Final Research Report

Project Title:	Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) use in the Critically Ill: A Scoping Review	
Project advisor name & email:	Brian Erstad, PharmD	erstad@pharmacy.arizona.edu
Project co-author	Jennifer Martin	jenmartin@arizona.edu
Student name & email:	Renita Daniel	rdaniel@email.arizona.edu
Student name & email:	Lorenz Laurel	llaurel@email.arizona.edu
Student name & email:	William Leung	williamleung@email.arizona.edu
Student name & email:	Madeline Yu	madelineyu@email.arizona.edu

PROPOSAL CHECKLIST

Completed (Y)	Checklist item
Y	Project title is clear and concise.
Y	Names and emails for project advisor(s) and up to five students per group are provided.
Y	Problem statement states general issues under consideration.
Y	Literature review contains at least four reviews (at least one review uses a similar method to the proposed project), is sufficient to develop a sound reason to conduct the project, and clearly leads to the purpose statement.
Y	Purpose statement is clearly stated.
Y	Up to three specific aims with corresponding hypotheses are clearly stated.

Y	Methods is written in future tense and includes appropriate and clear: study design, subject/data selection, human subjects, sample size, instruments, variables (independent, dependent, descriptive/demographic), data collection procedures, data storage/access procedures, project assumptions and limitations, and planned data analysis.
Y	Planned data analysis is appropriate and addresses the hypotheses.
Y	Timeline for project completion is provided and is reasonable.
Y	Budget describes all applicable costs even if they will not actually be paid (e.g., personnel time, cost of lab equipment, photocopying charge).
Y	Reference list is complete and contains appropriate references, and reference style is applied correctly and consistently.
Y	Appendix A (Literature Search Strategy), Appendix B (Type of IRB Approval Required), Appendix C (Data Collection Forms/Data Dictionary), and any additional appendices (as necessary) are provided on a new page at the end of the proposal.
Y	Proposal and IRB (if required) submitted to D2L and project advisor(s).
Y	Template structure is maintained and all required sections are included. Red text instructions/examples are removed. Proposal is written in Times New Roman 12-point font and does not exceed 10 single-spaced pages (excluding appendices). Proposal has been spell-checked and grammar-checked.

INTRODUCTION

Opioids and other analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) are important medications for pain management; however, the use of these agents raises important adverse effect concerns in critically ill patients already predisposed to organ dysfunction. Pain medication properties that apply to an otherwise healthy individual with pain may or may not translate to the critically ill. Appropriate patient selection with ongoing monitoring for drug efficacy and adverse effects can help optimize the benefit: risk consideration.[1] Opioids are a staple of pain management in the acute care setting but have well known adverse effects including constipation, central nervous system and respiratory depression, and opioid use disorder with prolonged inappropriate use.[2] Because of these adverse effect concerns of opioids, current clinical practice guidelines pertaining to critically ill patients recommend the use of

opioid-sparing therapies such as NSAIDs.[3] Some of the NSAID adverse effects of most concern in the critically ill population include gastrointestinal bleeding and acute kidney injury.[4] These adverse effects of NSAIDs may be masked or amplified in critically ill patients prone to variable and compromised health states during their intensive care unit (ICU) stay.[5]

The purpose of this scoping review is to conduct a thorough search of the current literature concerning NSAID adverse effects in critically ill patients. Our aim is to collect data on the rate and types of NSAID adverse effects in this patient population in order to help guide therapy recommendations and monitoring parameters. We also intend to provide information on gaps in the literature to guide further research and clinical decision making concerning NSAID use in critically ill patients.

METHODS

Protocol and Registration

The protocol was drafted and revised using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) by the research team; review protocols are to be reported for advisory board review in future references. The research team included a librarian with expertise in conducting scoping reviews.

Eligibility Criteria

To be included in the review, all literature consisting of randomized control trials, case series, and retrospective studies were included. Case reports, letters, review articles, and commentaries were excluded. The focus was on critically ill patient populations. Studies restricted to patients in emergency medicine settings were excluded in the search.

Human Subjects

Because this project did not involve human subjects, IRB approval was not necessary.

