



PEARL

Exploring incidence and risk factors for persistent postoperative opioid use in adult surgical patients: a systematic review protocol

Griffiths, Harry; Kent, Bridie; Martin, Daniel

Published in:

JBI evidence synthesis

DOI:

[10.11124/jbies-22-00106](https://doi.org/10.11124/jbies-22-00106)

Publication date:

2023

Link:

[Link to publication in PEARL](#)

Citation for published version (APA):

Griffiths, H., Kent, B., & Martin, D. (2023). Exploring incidence and risk factors for persistent postoperative opioid use in adult surgical patients: a systematic review protocol. *JBI evidence synthesis*, 21(4), 805-811. <https://doi.org/10.11124/jbies-22-00106>

All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Wherever possible please cite the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.

1 **Exploring incidence and risk factors for persistent postoperative opioid use in**
2 **adult surgical patients: a systematic review protocol**

3 **Abstract**

4 **Objective:** To determine the incidence of persistent postsurgical use of opioids in adult patients and
5 the risk factors associated.

6 **Introduction:** Surgery has been identified as an independent risk factor for unwarranted chronic
7 opioid use, contributing to opioid-related harm in the community. Persistent opioid use after surgery
8 is associated with morbidity and mortality from opioid-related adverse events, indicating a
9 significant yet mitigable public health concern. There is substantial variation in the reported
10 incidence and risk factors for postoperative opioid use, which require evaluation for future evidence-
11 based risk reduction strategies.

12 **Inclusion criteria:** This review will include studies investigating the persistent use of opioids after 90
13 postoperative days in adult (≥ 18 years) patients undergoing surgery of any type, including cancer
14 pain patients. Selected evidence must report on opioid use prior to surgery. Included study designs
15 are analytical and descriptive observational studies, and experimental and quasi-experimental
16 studies, published in the last decade.

17 **Methods:** The proposed study methods follow guidance from the JBI Methodology for Systematic
18 Reviews of Prevalence and Incidence. A systematic search will include PubMed, EMBASE, CINAHL,
19 Cochrane Central, Web of Science, and the gray literature. Study selection, critical appraisal, and
20 data extraction are to be performed by two independent reviewers, aided by relevant JBI systematic
21 review tools. We aim to produce a narrative synthesis of results and conduct a meta-analysis where
22 feasible, in addition to subgroup analyses of suitable populations. The results are intended to
23 promote safe, evidence-based postoperative opioid prescribing when considering risk factors for
24 persistent postoperative opioid use.

25 **Keywords:** Opioid; Incidence; Postoperative; Pain.

26 **Abstract word count: 247**

27 **Total manuscript word count: 2495**

28 Introduction

29 For centuries, opioids have successfully alleviated pain and suffering for patients, including those
30 undergoing surgery.⁽¹⁾ Over the past two decades, prescription rates for opioids have increased
31 sharply in the United States (US), where the “opioid epidemic” is said to have originated,⁽³⁾ with
32 many other nations following this trend, including the United Kingdom (UK).^(4, 5) However, despite
33 their strengths, prescription opioids carry significant potential for abuse and addiction similar to
34 non-prescription opioids, and the risk of transition towards illicit opioid use has been documented.⁽⁶⁾
35 As a result, health, societal, and economic burden from inappropriate opioid prescribing is
36 increasing, resulting in significant morbidity, mortality, and public health expenditure.^(1, 3, 7) In the UK,
37 between 1998 and 2016, opioid prescription counts rose by 34%, compounded by a 127% increase in
38 the average oral morphine equivalent (OME) dose prescribed (mg day⁻¹),⁽¹⁾ and it is now estimated
39 that 5% of the UK population take opioids regularly.⁽⁸⁾ Consequently, these data have prompted
40 issues of warning by the Chief Medical Officer and numerous UK pain associations to promote
41 evidence-based, judicious prescribing of opioids.^(1, 2)

