http://dx.doi.org/10.2106/JBJS.17.01239

Appendix

TABLE E-1 PRISMA 2009 Checklist*

Section/Topic	No.	Checklist Item	Reported [in Submitted Manuscript] on Page No.
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7-8
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., web address), and, if available, provide registration information including registration number.	9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	9-10
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	9
Search	8	Present full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	8, Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9-10
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9-10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	12-13
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	11-18
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	11-18, Appendix
Results			

Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4, 9-10, 14 (Fig. 1)
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	14-15
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see Item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-18, Appendix
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	14-15
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Appendix
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19-20
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20-21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21-22
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	10

*Reproduced from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. For more information, visit: www.prisma-statement.org.

Search Strategy

General search strategy was designed by an experienced librarian for PubMed and later adopted for searching Embase, Web of Science, EBM Reviews - Cochrane Database of Systematic Reviews, and ClinicalTrials.gov.

PubMed Search Strategy

("Analgesics, Opioid" [Pharmacological Action] OR "Analgesics, Opioid"[MeSH] OR (opioid analgesic[Title/Abstract] OR opioid analgesics[Title/Abstract] OR codeine[Title/Abstract] OR fentanyl[Title/Abstract] OR hydrocodone[Title/Abstract] OR hydromorphone[Title/Abstract] OR levorphanol[Title/Abstract] OR meperidine[Title/Abstract] OR methadone[Title/Abstract] OR morphine[Title/Abstract] OR opiate[Title/Abstract] OR opiates[Title/Abstract] OR opioid[Title/Abstract] OR opioids[Title/Abstract] OR oxycodone[Title/Abstract] OR oxymorphone pentazocine[Title/Abstract] OR propoxyphene[Title/Abstract] OR sufentanil[Title/Abstract] OR tramadol[Title/Abstract]))

AND

(("Surgical Procedures, Operative"[MesSH]) OR "Wounds and Injuries"[MeSH]) OR (postoperative[Title/Abstract] OR postoperatively[Title/Abstract] OR "post operative"[Title/Abstract] OR "post operatively"[Title/Abstract] OR postsurgical[Title/Abstract] OR "post surgical"[Title/Abstract] OR "post procedure"[Title/Abstract] OR "surgical trauma"[Title/Abstract] OR "surgical traumas"[Title/Abstract])

AND

("Odds Ratio"[MeSH] OR "Protective Factors"[MeSH] OR "Risk"[MeSH:NoExp] OR "Risk Assessment"[MeSH:NoExp] OR "Risk Factors"[MeSH]) OR "cumulative incidence ratio" OR "cumulative incidence ratios" OR "hazard ratio" OR "hazard ratios" OR "odds ratio" OR "odds ratios" OR predictor OR predictors OR probability OR "probability risk" OR "probability risks" OR "protective factor" OR "protective factors" OR risk OR "risk assessment" OR "risk factor" OR "risk factors" OR "number needed to treat" OR "number needed to harm" OR nnt OR nnh

NOT

((news[Title] OR letter[Title] OR letter[Title] OR comment[Title] OR comments[Title] OR editorial[Title] OR case report[Title] OR case reports[Title]) OR (news[Publication Type] OR letter[Publication Type] OR letter[Publication Type] OR comment[Publication Type] OR comments[Publication Type] OR editorial[Publication Type] OR case report[Publication Type] OR case reports[Publication Type]) OR (animals[MeSH] NOT (humans[MeSH] AND animals[MeSH]))

TABLE E-2 The Critical Appraisal of Included Studies Using Newcastle-Ottawa Scale (NOS)

		Score by NOS Category			
	Study, by First Author	Selection	Comparability	Out-come/Exposure	Overall Score
1	Massey et al.[48]	4	0	3	7
2	Singh and Lewallen (2010)[52]	3	2	2	7
3	Alam et al.[9]	3	2	3	8
4	Singh and Lewallen (2012)[53]	3	2	2	7
5	Holman et al.[45]	4	2	3	9
6	Armaghani et al.[40]	4	2	2	8
7	Berecki-Gisolf et al.[42]	3	2	3	8
8	Fuzier et al.[44]	4	2	3	9
9	Helmerhorst et al.[20]	3	2	2	7
10	Raebel et al.[50]	4	2	3	9
11	Rozet et al.[27]	4	2	3	9
12	Singh and Lewallen (2014)[54]	3	2	2	7
13	Anderson et al.[39]	4	2	3	9
14	Valdes et al.[55]	3	2	2	7
15	Zwisler et al.[56]	4	0	3	7
16	Al Dabbagh et al.[30]	4	2	3	9
17	Bateman et al.[41]	4	2	3	9
18	Goesling et al.[22,23]*	3	2	2	7
19	Inacio et al.[46]	4	2	3	9
20	Carroll et al.[29]	4	2	2	8
21	Clarke et al.[10]	4	2	3	9
22	Lindestrand et al.[17]	4	2	3	9
23	Sun et al.[18]	4	2	3	9
24	Jiang et al.[47]	3	2	3	8
25	Johnson et al.[11]	4	2	3	9
26	Rosenbloom et al.[51]	4	2	2	8
27	Brummett et al.[43]	4	2	3	9
28	Bedard et al.[25]	4	2	3	9
29	Hansen et al.[19]	4	2	3	9
30	Mudumbai et al.[28]	4	2	3	9
31	Mulligan et al.[49]	4	2	2	8
32	Westermann et al.[26]	4	2	3	9
33	Connolly et al.[57]	4	2	3	9
34	Chaudhary et al.[31]	4	2	3	9
35	Kim et al.[58]	4	2	3	9
36	Schoenfeld et al.[32]	4	2	3	9
37	Shah et al.[59]	4	2	3	9