Information Resources

To identify potentially relevant documents, the following bibliographic databases were searched from January 2016 to January 2020: PubMed, Cochrane Library, EMBASE, Stat!Ref, Access Pharmacy. The search strategies were drafted by the librarian and further with further refinement through team discussion. The final search results were exported into Mendeley with duplicate removal by the librarian. The electronic database search was supplemented by consulting sources guidelines: Society of Critical Care Medicine (SCCM), American Pain Society Guidelines (APS), American Thoracic Society (ATS), and American College of Chest Physicians (ACCP), 2020 ACS TQP best practice guidelines.

Selection of Sources of Evidence

To increase consistency among reviewers, all reviewers screened 2250 articles split evenly in the reviewers, discussed the results and amended the screening and data extraction manual before beginning screening for this review. Four reviewers working in pairs sequentially evaluated the

titles, abstracts and full text of all publications identified by our searches for potentially relevant publications. We resolved disagreements on study selection and data extraction by consensus and discussion with other reviewers if needed.

Data Charting Process

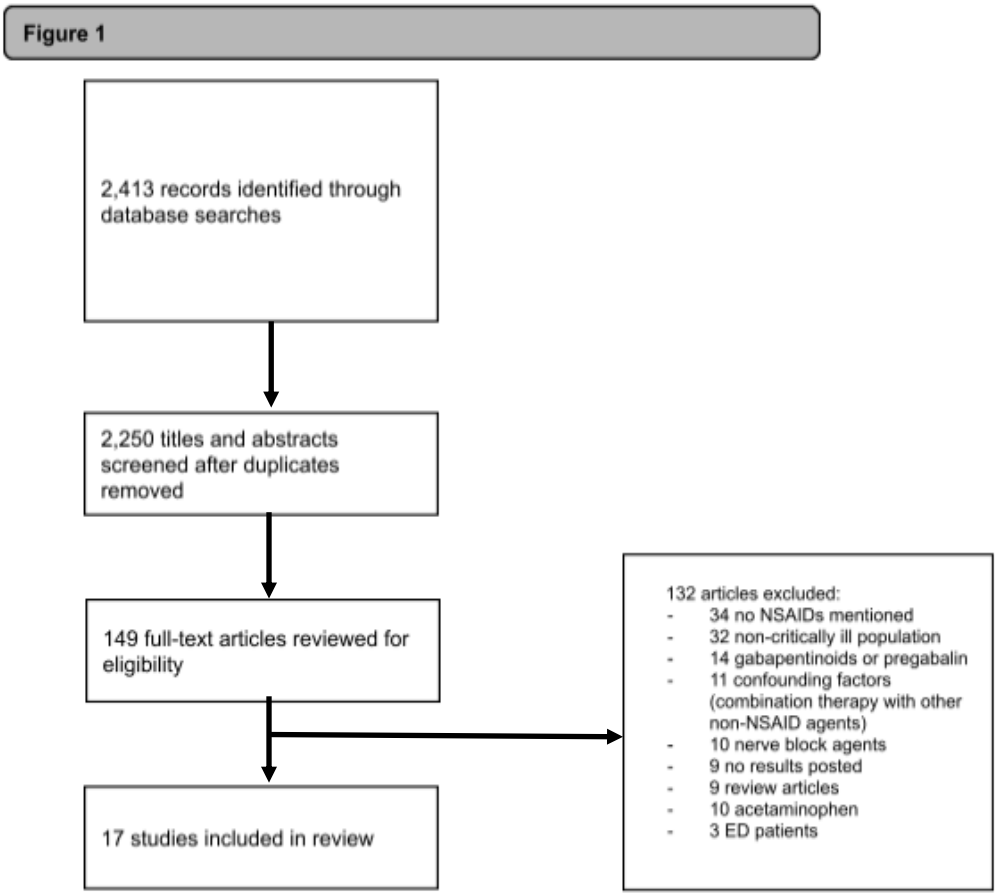
In accordance with the metadata that has been used in previous scoping review protocols,[6] decisions were made for key study characteristics and detailed information on all metrics to determine adverse effect incidence based on eligibility of an article. Discussions were held to resolve disagreements on criteria with further adjudication by a third or fourth reviewer.