42 Highlighting opioid-related harm, a Cochrane systematic review of 18,679 randomized patients
43 found that chronic opioid use, compared with placebo, caused a higher risk of experiencing any
44 adverse event (risk ratio (RR) 1.42, 95% confidence interval (CI) 1.22-1.66) or serious adverse event
45 (RR 2.75, 95% CI 2.06-3.67).⁽⁹⁾ Notable serious opioid-related adverse events (ORAEs) include
46 dependence, hospitalization, death or hypoxia via opioid-induced ventilatory impairment, and fatal
47 or non-fatal overdose.^(1, 3) More recently, evidence suggests that surgery is an isolated risk factor for
48 developing chronic opioid consumption, a phenomenon termed persistent postoperative opioid use
49 (PPOU),^(1, 7, 10) which is associated with morbidity and mortality from ORAEs.⁽²⁾ The definition of PPOU
50 varies within the literature;⁽¹¹⁾ however, the most recent national and international guidelines define
51 PPOU as ≥ 1 opioid prescription (OP) in postoperative days 90-365 for patients opioid-naïve prior to
52 surgery, and any baseline increase in OME from the 90 days preceding surgery to postoperative days
53 90-365 for presurgical users.^(1, 7, 12) Depending on the selected definition, the reported risk of
54 developing PPOU from US observational research ranges from 0.6-26% for opioid-naïve patients to
55 35-77% for presurgical chronic opioid users.⁽¹³⁾ Moreover, the responsibility held by surgeons,
56 anesthetists and other disciplines in mitigating this risk is increasingly evident, with clinical and
57 research interest in perioperative opioid stewardship gaining significantly.^(2, 12)

58 PPOU has been reported in recent observational studies for patients undergoing both major and

59 minor surgery, regardless of preoperative opioid exposure. Therefore, all patients undergoing
 60 surgery are currently deemed at risk.⁽¹⁴⁻¹⁶⁾ Successful harm reduction strategies, such as gradual
 61 preoperative opioid tapering, will require targeting patient risk factors and modifying potential
 62 drivers of PPOU where possible via supportive evidence.⁽¹⁷⁾ In attempt to facilitate this, many
 63 observational studies have characterized the relationship between patient baseline characteristics as
 64 risk factors and PPOU.^(14, 15) For example, Chaudhary *et al.* performed a retrospective case-control
 65 study in 86,356 adult surgical patients, where 6,365 (7.4%) met criteria for PPOU, and found that the
 66 strongest risk factors were preoperative sustained opioid use (odds ratio (OR) 13.00, 95% CI 11.88-
 67 14.23), preoperative opioid exposure (OR 3.21, 95% CI 2.96-3.47), and nonhome discharge (OR 2.14,
 68 95% CI 1.62-2.83).⁽¹⁵⁾ In comparison, Khazi and colleagues found that in 12,038 adult patients
 69 undergoing total shoulder arthroplasty, continued OPs at 12 months were most associated
 70 preoperative chronic opioid use (OR 10.32, 95% CI 8.69-12.3), preoperative opioid exposure (OR
 71 2.54, 95% CI 1.89-3.39), and concurrent chronic lung disease (OR 2.14, 95% CI 1.62-2.82).⁽¹⁸⁾
 72 Therefore, variation in estimates of PPOU incidence, and the magnitude of risk factors contributing,
 73 warrants an evidence synthesis for clinicians to aid accurate risk stratification in surgical patients
 74 who may transition to long-term opioid therapy.⁽¹⁾