*The 2 articles by Goesling et al. involved the same patient cohort.

http://dx.doi.org/10.2106/JBJS.17.01239

TABLE E-3 Sensitivity Analysis*

Risk Factors	No. of Studies	No. of Patients	Pooled OR (95% CI)	P Value	NNH (95% CI)	Heterogeneity: I^2 (P Value)	Grade of Evidence
Mental health factors							
Depression	13[18,20,23,39,40,46,50-54,57,59]	1,326,398	1.42 (1.21-1.65)	<0.001	59 (38-117)	93% (<0.001)	II-A
Pain catastrophizing	4[20,23,51,55]	1,693	1.19 (1.05-1.35)	0.006	129 (70-487)	87% (<0.001)	III
Anxiety	10[20,23,40,43,46,50-54]	65,889	1.08 (1.00-1.16)	0.043	NA	70% (<0.001)	II-A
Posttraumatic stress disorder (PTSD)	3[20,27,51]	412	1.04 (0.92-1.17)	0.566	NA	83% (0.002)	III
Injury or surgery-related factors							
Longer hospital stay	4[19,44,58,59]	750,031	1.42 (1.04-1.96)	0.030	59 (26-609)	83% (0.001)	II-A
Total knee arthroplasty vs. total hip arthroplasty	5[18,23,44,55,58]	672,690	2.02 (1.01-4.03)	0.046	25 (9-2431)	98% (<0.001)	II-A
More invasive surgery	6[10,40,43-45,55]	79,304	1.75 (1.21-2.54)	0.003	33 (17-117)	89% (<0.001)	II-A
Revision surgery	3[39,40,57]	9,962	1.83 (1.16-2.88)	0.009	30 (14-153)	77% (0.012)	II-A
Extended time out of work	2[39,42]	47,946	3.02 (0.92-9.95)	0.069	NA	96% (<0.001)	II-A
Pain intensity	4[23,44,51,55]	3,487	1.48 (0.99-2.20)	0.052	NA	85% (<0.001)	III
Previous medication or substance use							
Opioids	13[17,23,25-27,39,45,48-50,56-58]	189,485	9.85 (7.50-12.94)	<0.001	4 (3-5)	91% (<0.001)	II-A
Alcohol abuse	9[11,18,25,27,43,46,49,58,59]	1,524,515	1.53 (1.19-1.96)	0.001	47 (26-129)	74% (<0.001)	II-A
Benzodiazepine	6[10,18,41,46,50,58]	808,760	1.82 (1.45- 2.30)	<0.001	31 (20-55)	88% (<0.001)	II-A
Smoking	10[11,25,27,41,43,49,50,57-59]	1,002,212	1.45 (1.13-1.86)	0.003	55 (29-188)	95% (<0.001)	II-A
Antidepressants	3[10,41,58]	176,812	1.68 (0.92-3.05)	0.091	NA	96% (<0.001)	II-A
Demographics and comorbidities							
History of pain conditions (back pain)	9[19,25,26,39,41,43,46,55,58]	309,362	2.70 (1.97-3.70)	<0.001	15 (10 -26)	98% (<0.001)	II-A
History of pain conditions (migraine)	3[41,46,58]	147,197	1.78 (1.04-3.17)	0.049	32 (12-609)	86% (0.001)	II-A
History of pain conditions (chronic pain)†	5[11,27,49-51]	70,767	1.36 (1.22-1.50)	<0.001	69 (50-112)	52% (0.078)	II-A
History of pain conditions (fibromyalgia)	3[26,41,58]	172,827	1.78 (1.07–2.97)	0.028	32 (13-348)	70% (0.067)	II-A
Pulmonary comorbidity	4[10,27,46,59]	724,337	1.77 (1.50-2.08)	0.001	33 (24-50)	36% (0.196)	I
Cardiovascular comorbidity	3[10,27,46]	48,810	1.43 (1.13-1.81)	0.003	NA	25% (0.264)	I
Female sex	21[11,17-19,23,25,27,42-47,50,52-58]	1,022,351	1.12 (1.03-1.22)	0.001	204 (112-811)	84% (0.001)	II-A
High comorbidity index	12[11,17,19,27,40,43,50,52-54,57,59]	814,730	1.08 (1.02-1.13)	0.007	305 (188-1,216)	73% (<0.001)	II-A
Obesity	6[47,52-55,57]	96,472	1.35 (0.98-1.86)	0.068	NA	75% (0.001)	II-A
Diabetes	3[10,44,46]	50,604	1.13 (0.76-1.70)	0.541	NA	57% (0.096)	II-A
Lower income	4[10,11,42,59]	821,336	1.05 (0.88-1.26)	0.586	NA	77% (0.004)	II-A
Race (Caucasian vs. African-American)	6[23,27,43,47,50,59]	802,189	0.90 (0.69-1.17)	0.426	NA	82% (<0.001)	II-A