Critical Appraisal of Individual Sources of Evidence

Critical appraisals are not applicable for this scoping review.

Data Analysis and Synthesis of Results

After an initial screening, full text-articles were assessed for eligibility. See attached PRISMA diagram for a depiction of the process used in the synthesis of information for this scoping review (Figure 1). NSAIDs that were included could be any NSAID commercially available in the US or internationally, while adverse effects could be any adverse reaction that could be associated with NSAID use.



Risk of Bias Assessment

Risk of Bias Assessment was not necessary for this scoping review.

Results

The PRISMA diagram for the scoping review is outlined in Figure 1. Of the 2,413 citations and titles identified in the search, 2,250 titles remained after removal of duplicates, 2,101 were excluded at title and abstract screening, and 149 articles remained for full-text review. Only 17 studies that met eligibility criteria were included in the scoping review. Of these, four studied ketorolac (11,14, 15, 22), three studied diclofenac (10, 20, 24), three studied parecoxib (13, 21, 23), one studied meloxicam (12), one studied celecoxib (20), one studied etoricoxib (24), one studied ketoprofen (17), and one studied ibuprofen (18). Most studies (8/17 47%) focused on surgical orthopedic patients, the remainder were a mixed medical-surgical population and critical illness. Full characteristics of the studies included in this analysis are described in Table 1 and Table 2.

Table 1: Study Characteristics

References	Opioid	Adjuvant Used	Duration of Intervention	Patient Subgroup	Mean Age (yrs) Intervention group	% female patients intervention group
Arslans et al. (10)	Tramadol IV	Diclofenac IM	24hr	Surgical-cardiac	56	16%
Bakr et al. (11)	Morphine IV	Ketorolac IV	24hr	Surgical-oncology	46	100%
Bergese et al. (12)	None	Meloxicam IV	28hr	Surgical-orthopedic	53	58%
Camu et al. (13)	Morphine IV	Parecoxib IV	48hr	Surgical-orthopedic	65	42%
Claus et al. (14)	None	Ketorolac IV	48hr	Surgical-orthopedic	61	53%
Dehghanpishesh et al. (15)	None	Ketorolac IV	12hr	Surgical-general	26	100%
Eftekharian HR et al. (16)	None	Ketorolac IV	4hr	Surgical-mandibular	30	40%
Eljezi et al. (17)	Morphine IV	Ketoprofen IV	48hr	Surgical-cardiac	61	16%
Erdogan et al. (18)	Morphine IV	Ibuprofen IV	24hr	Surgical-bariatric	37	34%
Liu et al. (19)	Morphine IV	Parecoxib IV	5days	Surgical-general	63	38%
Liu et al. (20)	Morphine*	Diclofenac*	28days	Critical illness-oncology	55	45%

	Morphine*	Celecoxib PO	28days	Critical illness-oncology	54	44%
Mu et al. (21)	Morphine IV	Parecoxib IV	5days	Surgical-orthopedic	69	74%
Sivasundaram et al. (22)	Oxycodone-APAP	Ketorolac IV	5days	Surgical-orthopedic	56	25%
	Oxycodone-APAP	Ketorolac PO	5days	Surgical-orthopedic	56	25%
Wang et al. (23)	Fentanyl IV	Parecoxib IV	48hr	Surgical-hepatic	55	17%
Winkler et al. (24)	None	Etoricoxib PO	9days	Surgical-orthopedic	62	46%
	None	Diclofenac PO	9days	Surgical-orthopedic	60	47%

*unspecified administration route

Table 2: Adverse Events

Study Name	Adverse Event	Adjuvant Group	Control Group
Ketorolac			
Bakr 2016	Nausea and vomiting	0/20	N/A
	Respiratory depression	0/20	N/A
Claus 2022	AKI	2/119	2/127
	Wound hematoma	1/119	0/127
Dehghanpisheh 2021	Hypotension	16/49	16/48
	Bradycardia	3/49	4/49
Sivasundaram 2021	Nausea and vomiting	2/20	2/19
	Abdominal pain	1/20	0/19
	Drowsiness	1/20	4/19
	Insomnia	2/20	1/19
	Headache	2/10	1/19
Diclofenac			
Arslans 2018	Nausea and vomiting	3/50	5/50

