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APPENDIX

Post-operative Opioid Use

Neither pre-operative opioid use nor any post-operative opioid use had a statistically significant range of relative risks for post-operative opioid use. However, the risk of post-operative opioid use after pre-operative opioid use was reported up to 220 times the risk of non pre-operative users (RR 0.29-219.95) (Appendix Table 1).

Trauma Surgery

Four studies were included within the trauma surgery category[71-74]. Timepoints of post-operative opioid use were 2 months[72], 3 months[73], 4 months[74], and 6 months[71]. A total of 779 patients were included with 313 (40.2%) prolonged post-op OU and 466 (59.8%) NOU. Past or active diagnosis of cancer had a 3 times higher risk of chronic post-op use (RR 3.13) while any pre-operative opioid use had up to a six-fold risk (6.25). Post-operative opioid use was associated with decreased risk of prolonged post-operative use (RR0.45) (Appendix Table 2).

Shoulder Arthroplasty

Two studies were included with one study reporting on total shoulder arthroplasty post-operative opioid[75] and another combining total and hemi shoulder arthroplasties[76]. Both studies reported opioid use at a maximum timepoint of 1 year. A total of 7,538 patients were included with 5,198 chronic post-op OU and 2,340 NOU. Factors with higher risk of post-op opioid use included age greater than 50 years (RR 1.26-1.40), any psychiatric history (RR 1.01-1.54), chronic kidney disease (RR 1.02-1.06), arthritis (RR 1.01-1.13), chronic pulmonary disease (1.04-1.09), chronic back pain (RR 1.03-1.37), and history of back surgery (RR 1.27-1.43). BMI greater than 30 had up to a decreased risk of post-op opioid use (RR 0.88-0.96). Other protective factors included peripheral vascular disease (RR 0.76-0.95), liver disease (RR 0.90-0.97), blood loss anemia (RR 0.78-0.85), paralysis (RR 0.71-0.99), and diabetes (RR 0.93-0.98) (Appendix Table 3).

Combined Data for Total Knee and Hip Arthroplasty

Three studies combined data for both total knee and hip arthroplasties with 1 study reporting post-operative opioid use at 6 months[69] and 2 studies reporting at 12 months[34,70]. A total of 58,906 patients were included with 58,520 (99.3%) OU and 386 (0.7%) NOU. Age >50 had slightly increased risk of post-op opioid use (RR 1.02) (Appendix Table 4). Prior substance use, psychiatric history, and higher Elixhauser Comorbidity scores also had increased risk of post-op opioid use (Appendix Table 4).

Improved post-operative Brief Pain Inventory scores was protective (RR 0.8) whereas any pre-operative opioid use increased risk for post-operative opioid use (RR 2.6-3.9).

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Table 1. Opioid Use Before and After Surgery

	Total Number of Patients	Post-operative opioid use		Opioid Use Summary Values		Summary Values Stratified by Prolonged Post-operative opioid use						Preoperative Relative Risks for Post-operative Opioid Use		Post-operative opioid use Stratified by Pre-operative Opioid Use		
						NOU			OU					NOU	OU	
		NOU	OU	Nª	Mean SD	Nª	Mean	SD	Nª	Mean	SD	RR Min	RR Max	RR Min RR Max	RR Min	RR Max
Any Pre-operative Opioid Use	22,002	120	21,882									0.29	1674.00		0.29	219.95
Any Post-operative Opioid Use	64,201		64,201									0.45	10.20		0.45	10.20
Opioid Refills																
Patients with 1 opioid prescription refill after surgery	157		157												**2.78**	**2.78**
Patients with 2 opioids prescription refills after surgery	58		58												**5.93**	**5.93**
Patients with 3 Post-operative Refills Patients with 4 Post-operative Refills															**15.05** **2.34**	**15.05** **2.34**
Prescription OME																
Pre-operative Total OME				2.00	10,256.70	1.00	4,256.30		1.00	16,257.10						
Post-operative Total OME				24.00	3,835.31	2.00	2,609.35		22.00	3,946.76						
Total Number of Post-operative Prescriptions				4.00	1.85				4.00	1.85						
Post-operative Daily OME				2.00	60.10	1.00	47.90		1.00	72.30						
Number of Post-operative Days on Opioids				4.00	300.30	1.00	98.30		3.00	367.63						

NOU: non-opioid users; OME: oral morphine equivalents; OU: opioid users; RR Max: relative risk maximum; RR Min: relative risk minimum; SD: standard deviation

ª Number of patient cohorts included (ex: 1 cohort of non-opioid users versus 1 cohort of opioid users)

Table 2. Chronic Opioid User Demographics for Orthopaedic Trauma

4 studies included. Post-op timepoints include 1 study reporting opioid use at 2 months, 1 study reporting opioid use at 4 months, 1 study reporting opioid use at 5 months, and 1 study reporting opioid use at 6 months.