*Risk factors for prolonged opioid use; analysis was done using "remove 1" random-effect meta-analysis. NA = not applicable. †Chronic pain inclusive of joint pain, nerve pain, back/neck pain, headache, and psychological pain.

Statistical Approach

1. Definition of each risk factor based on original studies

A) Mental health factors:

1. Depression defined by high probability of depression using Hospital Anxiety and Depression Scale (HADS) (Goesling et al.[22], Rosenbloom et al.[51]), score of >16 on Center for Epidemiologic Studies Depression Scale (CES-D28) (Helmerhorst et al.[20]), score of ≥33 on Zung Depression Scale (ZDS) (Armaghani et al.[40]), Beck Depression Inventory II (Carroll et al.[29]), or clinical diagnosis (Anderson et al.[39], Chaudhary et al.[31], Connolly et al.[57], Inacio et al.[46], Mudumbai et al.[28], Schoenfeld et al.[32], Singh and Lewallen [2010[52], 2012[53], 2014[54]], Raebel et al.[50], Sun et al.[18])
2. Anxiety defined by high probability of anxiety using Hospital Anxiety and Depression Scale (HADS) (Goesling et al.[22]), score of ≥12 on Modified Somatic Perception Questionnaire (MSPQ) (Armaghani et al.[40]), the Pain Anxiety Symptoms Scale (PASS-2030) (Helmerhorst et al.[20], Rosenbloom et al.[51]), or clinical diagnosis and medical history (Brummett et al.[43], Chaudhary et al.[31], Inacio et al.[46], Mudumbai et al.[28], Raebel et al.[50], Schoenfeld et al.[32], Singh and Lewallen [2010[52], 2012[53], 2014[54]])
3. Posttraumatic stress disorder (PTSD) defined by a score >17 on the PTSD Checklist, civilian version (PCL-C26) (Helmerhorst et al.[20], Rosenbloom et al.[51]), or clinical diagnosis of PTSD (Mudumbai et al.[28], Rozet et al.[27])
4. Pain catastrophizing thinking defined by Pain Catastrophizing Scale (PCS29) (Helmerhorst et al.[20], Goesling et al.[22], Rosenbloom et al.[51], Valdes et al.[55])

B) Injury or surgery-related factors:

1. Revision surgery defined as additional lumbar surgery (Anderson et al.[39], Connolly et al.[57]) or primary versus revision surgery (Armaghani et al.[40])
2. More invasive surgery defined as tier-3 spinal surgery (i.e., lumbar fusion/posterior cervical) (Armaghani et al.[40]), surgery on the pelvis or acetabulum versus lower extremity (Holman et al.[45]), minor versus major surgery (Brummett et al.[43]), and total knee arthroplasty versus unicompartmental knee replacement (Fuzier et al.[44])
3. Pain intensity defined by visual analog scale (VAS) of >5 (Valdes et al.[55]) or Brief Pain Inventory (Goesling et al.[22], Rosenbloom et al.[51]), high level of preoperative pain defined by receiving painkillers 2 months prior to surgery (Fuzier et al.[44])
4. Extended time out of work (i.e., work loss of >12 weeks in Anderson et al.[39] or >14 days in Berecki-Gisolf et al.[42])
5. Longer hospital stay: >7 days in Mudumbai et al.[28], >9 days in Fuzier et al.[44], >14 days in Shah et al.[59], >21 days in Hansen et al.[19], or number of days for in-hospital stay in Chaudhary et al.[31], Kim et al.[58], and Schoenfeld et al.[32]
6. Severe injury defined by Injury Severity Score (ISS) in Al Dabbagh et al.[30] and Chaudhary et al.[31]

C) Prior medication or substance use:

1. Opioid use

2. Non-narcotic analgesics
3. Nonsteroidal anti-inflammatory drugs (NSAIDs)
4. Benzodiazepines
5. Antidepressants (general term in Bateman et al.[41], Kim et al.[58] or specified as selective serotonin reuptake inhibitor [SSRI] in Clarke et al.[10])
6. Smoking
7. Alcohol abuse

D) Demographics and comorbidities:

1. Sex
2. Race (Caucasian versus African-American)
3. Marital status
4. Cardiovascular comorbidity
5. Pulmonary comorbidity
6. Obesity
7. Diabetes
8. History of pain conditions such as back pain (Anderson et al.[39], Bateman et al.[41], Bedard et al.[25], Brummett et al.[43], Hansen et al.[19], Inacio et al.[46], Kim et al.[58], Valdes et al.[55], Westermann et al.[26]), fibromyalgia (Bateman et al.[41], Kim et al.[58], Westermann et al.[26]), migraine (Bateman et al.[41], Inacio et al.[46], Kim et al.[58]), or chronic pain (Johnson et al.[11], Mulligan et al.[49], Raebel et al.[50], Rosenbloom et al.[51], Rozet et al.[27])
9. High comorbidity index, as defined by Deyo-Charlson Comorbidity Index (Brummett et al.[43], Chaudhary et al.[31], Hansen et al.[19], Mudumbai et al.[28], Singh and Lewallen [2010[52], 2012[53], 2014[54]], Shah et al.[59], Schoenfeld et al.[32]), American Society of Anesthesiologists (ASA) score of >2 (Armaghani et al.[40], Lindestrand et al.[17], Rozet et al.[27]), or Elixhauser Comorbidity Index (Connolly et al.[57], Johnson et al.[11], Raebel et al.[50])
10. Lower income defined as first and second deciles of socioeconomic index of the area of residential postcode (Berecki-Gisolf et al.[42]), lowest 20% versus highest 20% of the median income of the neighborhood (Clarke et al.[10]), median household income in area of residence <$40,000 (U.S.) (Johnson et al.[11]), highest versus lowest interquartile income of the area of residence (Shah et al.[59])

2. Grading evidence based on sample size and heterogeneity

In order to increase the comprehensibility of the findings, the effect of risk factors was graded by pooled sample size and heterogeneity[39]:

"Grade I evidence" defined as both a pooled population of >5,000 and lower heterogeneity (I^2 <50%)

"Grade II-A evidence" defined as a pooled population of >5,000 but with higher heterogeneity (I^2 ≥50%)

"Grade II-B evidence" defined as lower heterogeneity (I^2 <50%) but with pooled population of <5,000

"Grade III evidence" defined as both pooled population of <5,000 and higher heterogeneity (I^2 ≥50%).

3. Formula used for number needed to harm (NNH) calculation:

In order to increase the clinical and public relevance of the results, we calculated an NNH from the pooled odds ratios (ORs) and hazard ratios (HRs) and the pooled event rate of prolonged opioid use. NNH was calculated using a population event rate (PER) of 4.3% based on the pooled rate of prolonged opioid use seen in population-based studies, and assuming the risk ratio (RR) is equal to the OR—an acceptable assumption in uncommon diseases[35]—using the following formula[36]:

$$\text{NNH} = \frac{[PER \times (OR - 1)] + 1}{[PER \times (OR - 1)] \times (1 - PER)}$$

The NNH for HR was calculated as follows[37]:

$$\text{NNH} = \frac{1}{[PER^{HR^{-1}}] - PER}$$

http://dx.doi.org/10.2106/JBJS.17.01239

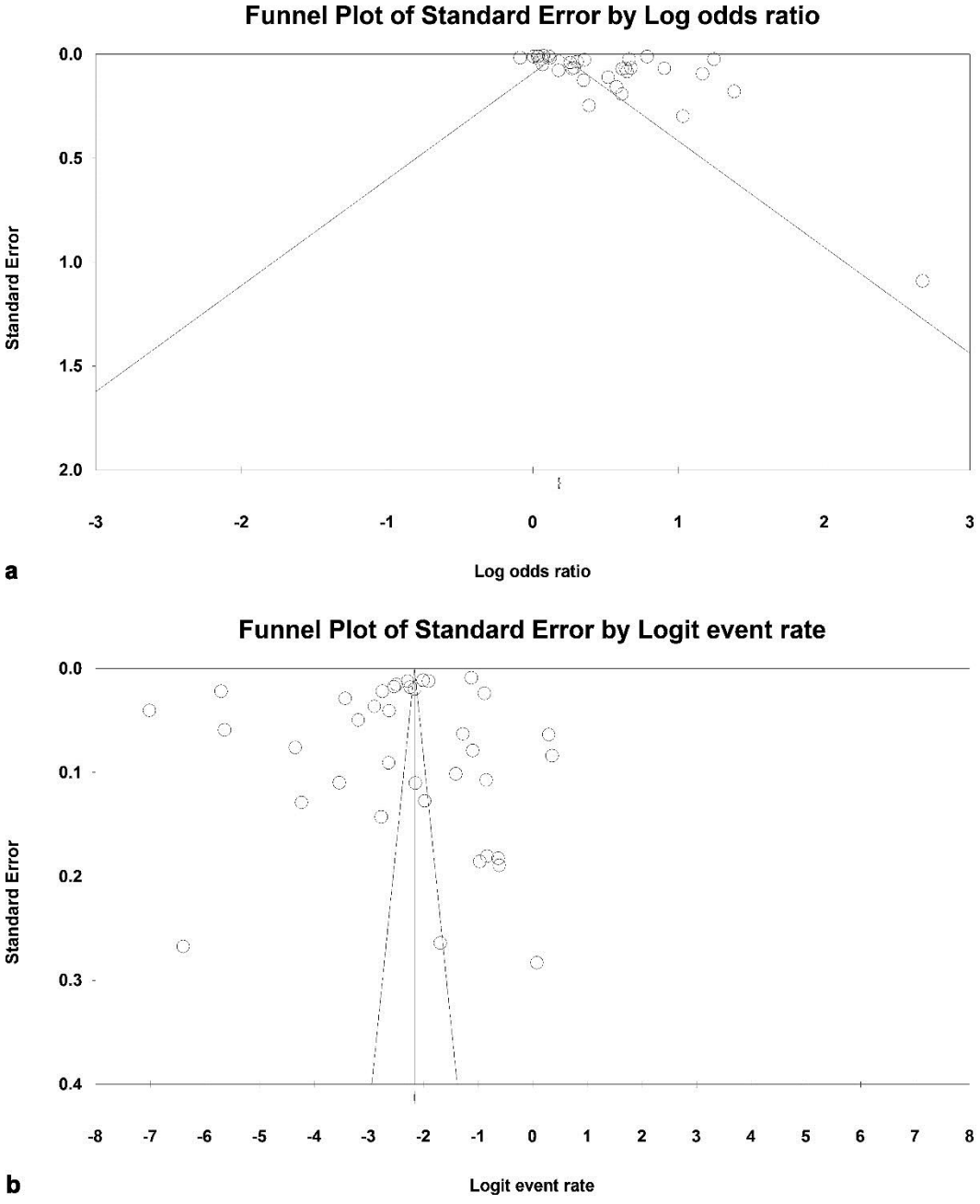

Fig. E-1
Funnel plots assessing publication bias in the systematic review. **Fig. E-1A** The risk factors of prolonged opioid use. The Egger regression test (p = 0.136) was not indicative of significant publication bias. **Fig. E-1B** The rate of prolonged opioid use. The Egger regression test (p = 0.206) did not show significant publication bias.

http://dx.doi.org/10.2106/JBJS.17.01239

TABLE E-4 Descriptive Data from Included Studies*

Study, by First Author	Yr	Country	Surgery/Injury	ONP	Mean Age *(yr)*	Male	Follow-up/Definition of POU	Substance of Study	No. of Patients	No. of ONP	POU	POU in ONP	Risk Factors
Massey et al.[48]	2005	U.S.	Femoral shaft fractures, acetabulum, tibial shaft, tibial plateau, subtrochanteric femur, open fracture, multiple fractures	Some, not all	38	60%	6 mo	NS	50	14 (28%)	26 (52%)	1 (7.14%)	Positive toxicology on admission
Singh and Lewallen (2010)[52]	2010	U.S.	Primary THA	NS	64.9	48%	24 mo	NS	3,005	NR	85 (2.83%)	NR	Female, depression, BMI 30-34.9 kg/m^2
Alam et al.[9]	2012	Canada	Short-stay surgery (cataract surgery, laparoscopic cholecystectomy, TURP, or varicose vein stripping)	Yes	76.7	38%	1 yr (± 60 days)	Codeine, fentanyl patch, hydromorphone, meperidine, morphine, oxycodone, long-acting oxycodone	27,636	27,636 (100%)	2,857 (10.34%)	2,857 (10.34%)	Early opioid prescription (compared with normal population)
Singh and Lewallen (2012)[53]	2012	U.S.	Primary TKA	NS	68	80%	2 and 5 yr postop.	NS	4,234	NR	61 (1.44%)	NR	Female, <60 yr of age, anxiety
Holman et al.[45]	2013	U.S.	Isolated MSK trauma	Some, not all	NR	NR	12 wk	NS	613	518 (84.50%)	121 (19.74%)	63 (12.16%)	Preinjury opioid use, advanced age, pelvic or acetabular surgery
Armaghani et al.[40]	2014	U.S.	Spine surgery	Some, not all	57	46%	12 mo postop.	NS	583	262 (44.94%)	343 (58.83%)	68 (25.95%)	Invasive surgery, anxiety, revision surgery, greater preop. opioid use
Berecki-Gisolf et al.[42]	2014	Australia	Occupational injury (85% MSK injury)	Some, not all	NR	66%	2 yr	Codeine, tramadol, oxycodone, fentanyl, dextropropox-	46,944	NR	3,446 (7.34%)	NR	Age, female, laborers, lower socioeconomic status, greater