75 A preliminary search of PROSPERO, PubMed, the Cochrane Database of Systematic Reviews, and *JBIC*
 76 *Evidence Synthesis* was conducted. PubMed revealed three systematic reviews investigating PPOU
 77 across multiple surgical disciplines,^(12, 19, 20) one was confined to the US and Canada,⁽¹²⁾ and another
 78 confined to Europe.⁽¹⁹⁾ The former review did not create a pooled estimate of risk factors but only
 79 assessed the quality of evidence for studies that mentioned them;⁽¹²⁾ the latter only assessed
 80 incidence and found insufficient evidence to make robust conclusions on the current extent of
 81 PPOU.⁽¹⁹⁾ The third review examined both incidence and risk factors of PPOU with no geographical
 82 limitations to studies, but included historical data dating back to 1995 in a fast-changing health issue,
 83 and excluded cancer patients.⁽²⁰⁾ Despite excluding a large proportion of the opioid-using population
 84 and thus reducing generalizability, some studies exclude cancer patients due to their inherent
 85 differences in pain management, particularly as many may be palliative.⁽⁵⁾ Interestingly, use of
 86 historical data and handling of cancer diagnoses were among the greatest methodological
 87 weaknesses found in an analysis of current prescription opioid safety research.⁽²¹⁾ It is suggested that
 88 examining the effect or interaction due to cancer patients, rather than excluding them or simply
 89 combining the pooled estimates, will help inform whether separate opioid safety guidelines may or
 90 may not be required for cancer-related postsurgical pain.⁽²¹⁾

91 Our proposed review will include cancer patients and enable geographical comparisons of incidence
92 and risk factors of PPOU, to evaluate whether data from the US may be used cautiously to aid
93 decision-making where raw data is still scarce.⁽¹⁶⁾ Additionally, owing to both the rapidly changing
94 picture of the opioid epidemic and the recent surge in research interest,^(15, 16) we believe an updated
95 review of existing evidence is warranted. The objective of this review is to measure the incidence of
96 PPOU across existing literature and determine the overall risk of individual patient characteristics
97 contributing to PPOU in adult surgical patients, thus contributing to the knowledge of opioid
98 prescription safety. This will help evidence local policy decisions enforcing opioid stewardship
99 practices and facilitate the identification and management of surgical patients susceptible to opioid-
100 related harm.

101 **Review question**

- 102 1. What is the incidence of persistent postoperative opioid use in adult surgical patients in
103 varying populations and backgrounds?
- 104 2. What are the pooled estimates of **risk factors** for persistent postoperative opioid use?

105 **Inclusion criteria**

106 The inclusion criteria outlined utilizes the Population, Condition, Context (PCC) structure for the first
107 research question, and the Population, Exposure, Outcome (PEO) structure for the second research
108 question, as described by the JBI Methodology for Systematic Reviews.⁽²²⁾ The Population criteria for
109 both questions are synonymous.

110 *Population*

111 This review will consider studies that include surgical patients aged 18 years or older requiring any
112 formulation or duration of opioid-based analgesia postoperatively. This includes operations for cancer
113 diagnoses. Contrary to existing reviews, no minimum participant number applies, permitting inclusion
114 of smaller studies. The intervention in this review will include any form of major or minor: elective,
115 emergency, day-case, or reoperative surgery, given sufficient postdischarge data is presented.
116 Consistent with other literature, studies involving $\geq 75\%$ of participants meeting inclusion criteria will
117 be accepted in the event of mixed populations.⁽²³⁾

118 *Condition*

119 This review will consider studies evaluating PPOU, including a limited variety of associated definitions.
120 Currently, no standardized definition for PPOU exists, which remains an issue with current research.^{(1,}
121 ¹²⁾ For inclusion, studies investigating PPOU must attempt to quantify postoperative opioid
122 consumption at least 90 days after discharge; studies mentioning PPOU but measuring OPs received
123 or prescribed only at discharge, or before 90 postoperative days, will not meet the definition
124 requirements and are therefore excluded.⁽¹⁶⁾ This threshold is frequently agreed in existing evidence
125 and is in line with the definition of persistent postsurgical pain.^(12, 20) Similarly, studies failing to provide
126 details on the timing of opioid initiation or duration are excluded. Studies with postdischarge data
127 limited to 90 days are included if OP data is indexed to the corresponding surgical event.