Liu 2017	Nausea	15/111	N/A
	Dizziness	31/111	N/A
	Constipation	35/111	N/A
	Drowsiness	46/111	N/A
	Respiratory inhibition	6/111	N/A
	Peripheral edema	3/111	N/A
Winkler 2015	Nausea	6/50	N/A
	Vomiting	4/50	N/A
	Dizziness	4/50	N/A
	Diarrhea	3/50	N/A
	Hypertension	2/50	N/A
Meloxicam			
Bergese 2018	Nausea	123/539	51/183
	Constipation	51/539	17/183
	Vomiting	27/539	14/183
	Bleeding	26/539	7/183
	Hepatic	35/539	15/183
	Wound Healing Complications	31/539	7/183
Celecoxib			
Liu 2017	Nausea	17/115	N/A
	Dizziness	30/115	N/A
	Constipation	36/115	N/A
	Drowsiness	43/115	N/A
	Respiratory inhibition	6/115	N/A
	Peripheral edema	1/115	N/A
Etoricoxib			
Winkler 2015	Nausea	7/50	N/A

	Vomiting	5/50	N/A
	Dizziness	1/50	N/A
	Diarrhea	2/50	N/A
	Hypertension	2/50	N/A
Parecoxib			
Camu 2017	Hypotension	2/72	0/38
	Fever	5/72	7/38
	Nausea	34/72	22/38
	Vomiting	19/70	11/38
Mu 2017	Delirium	19/310	34/310
Wang 2020	Nausea/Vomiting	6/40	10/40
	Pruritus	2/40	3/40
	Hypotension	1/40	1/40
	Respiratory depression	0/40	0/40
	Wound infection	3/40	4/40
	Lung infection	1/40	2/40
Ketoprofen			
Eljezi 2017	Nausea	4/25	5/23
	Vomiting	1/25	5/23
	Delayed acute renal insufficiency	3/25	3/25
	Fever	5/25	5/25
Ibuprofen			
Erdogan 2018	Nausea and vomiting	24/35	28/39
	Headache	7/35	7/39
	Dizziness	15/35	6/39
	Dyspepsia	7/35	7/39

Adverse Events:

The included studies had limited adverse events reported. Dissemination of the

types of adverse events reported are quantitatively summarized in Table 2.

Discussion

The results of this scoping review demonstrate a paucity of evidence supporting the safety of NSAIDs in critically ill patients and lend support to the recommendation in the most recent SCCM PADIS clinical practice guideline to avoid routine use of COX-1 selective NSAIDs as adjuncts to opioid therapy in critically ill patients.[3] None of the available studies evaluated an NSAID in a heterogeneous critically ill population, but instead most of the investigations were limited to postoperative cardiac surgery patients. Of the limited studies involving NSAIDs available in an injectable form, some involved products such as ketoprofen that do not have an injectable formulation approved for human use in the US. Other issues common to all of the published studies include the difficulty in attribution of adverse drug events given the frequent occurrence of complications such as bleeding and acute kidney injury in critically ill patients and limited duration of NSAID administration. For these reasons, our findings suggest that the SCCM PADIS recommendation is applicable to all NSAIDs, not just COX-1 selective agents.