								yphene, buprenorphine, morphine, or methadone					work disability, and greater hospital expense
Fuzier et al.[44]	2014	France	Unicompartmental knee replacement and TKA	Some, not all	72	40%	1 yr	Codeine, tramadol, combinations with paracetamol, opium, morphine sulfate, morphine hydrochloride fentanyl, hydromorphone, oxycodone	1,939	NR	130 (6.7%)	NR	Younger age, female sex, increased length of hospital stay†, psychiatric disorders†
Helmerhorst et al.[20]‡	2014	U.S.	Operative treatment of MSK trauma	NS	NR	NR	1-2 mo	NS	145	NR	40 (27.59%)	NR	Catastrophic thinking, anxiety, posttraumatic stress disorder, depression, magnitude of disability as measured by the Short Musculoskeletal Function Assessment score
Raebel et al.[50]	2013	U.S.	Bariatric surgery (gastric sleeve, lap band, lap gastric bypass, open gastric bypass)	Some, not all	47	18.40 %	≥10 prescription fillings in ≥90 days or >120 days total supply	NS	10,643	6,483 (60.91%)	421 (3.96%)	84 (1.30%)	Pre-surgery opioid use, pre-surgery non-narcotic analgesic use, antianxiety agents, tobacco use, younger age, laparoscopic bypass (compared with band)
Rozet et al.[27]	2014	U.S.	Knee arthroscopy, veterans setting	Some, not all	38.9	87.60 %	3.5 mo after surgery	NS	145	101 (69.66%)	44 (30.34%)	8 (7.92%)	Whole cohort: preop. opioid, female, higher ASA, hypertension, smoking,

													PTSD; opioid-naive cohort: PTSD
Singh and Lewallen (2014)[54]	2014	U.S.	Revision TKA	NS	69	50%	2 and 5 yr postop	NS	881	NR	52 (5.90%)	NR	Younger age, depression
Anderson et al.[39]	2015	U.S.	Lumbar fusion for degenerative disc, Workers' Compensation setting	Some, not all	44.5	66.10 %	1 yr	NS	1,002	NR	575 (57.39%)	NR	Chronic preop. opioid use, failed back syndrome, additional surgery, clinically diagnosed depression, extended work loss before fusion
Valdes et al.[55]	2015	U.K.	TKA and THA	NS	73.7	43.30 %	4 yr	Buprenorphine, fentanyl, morphine, Nurofen Plus (Crookes Healthcare) and combinations (ibuprofen and codeine phosphate), Oramorph (Boehringer Ingelheim), oxycodone, tramadols and Transtec patch (buprenorphine)	852	NR	214 (25.12%)	NR	Back pain, body pain, illness behavior >4, VAS >5, obese, PCS highest tertile, WOMAC pain >10, female, TKA (compared with THA), both THA and TKA (compared with only TKA or only THA)
Zwisler et al.[56]	2015	Denmark	Trauma unspecified	Some, not all	36.6	70%	Redemption of ≥2 prescriptions for opioids 6 mo or later after	Tramadol, ketobemidone chloride, oxycodone, buprenorphine, morphine, fentanyl, pethi-	877	812 (92.59%)	92 (10.49%)	62 (7.64%)	Severe injury, lower extremity injury

							multi-trauma	dine, and ni-comorphine					
Al Dabbagh et al.[30]	2016	Sweden	Femoral shaft fractures	Yes	75	44%	6 and 12 mo (IQR, 11-20 mo)	Morphine, ox-ycodone, fen-tanyl, tramadol, co-deine	1,471	1,471 (100%)	529 (35.96%)	529 (35.96%)	Younger age
Bateman et al.[41]	2016	U.S.	Cesarean deliv-ery	Yes	NR	0%	12 mo postop.	NS	80,127	80,127 (100%)	285 (0.36%)	285 (0.36%)	Cocaine abuse, other illicit sub-stance abuse, tobacco use, back pain, migraines, antidepressant use, benzodiaze-pine use
Goesling et al.[23]‡	2016	U.S.	TKA and THA	Some, not all	63.3	46.90 %	6 mo	NS	574	407 (70.91%)	70 (12.20%)	20 (4.91%)	Higher WOMAC scores for pain, functioning, stiff-ness, and total, higher overall pain severity, depression, CSQ catastrophizing
Inacio et al.[46]	2016	Austral-ia	THA, veterans setting	Some, not all	80	48.70 %	90 days of continu-ous use or 120 days of non-continu-ous use	NS	9,525	8,932 (93.77%)	644 (6.76%)	38 (0.43%)	Younger age, back pain, complicated diabetes, hypnot-ics use, prior use; risk factors for chronic opioid use in opioid-naive subgroup: female, back pain, depression, gas-tric acid disease, migraine, liver disease, weight loss, dementia, hyperlipidemia, hypnotics use, antineuropathic pain medication