128 *Context*

129 This review will consider studies conducted in any cultural, racial, or gender-based contexts. There are
130 no geographical or temporal limitations for included studies, provided they were published in the last
131 decade.

132 *Exposure*

133 The exposure of interest is preoperative opioid use, including patients that were: opioid-naïve
134 (defined as no OPs in the year preceding surgery), opioid-exposed (≥ 1 OP in the year preceding
135 surgery), or chronic users (≥ 60 days duration of OPs in the year preceding surgery) prior to admission.
136 Potential candidate studies must include opioids that are indicated and prescribed for pain; unless
137 specifically indicated for pain, studies investigating opioids regularly prescribed for other purposes are
138 excluded. There are no exclusions regarding medication formulation or route. Further exposures of
139 interest include patient characteristics that have been examined in included studies, such as
140 depression and concurrent benzodiazepine use, among others. To facilitate comparisons between
141 patients that are either opioid-naïve or experienced prior to surgery, studies with mixed cohorts which
142 prevent subgroup analyses of these exposures are excluded.

143 *Outcome*

144 The outcome of interest for the pooled rates of **risk factors** is PPOU.

145 *Types of studies*

146 This review will consider analytical observational studies including prospective and retrospective
147 cohort studies, case-control studies, and cross-sectional studies. Additionally, descriptive
148 observational study designs that may contribute to incidence data will be considered. Similarly,
149 experimental and quasi-experimental studies, including *post hoc* analyses of these, will be included if
150 they contribute toward incidence data or test an intervention where the outcome directly addresses
151 postsurgical opioid use and meets the criteria.⁽²⁴⁾ Further, conference proceedings will be searched
152 for contributable incidence data given the scarcity of available published information. Studies in
153 English will be included for feasibility purposes, despite potential language bias and the possibility of
154 an incomplete dataset.⁽²⁵⁾ Qualitative studies will be excluded.

155 **Methods**

156 The methodology proposed in this protocol will be conducted in accordance with the JBI
157 Methodology for Systematic Reviews of Prevalence and Incidence,⁽²²⁾ and adheres to the Preferred
158 Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).⁽²⁶⁾ This protocol has
159 been registered in PROSPERO (CRD42022320691).

160 *Search strategy*

161 The search strategy will retrieve both published and unpublished literature. The first stage of the
162 search strategy is an initial search of PubMed to identify articles and relevant key terms. The second
163 stage involves creating a full search strategy developed for PubMed, using text words identified from
164 the titles and abstracts of relevant articles and associated index terms (Appendix I). The full search
165 strategy, with all identified keywords and index terms, will be adapted for searching additional
166 databases, including CINAHL (EBSCOhost), CENTRAL (Cochrane Library), EMBASE (Ovid), and Web of
167 Science (Clarivate). Sources of unpublished studies and gray literature will be searched, including
168 Google Scholar and ClinicalTrials.gov. As the final stage of the strategy, additional studies will be
169 sought by hand-searching bibliographies of relevant articles that were selected for critical appraisal.
170 The results of all searches, including the number of results and the date each search was performed,
171 in addition to any limits applied to each database, will be recorded as a supplement, to develop a
172 fully reproducible search and improve transparency.⁽²⁶⁾ Studies published from 1 January 2012 until
173 present will be included to better capture recent trends in incidence and ensure that the most

174 relevant studies will be analyzed.