The SCCM PADIS clinical practice guideline has a conditional recommendation based on low quality evidence, which states that NSAIDs (by a variety of routes) are alternatives to opioids for discrete or infrequent procedures. The basis for this suggestion is one study in which patients were randomized to a single 4 mg dose of IV morphine or a single 30 mg dose of IV ketorolac for alleviating pain in association with chest tube removal in patients on a cardiac surgery service.[7] We recommend caution in extrapolating the results of this single study to heterogeneous critically ill patients. In addition to using the lowest effective dose for the shortest duration possible, potential candidates for NSAID therapy in the ICU should not have any of the following, most of which are listed as contraindications in NSAID product labeling: active gastrointestinal ulceration or bleeding, recent gastrointestinal bleeding or perforation, or history of peptic ulcer disease or gastrointestinal bleeding; confirmed cerebrovascular bleeding, hemorrhagic diathesis, incomplete hemostasis or high risk of bleeding including major surgery; advanced kidney impairment, substantial risk for kidney impairment including hemodynamic instability such as volume depletion, or concurrent nephrotoxins; active liver disease or moderate-severe liver disease (Child-Turcotte-Pugh score > 7); decompensated heart failure; or inflammatory bowel disease. These conditions would preclude most critically ill patients from receiving NSAIDs of any dose or duration of therapy.

Because of legitimate concerns related to inappropriate opioid use, there is a tendency to overgeneralize regarding the preference for non-opioid alternatives as adjuncts or replacements for opioids. For example, in a recent systematic review and meta-analysis evaluating the efficacy and safety of nonopioid adjunctive analgesics in critically ill patients, the authors concluded that, “Clinicians should consider using adjunct agents to limit opioid exposure and improve pain scores in critically ill patients.”[1] With respect to NSAIDs, there were six investigations included in the analysis involving indomethacin, diclofenac, and ketoprofen. Of

the latter agents, only indomethacin and diclofenac are available in injectable forms and the commercially available indomethacin formulation (1 mg single dose vial) is not useful in adult ICU settings given its sole approved indication of closing a hemodynamically significant patent ductus arteriosus in premature infants. Similar to these conclusions, despite non-opioid analgesics demonstrating a reduction in both consumption of opioids and adverse effects such as nausea and vomiting, documentation of total opioid consumption was not included in the study and therefore could not provide a conclusive correlation with reduction of opioid consumption.[9] Of note, the discussion section of the systematic review does refer to the SCCM PADIS recommendations and adverse effect concerns related to bleeding and kidney dysfunction.

Injectable products, particularly IV formulations, are frequently preferred for pain management in the ICU setting because of more rapid onset of action in comparison to oral administration and concerns related to absorption. Besides diclofenac, the only two NSAIDs available in injectable formulations in the US are ibuprofen (approval in 2009) and ketorolac (approval in 1997). Ketorolac is the most studied injectable NSAID, particularly for postoperative pain, as indicated by the results of a systematic review conducted by the Cochrane organization that included participants in randomized, double-blind studies receiving single IV dose ketorolac for various types of surgical procedures.[8] The review included 12 studies (1905 participants) with ketorolac comparisons to placebo and other NSAIDs. The authors concluded that while ketorolac has the potential to offer substantial pain relief in most patients, adverse events occurred at somewhat higher rates compared with other NSAIDs (76% versus 68%, respectively; RR 1.11, 95% CI 1.00 to 1.23; NNTH 12.5, 95% CI 6.7 to infinite, moderate-certainty evidence). Furthermore, there was insufficient information to evaluate serious adverse events such as gastrointestinal bleeding and kidney dysfunction, which are of particular concern in critically ill patients who are predisposed to such complications.

The primary limitations of this scoping review are similar to those of other systematic and scoping reviews, which include the potential for missing studies or publication bias due to unpublished investigations.

Conclusions

While there is data primarily from postoperative populations that NSAIDs are efficacious for the management of mild to moderate pain, there is insufficient evidence to conclude that NSAIDs have an acceptable safety profile in heterogeneous critically ill patient populations predisposed to complications such as bleeding and acute kidney injury that are also adverse effect concerns of NSAIDs. In most (if not all) critically ill patients, it is best to avoid NSAIDs regardless of COX-1 selectivity with preference being given to other adjunctive therapies for minimizing opioid use. When NSAIDs are undergoing consideration for single dose or short-term use in critically ill patients, careful patient selection and ongoing monitoring must occur given the well-known adverse effect profile of NSAIDs.