	Total Number of Patients	Post-operative		Relative Risk for	
		NOU	OU	RR Min	RR Max
General Demographics					
Total Patients Included	779	313	466		
Males	273	225	48		
Females	311	219	92		
Substance Use					
Other unspecified substance abuse	50	0	50		
Medical Comorbidities					
Chronic Kidney Disease	6	4	2		
Cancer	70	50	20	**3.13**	**3.13**
Diabetes	39	27	12		
Heart Failure	27	18	9		
Chronic Pulmonary Disease	35	23	12		
Opioid Use					
Any Pre-operative Opioid Use				**6.25**	**6.25**
Any Post-operative Opioid Use	20	0	20	**0.45**	**0.45**

NOU: non-opioid users; OU: opioid users; RRMax: relative risk maximum; RRMin: relative risk minimum; SD: standard deviation

[a] Number of patient cohorts included (ex: 1 cohort of non-opioid users versus 1 cohort of opioid users)

Table 3. TSA

2 Studies Included. Procedures included TSA and HA. Post-op time points included 1 study reporting opioid use at 6 months and 1 study reporting opioid use at 12 months.

	Total Number of Patients	Post-operative opioid use		Relative Risk for Prolonged Post-op Opioid Use	
		NOU	OU	RR Min	RR Max
General Demographics					
Total Patients Included	7,538	2,340	5,198		
Males				Ref.	Ref.
Females				0.96	1.10
Age =<50 years				ref	ref
Age between 50-70 years				**1.26**	**1.40**
BMI >=30				**0.88**	**0.96**
Race					
White				Ref.	Ref.
Black				0.88	1.06
Asian				0.88	1.17
Hispanic				0.99	1.09
Psychiatric History					
Anxiety				**1.06**	**1.18**
Depression				**1.01**	**1.08**
PTSD				**1.25**	**1.54**
Fibromyalgia				**1.03**	**1.20**
Medical Comorbidities					
Peripheral Vascular Disease				**0.76**	**0.95**
Chronic Kidney Disease				**1.02**	**1.06**
Liver Disease				**0.90**	**0.97**
Arthritis				**1.01**	**1.13**
Coagulation Deficiency				0.96	1.24
Fluid Electrolyte Abnormality				0.93	1.03
Blood Loss Anemia				**0.78**	**0.85**
Paralysis				**0.71**	**0.99**
Diabetes				**0.93**	**0.98**
Heart Failure				0.93	1.08
Valvular abnormality				**0.92**	**0.97**
Chronic Pulmonary Disease				**1.04**	**1.09**
Chronic Pain Conditions					
Chronic Back Pain				**1.03**	**1.37**
History of Back Surgery				**1.27**	**1.43**

BMI: body mass index; NOU: non-opioid users; OU: opioid users; PTSD: post-traumatic stress disorder; RRMax: relative risk maximum; RRMin: relative risk minimum; SD: standard deviation

Table 4. Chronic Opioid User Demographics for Studies Combining Results from TKA and THA Patients

3 studies included. Post-op timepoints include 1 study reporting opioid use at 6 months and 2 studies reporting opioid use at 12 months.

	Total Number of Patients	Post-operative opioid use		Overall Summary Values			Summary Values Stratified by Prolonged Post-op opioid use						Relative Risk for Prolonged Post-op Opioid Use	
		NOU	OU	N[a]	Mean	SD	NOU			OU			RR Min	RR Max
							N[a]	Mean	SD	N[a]	Mean	SD		
General Demographics														
Total Patients Included	58,906	386	58,520											
Males	70	44	26										Ref.	
Females	386	342	44										1.03	
Age between 50-70 years													1.02	
Age >=70yrs													1.02	
Race														
White	417	370	47										2.00	
Other													Ref.	
Substance Use														
Alcohol Abuse													0.93	
Cocaine													3.59	
Marijuana													1.14	
Benzodiazepines													1.42	
NSAIDs													1.01	
Oral Steroids													1.02	
Gabapentin or Pregabalin													1.10	
Other unspecified substance abuse													1.17	
Psychiatric History														
Any Psychiatric History													1.38	
Migraines													1.19	
Medical Comorbidities														
Peripheral Vascular Disease													1.46	
Elixhauser Comorbidity Scores														
Elixhauser Comorbidity Score >=3													1.00	
Pre-Operative Patient Reported Outcomes														
Pre-operative HADS Depression Score										1	2.30	3.91		
Pre-operative HADS Anxiety Score				2	5.59	3.84	1	5.14	3.50	1	6.03	4.17		
Pre-operative CSQ Catastrophizing Score				2	5.41	6.71	1	4.01	4.99	1	6.81	8.42		
Post-op PROs														
Post-operative WOMAC Pain Score				2	11.2	3.46	1	10.27	3.25	1	12.17	3.67		
Post-operative WOMAC Functioning Score				2	37.6	11.35	1	35.24	10.20	1	39.90	12.50		
Post-operative WOMAC Stiffness Score				2	4.9	1.76	1	4.45	1.76	1	5.27	1.76		
Post-operative WOMAC Total Score				2	53.6	15.45	1	49.96	14.00	1	57.22	16.90	1.	1.0
Post-operative BPI Score				2	4.9	1.95	1	4.32	1.90	1	5.43	1.99	0.	0.88
Post-operative Knee Flexion ROM														
Opioid Use														
Any Pre-operative Opioid Use	70	20	50										3.9	

BPI: brief pain inventory; CSQ: coping strategies questionnaire; HADS: hospital anxiety and depression scale; NOU: non-opioid users; NSAIDs: nonsteroidal anti-inflammatory drugs; OU: opioid users; ROM: range of motion; RR Max: relative risk maximum; RR Min: relative risk minimum; SD: standard deviation; THA: total hip arthroplasty; TKA: total knee arthroplasty; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

[a] Number of patient cohorts included (ex: 1 cohort of non-opioid users versus 1 cohort of opioid users)