													use
Carroll et al.[29]	2012	U.S.	Mastectomy, lumpectomy, thoracotomy, TKA, THA	Some, not all	58	29%	150 days	NS	109	82 (75.23%)	17 (15.60%)	5 (6.10%)	Preop. opioid use, self-perceived risk of addiction, Beck Depression Inventory II score
Clarke et al.[10]	2014	Canada	Isolated coronary artery bypass graft surgery through sternotomy, open (thoracotomy) lung resection surgery, lung resection using video-assisted thoracoscopic surgery, open colon resection surgery, laparoscopic colon resection surgery, open radical prostatectomy, minimally invasive radical prostatectomy, open total or radical hysterectomy, and minimally invasive total or radical hysterectomy	Yes	NR	48%	180 days	NS	39,140	39,140 (100%)	1,229 (3.14%)	1,229 (3.14%)	Younger age, lower household income, diabetes, heart failure, pulmonary disease, preop. use of benzodiazepines, SSRIs, ACEI, the type of surgical procedure (open and minimally invasive thoracic procedures)
Lindestrand et al.[17]	2015	Denmark	Hip fracture	Some, not all	79.5	29.50 %	3-6 mo post-injury	NS	413	313 (75.79%)	124 (30.02%)	9 (2.88%)	Opioid use before admission, osteoporosis, ASA score >2†
Sun et al.[18]‡	2016	U.S.	TKA, THA, chol-	Yes	43.99	26.40	≥10 pre-	Fentanyl	611,78	611,780	2,039	2,039	Increased use

			ecystectomy, appendectomy, cesarean section, functional endoscopic sinus surgery, cataract, TURP			%	scriptions or >120 days' supply of an opioid in the first yr after surgery, excluding first 90 days	(patch or oral form), hydrocodone, hydromorphone, methadone, morphine, oxymorphone, and oxycodone	0	(100%)	(0.33%)	(0.33%)	associated with TKA, open cholecystectomy, THA, mastectomy, laparoscopic cholecystectomy, open appendectomy, cesarean section, male sex, age >50 yr, preop. use of benzodiazepines, antidepressants, clinical history of depression, clinical history of alcohol abuse, clinical history of drug abuse†
Jiang et al.[47]	2017	U.S.	Surgeries from all specialties	NS	NR	52.30 %	90 days	NS	79,123	NR	7,303 (9.23%)	NR	Female, African-American and Latino more likely, Asian less likely, multiple specialty visits, abnormal BMI
Johnson et al.[11]	2016	U.S.	Hand surgery procedures	Yes	NR	40%	90 days after surgery	Hydrocodone, oxycodone, tramadol, codeine phosphate, hydromorphone, propoxyphene, meperidine, morphine sulfate, fentanyl	59,725	59,725 (100%)	7,764 (13.00%)	7,764 (13.00%)	Elective surgery, younger age, female, lower income, comprehensive insurance, higher Elixhauser comorbidity index, mental health disorders, tobacco use
Rosenbloom et al.[51]	2017	Canada	Traumatic MSK injury undergoing corrective surgery	NR	44.8	66%	4 mo	NS	122	NR	43 (35.25%)	NR	Pain severity, pain self-efficacy, depression, pain anxiety, pain catastrophizing,

													sensitivity to pain traumatization scale, pain interference
Brummett et al.[43]	2017	U.S.	Minor surgical procedures (varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral prostate surgery, parathyroidectomy, carpal tunnel). Major surgical procedures (ventral incisional hernia repair, colectomy, reflux surgery, bariatric surgery, hysterectomy)	Yes	44.6	34%	90-180 days after surgery	NS	36,177	36,177 (100%)	2,176 (6.01%)	2,176 (6.01%)	Preop. tobacco use, alcohol and substance abuse disorders, mood disorders, anxiety, preop. pain disorders (back pain, neck pain, arthritis, centralized pain), preop. opioid use
Bedard et al.[25]	2017	U.S.	TKA	Some, not all	NR	36%	Trended monthly for 12 mo	NS (tramadol excluded)	73,959	29,801 (40.29%)	8,780 (11.87%)	969 (3.25%)	Preop. opioid use, female, younger age, anxiety, depression, low back pain, myalgia, drug dependence, alcohol dependence, smoker
Hansen et al.[19]	2017	Australia	TKA	Some, not all	79	50.5	Chronic opioid use defined as	Weak (codeine, dextropropoxyphene, tra-	15,020	9,223 (61%)	786 (5%)	64 (0.7%)	Younger age, female, low back pain, greater