REFERENCES

[1] Wheeler KE, Grilli R, Centofanti JE, et al. Adjuvant analgesic use in the critically ill: A systematic review and meta-analysis. Crit Care Explor. 2020;2(7):e0157. doi:10.1097/CCE.0000000000000157

[2] Erstad BL, Puntillo K, Gilbert HC, et al. Pain management principles in the critically ill. Chest. 2009;135(4):1075-1086. doi:10.1378/chest.08-2264

[3] Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46(9):e825-e873. doi:10.1097/CCM.0000000000003299.

[4] Erstad BL. Attempts to limit opioid prescribing in critically ill patients: Not so easy, not so fast. Ann Pharmacother. 2019;53(7):716-725. doi:10.1177/1060028018824724

[5] Dehcheshmeh H, Johnston TP, Joneidi-Jafari N, Mojtahedzadeh M, Panahi Y, Sahebkar A. Analgesic and sedative agents used in the intensive care unit: A review. J Cell Biochem. 2018;119(11):8684-8693. doi:10.1002/jcb.27141

[6] Ghalibaf AK, Nazari E, Gholian-Aval M, Tabesh H, Tara M. Comprehensive overview of computer-based health information tailoring: a scoping review protocol. BMJ Open. 2017;7(12):e019215. doi:10.1136/bmjopen-2017-019215

[7] Puntillo K, Ley SJ. Appropriately timed analgesics control pain due to chest tube removal. Am J Crit Care. 2004 Jul;13(4):292-301.

[8] McNicol ED, Ferguson MC, Schumann R. Single-dose intravenous ketorolac for acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2021, Issue 5.

[9] Zhao H, Yang S, Wang H, Zhang H, An Y. Non-opioid analgesics as adjuvants to opioid for pain management in adult patients in the ICU: A systematic review and meta-analysis. J Crit Care. 2019 Dec;54:136-144. doi: 10.1016/j.jcrc.2019.08.022. Epub 2019 Aug 13. PMID: 31446231.

[10] Arslan, Yaşar & Kudsioğlu, Türkan & Yapici, Nihan & Aykac, Zuhal. (2018). Administration of Paracetamol, Diclofenac Sodium, And Tramadol in Postoperative Analgesia After Coronary Artery Bypass Surgery. Journal Of Cardio-Vascular-Thoracic Anaesthesia And Intensive Care Society. 10.5222/GKDAD.2018.023.

[11] Bakr MA, Amr SA, Mohamed SA, et al. Comparison Between the Effects of Intravenous Morphine, Tramadol, and Ketorolac on Stress and Immune Responses in Patients Undergoing Modified Radical Mastectomy. Clin J Pain. 2016;32(10):889-897. doi:10.1097/AJP.0000000000000338

[12] Bergese, Sergio D, Timothy I Melson, Keith A Candiotti, Sabry S Ayad, Randall J Mack, Stewart W McCallum, Wei Du, Alexis Gomez, and Jorge E Marcet. "A Phase 3, Randomized, Placebo-Controlled Evaluation of the Safety of Intravenous Meloxicam Following Major Surgery." Clinical Pharmacology in Drug Development 8.8 (2019): 1062-072. Web.

[13] Camu F, Borgeat A, Heylen RJ, Viel EJ, Boye ME, Cheung RY. Parecoxib, propacetamol, and their combination for analgesia after total hip arthroplasty: a randomized non-inferiority trial. Acta Anaesthesiol Scand. 2017;61(1):99-110. doi:10.1111/aas.12841

[14] Claus, Chad F, Evan Lytle, Michael Lawless, Doris Tong, Diana Sigler, Lucas Garmo, Dejan Slavnic, Jacob Jasinski, Robert W McCabe, Ascher Kaufmann, Gustavo Anton, Elise Yoon, Ammar Alsalahi, Karl Kado, Peter Bono, Daniel A Carr, Prashant Kelkar, Clifford Houseman, Boyd Richards, and Teck M Soo. "The Effect of Ketorolac on Posterior Minimally Invasive Transforaminal Lumbar Interbody Fusion: An Interim Analysis from a Randomized, Double-blinded, Placebo-controlled Trial." The Spine Journal 22.1 (2022): 8-18. Web.