175 *Study selection*

176 Upon completion of the full search strategy, all identified citations will be collated and uploaded into
177 EndNote 20 (Clarivate Analytics, Philadelphia, USA), with duplicates removed. The final search
178 results and retrieved studies will be imported into the JBI System for the Unified Management,
179 Assessment and Review of Information (SUMARI).⁽²⁷⁾ Following an initial pilot test, two independent
180 reviewers will screen titles and abstracts for compliance with the inclusion criteria described
181 previously. The two reviewers will then undergo full-text screening of relevant citations to
182 determine their compatibility with the inclusion criteria. Reasons for exclusion of full-text studies will
183 be recorded in SUMARI and reported in the review. Any disagreements that occur between the
184 reviewers at each stage of the study selection process will be recorded and resolved through either
185 discussion or consultation with a third reviewer. The results of the search, study selection and
186 inclusion process will be reported in full in the final systematic review and presented in a Preferred
187 Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow diagram.⁽²⁸⁾

188 *Assessment of methodological quality*

189 Two independent reviewers will critically appraise candidate studies for methodological quality using
190 standardized critical appraisal instruments from JBI for experimental, quasi-experimental, and
191 observational studies within SUMARI.⁽²²⁾ As with the selection process, disagreements between
192 reviewers will be recorded and resolved by consensus or with the help of a third reviewer. Included
193 studies and their corresponding results for each critical appraisal criterion (yes, no, or unclear) will
194 be reported in a table with an accompanying narrative. Studies that meet $\geq 50\%$ of the criteria in the
195 JBI critical appraisal checklist for studies reporting incidence data will be included for improved
196 quality of contributing studies. Authors will be contacted for missing or additional data where
197 required.

198 *Data extraction*

199 Data extraction from included studies will be performed by two independent reviewers using the
200 standardized JBI data extraction tools.⁽²⁷⁾ The data extracted will include specific details about the
201 populations, study methods, exposures, and outcomes of significance to the review question. This

202 includes study design, sample size, follow-up duration, type of surgical admission, and selected
203 PPOU and preoperative opioid use definitions. Additionally, data will be organized into categories
204 relating to PPOU risk factors, such as sociodemographic information, comorbid status, and
205 preoperative opioid use status. Studies reporting odds ratios (ORs), risk ratios (RRs), or hazard ratios
206 (HRs) for risk factors are included since no limitations to extracted effect measurements apply.
207 Finally, sources of study funding, such as pharmaceutical companies or research funding institutions,
208 will be analyzed. Authors of papers will be contacted to request missing or additional data, where
209 required.

210 *Data synthesis*

211 Estimates of incidence will, where possible, be pooled with statistical meta-analysis using JBI
212 SUMARI.⁽²⁷⁾ Incidence data will be transformed using Freeman-Tukey transformation and
213 subsequently used to calculate a summary proportion using a random effects model.⁽²⁹⁾ Since the
214 overall prevalence of risk factors is expected to be low, we will regard ORs and RRs as equivalent
215 measures; pooled rates of HRs will undergo a separate analysis.⁽²⁰⁾ Effect sizes of PPOU risk factors
216 will be expressed as ORs and their 95% confidence intervals (CIs) for dichotomous variables and as
217 standardized mean differences (SMD) with 95% CIs for continuous variables, using a random effects
218 model. Included studies will be assessed for clinical, methodological, and statistical heterogeneity;
219 the latter will involve the standard χ^2 , τ^2 , and I^2 tests.⁽²²⁾ Subgroup analyses will be conducted to
220 explore any clinical heterogeneity where there are sufficient data concerning study, participant, and
221 exposure characteristics previously mentioned. Examples of this include cancer diagnosis, type of
222 surgical admission, extent of preoperative opioid use, and study location. As substantial variation in
223 PPOU definitions is expected, a sensitivity analysis of the pooled odds ratios is planned, testing
224 different definition thresholds in addition to our primary analysis. It is likely that significant
225 heterogeneity will prohibit meta-analysis as often seen in reviews of prevalence and incidence.⁽²²⁾ In
226 this instance, the findings will be presented in narrative form including tables and figures to aid in
227 data presentation, where appropriate. In the event of low heterogeneity between studies, a funnel
228 plot will be generated to assess publication bias if 10 or more studies are included in a meta-analysis.
229 Statistical tests for funnel plot asymmetry, including the Egger regression-based test, will be
230 performed if necessary.

