of filled opioid prescriptions and in continuous fashion during the 24 months following lumbar fusion.	Overall: 40% for 6 months 30% for 12 months 17% for 24 months	Duration of opioid use in the year prior Repeat surgery Depression	Anterior fusion (modest decrease in risk of long term opioid use)
Schoenfeld, 2017 ²⁵	Retrospective cohort (Opioid Naive)	TRICARE insurance claims (2006-2014)	1 of 4 common spinal surgical procedures (discectomy, decompression, lumbar posterolateral arthrodesis, or lumbar interbody arthrodesis)	9991	Proportion of patient using opioids up to 1 year	Opioid Naïve: 0.1% at 6 months 0.02% at 1 year	Lumbar interbody arthrodesis Depression Senior enlisted Low SES	
Mino 2017 ⁵⁹	Retrospective Cohort	Cigna's national claim database (2009-2011)	Lumbar Fusion	1422	Narcotic pharmacy claims (secondary variable) 2 years post surgery	62% continued to receive opioid refill more than 1 year. Within this group, an average of 23.5 opioid prescriptions were filled during the study period. 95% of patients on preoperative opioid continued use more than 1 year postoperatively.	Not measured.	
Butterman, 2018 ⁶⁰	Prospective observational	Single site, Patient report	Anterior cervical discectomy and fusion	159	Opioid use 10 year follow (secondary outcome)	53% preoperative use 29% use 7-12 months postoperatively 26% use during 9-11 year follow up		

O'Connell 2018 ⁶¹	Retrospective cohort	MarketScan Commercial Claims and Encounters Database and Medicare Supple- mental and Coordination of Benefits Database.	Lumbar Fusion	60,597	“Chronic use” was defined as at least 10 prescriptions (regardless of MMEs) or ≥ 120 days’ supply over the 3- to 12-month post-index visit period,	<u>Overall:</u> 19.5% 31.8% of depressed patients met authors definition 18.4% of controls met definition	Depression Preoperative Opioid Use	
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Supplemental Table 8: Patient Characteristics Associated with PPOU in Thoracic Surgery: Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3- Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

<u>Risk Variable</u>	<u>Study Limitations</u>	<u>Indirectness</u>	<u>Imprecision</u>	<u>Inconsistency</u>	<u>Level of Evidence</u>
Preoperative Opioid Use	2	3	2	2	++
Depression	3	3	3	3	+
Substance Abuse	3	3	3	3	+
Age	3	3	3	3	+
Psychotropic Drug Use (Benzodiazepine, antidepressant)	3	3	3	3	+
Anxiety	-	-	-	-	2 studies - No association
Preoperative Pain	-	-	-	-	1 study - No association
Gender	-	-	-	-	3 studies - No association
Smoking	-	-	-	-	2 studies - No association

Supplemental Table 9: Studies reviewed pertaining to Thoracic Surgery

Thoracic								
Study (Author, Yr)	Design	Data Source	Setting	Number of Patients	Definition PPOU	Incidence	Risk Factors	Notes
Carroll, 2012 ¹³	Prospective, longitudinal inception cohort	Single site, Patient Report	USA- Mastectomy, lumpectomy, thoracotomy, TKR, THR.	109 total enrolled (19 TKA/ 26 THA)	Time until opioid cessation.- The time from surgery until the first of 5 consecutive days of zero opioid use was defined as postoperative “time to opioid cessation,” and this was the primary end point.	<u>Overall:</u> Thoracotomy – 22% at 276 days	<u>Overall Sample:</u> Legitimate preoperative opioid use Self perceived susceptibility to addiction Depressive Symptoms	
Clarke, 2014 ⁸	Retrospective Cohort (Opioid Naive)	Canada – Population based administrative databases (2003-2010)	9 Major surgeries	39,140	Prolonged opioid use after hospital discharge was defined as one or more opioid prescriptions	8.5% open lung resection 6.3% minimally invasive lung	<u>Overall sample:</u> Younger Lower 5 th of neighborhood income	

					within 1 to 90 days after surgery along with one or more prescriptions for opioids within 91 to 180 days after surgery		Comorbidities (Diabetes/HF/Pulmonary disease) Benzodiazepine use ACE Inhibitor use SSRI use. Thoracic surgery	
Soneji, 2016 ³⁰	Retrospective Cohort (Opioid Naive)	Canada – Population based administrative databases (2003-2010)	<u>Surgeries Included:</u> coronary artery bypass graft surgery via sternotomy; open and minimally invasive lung resection surgery; open and minimally invasive colon resection surgery; open and minimally invasive radical prostatectomy; and open and minimally invasive hysterectomy	39,140	- Cessation defined by the absence of any opioid prescription within the preceding 90 days	<u>Overall Sample:</u> 0.4% continued to receive prescriptions at 1 year <u>Open Thoracic:</u> <2% at 1 year <u>Minimally Invasive Thoracic:</u> <2% at 1 year	- Open and minimally invasive lung resection	