							at least 90 days of continuous use or 120 days of non-continuous use within 275 days of potential utilization	madol), strong (buprenorphine, fentanyl, hydromorphone, hydrocodone, morphine, oxycodone, oxycodone + naloxone, pethidine hydrochloride)					number of comorbidities, longer length of stay at surgery
Mudumbai et al.[28]	2016	U.S.	Broadly categorized surgeries (MSK, cardiovascular, digestive, other, male genital, nervous, urinary, respiratory, integumentary)	Some, not all	NR	94%	Cessation as 90 days free of opioids	NS	64,391	29,419 (45.69%)	15,878 (24.66%)	1,029 (3.50%)	Preop. opioid use (short acting opioids on acute/intermittent basis, tramadol only, short acting chronic, long acting opioids)
Mulligan et al.[49]	2016	U.S.	Ankle and hindfoot reconstruction	Some, not all	55	85%	90 days after surgery	NS	132	89 (67.42%)	52 (39.39%)	14 (15.73%)	Preop. narcotic use, chronic pain disorder, mood disorder
Westermann et al.[26]	2017	U.S.	Rotator cuff repair	Some, not all	NR	53%	3 months after surgery	All common opioids excluding tramadol	35,155	19,925 (56.68%)	6,749 (19.20%)	1,594 (8.00%)	Preop. opioid use, psychiatric diagnoses (anxiety, depression), myalgia and low-back pain
Connolly et al.[57]	2017	U.S.	Lumbar fusion	Some, not all	49.6	43.87 %	2 yr	NS	8,377	1,332 (15.90%)	2,458 (29.34%)	29 (2.18%)	Preop. opioid use, re-fusion surgery, depression
Chaudhary et al.[31]	2017	U.S.	Major trauma	Yes	33.3	82.2%	1 yr	Oxycodone, hydromorphone, morphine, fentanyl, suboxone, hy-	13,624	13,624 (100%)	175 (1.3%)	175 (1.3%)	Lower socioeconomic status, higher injury severity, being married

								drocodone-acetamino-phen, oxyco-done-acetaminophen and methadone					
Kim et al.[58]	2017	U.S.	THA, TKA	Some, not all	61.5	43.0%	1 yr	Hydrocodone, codeine, oxycodone, meperidine, hydromorphone, morphine, fentanyl, methadone, and oxymorphone	57,545	7,425 (12.90%)	4,394 (7.64%)	48 (0.65%)	TKA vs THA, longer hospitalization stay, discharge to rehabilitation facility, preop. opioid use (e.g., a longer duration and greater dosage and frequency), higher comorbidity score, back pain, rheumatoid arthritis, fibromyalgia, migraine, smoking, and benzodiazepine use
Schoenfeld et al.[32]	2017	U.S.	Spine surgery (discectomy, decompression, lumbar posterolateral arthrodesis, lumbar interbody arthrodesis)	Yes	46.4	63.0%	1 yr	NS	8,388	8,388 (100%)	2 (0.02%)	2 (0.02%)	Lower socioeconomic status as reflected by junior enlisted sponsor rank, senior enlisted rank, depression, younger age, more intense surgical intervention (lumbar interbody arthrodesis)
Shah et al.[59]	2017	U.S.	Urological surgery (stone, pelvic major	Yes	62	NR	1 yr	NS	675,527	675,527 (100%)	608 (0.09%)	608 (0.09%)	Younger age, nonprivate insurance (Medicare

			oncologic, kidney major oncologic, inguinal, TURP)										<65 years old, Medicaid, self-pay/uninsured), inpatient procedure, longer length of hospitalization, depression, COPD, tobacco use, peptic ulcer disease, liver disease

*ACEI = angiotensin-converting-enzyme inhibitor, ASA = American Society of Anesthesiologists, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CSQ = Coping Strategies Questionnaire, IQR = interquartile range, MSK = musculoskeletal, NR = not reported, NS = not specified, ONP = opioid-naive patients, PCS = Pain Catastrophizing Scale, POU = prolonged opioid use, PTSD = posttraumatic stress disorder, SSRI = selective serotonin reuptake inhibitor, THA = total hip arthroplasty, TKA = total knee arthroplasty, TURP = transurethral resection of the prostate, VAS = visual analog scale, and WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index. †Derived from bivariate analysis.
‡Additional data were obtained from the corresponding author.