231 *Assessing certainty in the findings*

232 The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach,
233 adapted for prognostic studies, for grading the certainty of evidence, will be followed.⁽³⁰⁾ The
234 Summary of Findings will be created using GRADEpro GDT (McMaster University, ON, Canada) and
235 present the following information where appropriate: incidence rates, pooled estimates of risk, and
236 a ranking of the quality of the evidence based on methodological bias assessment, directness,
237 heterogeneity, precision, and risk of publication bias of the review results.

238 **References**

- 239 1. Srivastava D, Hill S, Carty S, Rockett M, Bastable R, Knaggs R, et al. Surgery and opioids:
240 evidence-based expert consensus guidelines on the perioperative use of opioids in the United
241 Kingdom. *British Journal of Anaesthesia*. 2021;126(6):1208-16.
- 242 2. Srivastava D, Wilkinson P. Surgery and opioids: some cracks in an enduring romance. *British*
243 *Journal of Anaesthesia*. 2021;126(6):1088-92.
- 244 3. Cade S, Haxby A, Ximena C, Philip C, Stefan L, Tim S, et al. The Surgeon's Role in the Opioid
245 Crisis: A Narrative Review and Call to Action. *Frontiers in Surgery*. 2020;7:4.
- 246 4. Levy N, Mills P, Fawcett WJ. Avoiding an opioid crisis in the UK. *BMJ*. 2019;364:l1033.
- 247 5. Jani M, Birlie Yimer B, Sheppard T, Lunt M, Dixon WG. Time trends and prescribing patterns
248 of opioid drugs in UK primary care patients with non-cancer pain: A retrospective cohort study. *PLoS*
249 *Med*. 2020;17(10):e1003270.
- 250 6. Harbaugh C, Suwanabol P. Optimising Pain Control During the Opioid Epidemic. *Surgical*
251 *Clinics of North America*. 2019;99(5):867-83.
- 252 7. Levy N, Quinlan J, El-Boghdadly K, Fawcett JW, Agarwal V, Bastable BR, et al. An international
253 multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical
254 patients. *Anaesthesia*. 2021;76(4):520-36.
- 255 8. Farias JC, Porter L, McManus S, Strang J, Hickman M, Reed K, et al. Prescribing patterns in
256 dependence forming medicines. *Public Health Research Consortium*. 2017.

- 257 9. Els C, Jackson TD, Kunyk D, Lappi VG, Sonnenberg B, Hagtvedt R, et al. Adverse events
258 associated with medium and long term use of opioids for chronic non cancer pain: an overview of
259 Cochrane Reviews. *Cochrane Database of Systematic Reviews*. 2017(10).
- 260 10. Dalton M, Chaudhary M, Tomas A, Daniel S, Learn P, Jarman M, et al. Patterns and predictors
261 of opioid prescribing and use after rib fractures. *Surgery*. 2020;168(4):684-9.
- 262 11. Naheed J, Faizal R, Jennifer B, Wijeyesundera D, Ladha K, Bateman B, et al. Persistent
263 Postoperative Opioid Use: A Systematic Literature Search of Definitions and Population-based
264 Cohort Study. *Anesthesiology*. 2020;132(6):1528-39.
- 265 12. Kent ML, Hurley RW, Oderda GM, Gordon DB, Sun E, Mythen M, et al. American Society for
266 Enhanced Recovery and Perioperative Quality Initiative-4 Joint Consensus Statement on Persistent
267 Postoperative Opioid Use. *Anesthesia & Analgesia*. 2019;Publish Ahead of Print(&NA;):&NA;.
- 268 13. Quinlan J, Lobo D, Levy N. Postoperative pain management: time to get back on track.
269 Blackwell Publishing Ltd; 2020.
- 270 14. Schoenfeld AJ, Belmont PJ, Blucher JA, Jiang W, Chaudhary MA, Koehlmoos T, et al.
271 Sustained Preoperative Opioid Use Is a Predictor of Continued Use Following Spine Surgery. *The*
272 *Journal of Bone and Joint Surgery*. 2018;100(11):914-21.
- 273 15. Chaudhary MA, Bhulani N, De Jager EC, Lipsitz S, Nicollette KK, Sturgeon DJ, et al.
274 Development and Validation of a Bedside Risk Assessment for Sustained Prescription Opioid Use
275 after Surgery. *JAMA Network Open*. 2019;2(7):e196673.
- 276 16. Daliya P, Adiamah A, Roslan F, Theophilidou E, Knaggs DR, Levy N, et al. Opioid prescription
277 at postoperative discharge: a retrospective observational cohort study. *Anaesthesia*.
278 2021;76(10):1367-76.
- 279 17. Levy N, Mills P. Controlled-release opioids cause harm and should be avoided in
280 management of postoperative pain in opioid naïve patients. Elsevier Ltd; 2019.
- 281 18. Khazi ZM, Lu Y, Patel BH, Cancienne JM, Werner B, Forsythe B. Risk factors for opioid use
282 after total shoulder arthroplasty. *Journal of Shoulder and Elbow Surgery*. 2020;29(2):235-43.