Lee, 2017 ¹²	Retrospective Cohort Insurance (Opioid Naive Patients)	Truven Health Marketscan Research Databases (2010-2014)	Curative intent procedures for melanoma, breast, colorectal, lung, esophageal, and hepato-pancreato-biliary/gastric cancer.	68,463	Filling opioid prescriptions 90 to 180 days after surgery	Opioid Naïve Thoracic: 13.7%	Adjuvant Chemotherapy Adjuvant Radiation Preoperative opioid prescription	
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Table 10: Patient Characteristics Associated with PPOU in Mastectomy: Limitations - #1 - No Serious Limit, #2- Serious Limitation, #3-Very Serious Limitation. Quality of Evidence: + Very Low Quality, ++ Low Quality, +++ Moderate Quality, ++++ High Quality.

<u>Risk Variable</u>	<u>Study Limitations</u>	<u>Indirectness</u>	<u>Imprecision</u>	<u>Inconsistency</u>	<u>Level of Evidence</u>
Preoperative Opioid Use	2	2	3	2	++
Anxiety	3	3	3	2	++
Depression	3	3	2	2	++
Substance Abuse	3	3	3	3	+
Age	3	3	3	3	+
Preoperative Pain	-	-	-	-	1 study - No association
Gender	-	-	-	-	2 studies - No association
Smoking	-	-	-	-	2 studies - No association
BMI	N/A	N/A	N/A	N/A	N/A
Psychotropic Drug Use (Anti-depressant, benzodiazepine)	N/A	N/A	N/A	N/A	N/A

Supplemental Table 11: Studies reviewed pertaining to Mastectomy

Breast Surgery								
<i>Study (Author, Yr)</i>	<i>Design</i>	<i>Data Source</i>	<i>Setting</i>	<i>Sample Size</i>	<i>Definition PPOU</i>	<i>Incidence</i>	<i>Risk Factors</i>	<i>Notes</i>
Carroll, 2012 ¹³	Prospective, longitudinal inception cohort	Single site, Patient Report	USA- Mastectomy, lumpectomy, thoracotomy, TKR, THR.	109 overall sample 25 radical mastectomy 12 lumpectomy	Time until opioid cessation defined as the time from surgery until the first of 5 consecutive days of zero opioid use was defined as postoperative “time to opioid cessation,” and this was the primary end point.	Overall 6% of patients continued taking new opioids 150 days after surgery. Rad Mastectomy 0% at 859 days Lumpectomy 0% at 158 days	<u>Overall mixed surgical cohort:</u> Legitimate preoperative opioid use Self perceived susceptibility to addiction Depressive Sxs (every 10 pt increase in BDI-II)	- Pain duration was not associated with rate of cessation in multivariate model
Marcusa, 2017 ¹⁰	Retrospective Cohort (Opioid Naive)	Truven Health Market Scan Research Database(2010-2014)	Mastectomy with immediate reconstruction	4113	Prolonged opioid refills between 90-120 days after surgery	Overall : 10% filled Rx beyond 3 months 74% of chronic opioid users continued to fill Rx with OME 89 mg per day	Depression Anxiety Postoperative complications	Depressed patients filled prescriptions with higher daily OME Autologous pedicled reconstruction or free tissue transfer filled lower daily OME prescriptions

Lee, 2017 ¹²	Retrospective Cohort Insurance (Opioid Naive Patients)	Truven Health Marketscan Research Databases (2010-2014)	Curative intent procedures for melanoma, breast, colorectal, lung, esophageal, and hepato-pancreato-biliary/gastric cancer.	68,463 total sample 22,379 breast	Filling opioid prescriptions 90 to 180 days after surgery	Opioid Naïve Breast: 11%	Adjuvant Chemotherapy Preoperative opioid prescription	
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