- 283 19. Sitter T, Forget P. Persistent postoperative opioid use in Europe: A systematic review. Eur J
284 Anaesthesiol. 2021;38(5):505-11.
- 285 20. Lawal OD, Gold J, Murthy A, Ruchi R, Bavry E, Hume AL, et al. Rate and Risk Factors
286 Associated With Prolonged Opioid Use After Surgery: A Systematic Review and Meta-analysis. JAMA
287 Netw Open. 2020;3(6):e207367.
- 288 21. Ranapurwala SI, Naumann RB, Austin AE, Dasgupta N, Marshall SW. Methodologic
289 limitations of prescription opioid safety research and recommendations for improving the evidence
290 base. Pharmacoepidemiol Drug Saf. 2019;28(1):4-12.
- 291 22. Aromataris E, Munn Z. JBI Manual for Evidence Synthesis Adelaide, Australia: JBI; 2020
292 [Available from: [https://jbi-global-](https://jbi-global-wiki.refined.site/space/MANUAL/3283910689/Chapter+5%3A+Systematic+reviews+of+prevalence+and+incidence)
293 [wiki.refined.site/space/MANUAL/3283910689/Chapter+5%3A+Systematic+reviews+of+prevalence+a](https://jbi-global-wiki.refined.site/space/MANUAL/3283910689/Chapter+5%3A+Systematic+reviews+of+prevalence+and+incidence)
294 [nd+incidence](https://jbi-global-wiki.refined.site/space/MANUAL/3283910689/Chapter+5%3A+Systematic+reviews+of+prevalence+and+incidence).
- 295 23. Gabrielle PM, Irina K, Vignon ZHT, Jordie C, Daniela Z, Patrice N, et al. A Systematic Review of
296 the Relative Frequency and Risk Factors for Prolonged Opioid Prescription Following Surgery and
297 Trauma Among Adults. Annals of Surgery. 2020;271(5):845-54.
- 298 24. Hah J, Heather H, Peter S, Rebecca M, Jodie T, Debra C, et al. <p>Preoperative Factors
299 Associated with Remote Postoperative Pain Resolution and Opioid Cessation in a Mixed Surgical
300 Cohort: Post Hoc Analysis of a Perioperative Gabapentin Trial</p>. Journal of Pain Research.
301 2020;Volume 13:2959-70.
- 302 25. Neimann Rasmussen L, Montgomery P. The prevalence of and factors associated with
303 inclusion of non-English language studies in Campbell systematic reviews: a survey and meta-
304 epidemiological study. Systematic Reviews. 2018;7(1):129.
- 305 26. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting
306 items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic
307 Reviews. 2015;4(1):1.
- 308 27. Munn Z, Aromataris E, Tufanaru C, Stern C, Porritt K, Farrow J, et al. The development of
309 software to support multiple systematic review types: the Joanna Briggs Institute System for the

310 Unified Management, Assessment and Review of Information (JB1 SUMARI). Int J Evid Based Healthc.
 311 2019;17(1):36-43.

312 28. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA
 313 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

314 29. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis?
 315 Common methodological issues in systematic reviews of effectiveness. Int J Evid Based Healthc.
 316 2015;13(3):196-207.

317 30. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, et al. Use of GRADE for
 318 assessment of evidence about prognosis: rating confidence in estimates of event rates in broad
 319 categories of patients. Bmj. 2015;350:h870.

320

321 **Appendix I: Search strategy**

322 Search conducted on 07 July 2022 in PubMed.

Search	Query	Records retrieved
Condition	("Persistent postoperative opioid use"[All Fields] OR opioid use prolonged postoperative[All Fields] OR postoperative opioid dependence[All Fields] OR opioid dependence surgery[All Fields] OR persistent opioid use surgery[All Fields] OR chronic opioid use surgery[All Fields] OR opioid use postsurgical[All Fields] OR postoperative chronic opioid use[All Fields] OR postoperative opioid use[All Fields])	1,358
Exposure	((("opioid"[MeSH] OR "opioid"[All Fields]) OR ("codeine"[MeSH] OR "codeine"[All Fields]) OR ("morphine"[MeSH] OR "morphine"[All Fields]) OR ("tramadol"[MeSH] OR "tramadol"[All Fields]) OR ("oxycodone"[MeSH] OR "oxycodone"[All Fields]) OR ("dihydrocodeine"[MeSH] OR "dihydrocodeine"[All Fields]) OR ("hydromorphone"[MeSH] OR "hydromorphone"[All Fields]) OR ("oxymorphone"[MeSH] OR "oxymorphone"[All Fields]) OR ("fentanyl"[MeSH] OR "fentanyl"[All Fields]) OR ("hydrocodone"[MeSH] OR "hydrocodone"[All Fields]) OR ("tapentadol"[MeSH] OR "tapentadol"[All Fields]) OR (anagles*[All Fields] AND	71,759

	<p>“opioid”[All Fields]) OR (“levorphanol”[MeSH] OR “levorphanol”[All Fields]) OR (“meperidine”[MeSH] OR “meperidine”[All Fields]) OR (“pentazocine”[MeSH] OR “pentazocine”[All Fields]) OR (“levopropoxyphene”[MeSH] OR “levopropoxyphene”[All Fields]) OR (“propoxyphene”[MeSH] OR “propoxyphene”[All Fields]) OR (“dextropropoxyphene”[MeSH] OR “dextropropoxyphene”[All Fields]) OR (“sufentanil”[MeSH] OR “sufentanil”[All Fields]) OR (“buprenorphine”[MeSH] OR “buprenorphine”[All Fields]))</p>	
Context	<p>(“Postoperative”[All Fields] OR “postsurgical”[All Fields] OR (“minor”[All Fields] AND “surgery”[All Fields] OR “operative”[All Fields] OR “procedure”[All Fields]) OR (“major”[All Fields] AND “surgery”[All Fields] OR “operative”[All Fields] OR “procedure”[All Fields]) OR “surgical procedures”[All Fields] OR “minor surgical procedures”[MeSH] OR “major surgical procedures”[MeSH] OR “general surgery”[All Fields] OR “elective surgery”[All Fields] OR emergen* surgery[All Fields] OR “day-case surgery”[All Fields] OR reoperative surgery[All Fields] OR “operative”[All Fields] OR “surgical”[All Fields] OR “surgery”[All Fields] NOT (“animals”[MeSH] NOT “humans”[MeSH]) NOT ((child[MeSH] OR adolescent[MeSH]) NOT adult[MeSH]))</p>	1,865,709
#4	#1 AND #2 AND #3	1,181
Limited to studies published from 1 January 2012.		