[15] Dehghanpisheh L, Azemati S, Feiz F, Karami MY. Pre-emptive intravenous paracetamol vs. ketorolac for shoulder pain in cesarean section under spinal anesthesia: A randomized double-blind placebo-controlled trial. Anaesth. pain intensive care 2021;25(3):359–366. DOI: doi.org/10.35975/apic.v25i3.1425

[16] Eftekharian HR, Ilkhani Pak H. Effect of Intravenous Ketorolac on Postoperative Pain in Mandibular Fracture Surgery; A Randomized, Double-Blind, Placebo-Controlled Trial. Bull Emerg Trauma. 2017;5(1):13-17.

[17] Eljezi V, Biboulet C, Boby H, Schoeffler P, Pereira B, Duale C. The Dose-Dependent Effects of Ketoprofen on Dynamic Pain after Open Heart Surgery. Pain Physician. 2017;20(6):509-520.

[18] Erdogan Kayhan G, Sanli M, Ozgul U, Kirteke R, Yologlu S. Comparison of intravenous ibuprofen and acetaminophen for postoperative multimodal pain management in bariatric surgery: A randomized controlled trial. J Clin Anesth. 2018;50:5-11. doi:10.1016/j.jclinane.2018.06.030

[19] Liu G, Ma Y, Chen Y, Zhuang Y, Yang Y, Tian X. Effects of parecoxib after pancreaticoduodenectomy: A single center randomized controlled trial. Int J Surg. 2021;90:105962. doi:10.1016/j.ijsu.2021.105962

[20] Liu Z, Xu Y, Liu ZL, Tian YZ, Shen XH. Combined application of diclofenac and celecoxib with an opioid yields superior efficacy in metastatic bone cancer pain: a randomized controlled trial. Int J Clin Oncol. 2017;22(5):980-985. doi:10.1007/s10147-017-1133-y

[21] Mu DL, Zhang DZ, Wang DX, et al. Parecoxib Supplementation to Morphine Analgesia Decreases Incidence of Delirium in Elderly Patients After Hip or Knee Replacement Surgery: A Randomized Controlled Trial. Anesth Analg. 2017;124(6):1992-2000. doi:10.1213/ANE.0000000000002095

[22] Sivasundaram, Lakshmanan, John Strony, Sunita Mengers, Nikunj Trivedi, Joseph Tanenbaum, Michael Salata, James Voos, Brian Victoroff, Michael Karns, and Robert Gillespie. "Oral Ketorolac as an Adjuvant Agent for Postoperative Pain Control following Arthroscopic Rotator Cuff Repair: A Prospective, Randomized, Controlled Study. (113)." Orthopaedic Journal of Sports Medicine 9.10_suppl5 (2021): 2325967121. Web.

[23] Wang, Run-Dong, Jian-Yu Zhu, Yu Zhu, Yong-Sheng Ge, Ge-Liang Xu, and Wei-Dong Jia. "Perioperative Analgesia with Parecoxib Sodium Improves Postoperative Pain and Immune Function in Patients Undergoing Hepatectomy for Hepatocellular Carcinoma." Journal of Evaluation in Clinical Practice 26.3 (2020): 992-1000. Web.

[24] Winkler, Sebastian, Hans-Robert Springorum, Tobias Vaitl, Martin Handel, Sabine Barta, Victoria Kehl, Benjamin Craiovan, and Joachim Grifka. "Comparative Clinical Study of the Prophylaxis of Heterotopic Ossifications after Total Hip Arthroplasty Using Etoricoxib or Diclofenac." International Orthopaedics 40.4 (2016): 673-80. Web.

APPENDIX A: Literature Search Strategy

DATABASE	KEY WORDS
PubMed	- Critical Care - NSAIDs - Pain - Adjuvant - Limits: English, Human, Adult 19+ years - Publication date: 2016-Present - **Final Results 73**
Cochrane Library	- Critical Care - Comment: NSAID 12.9.21 - **Final Results 203**
Embase	- Critical Care - NSAIDs - Pain - Adjuvant - Limits: English, Human, Adult 19+ years, Randomized controlled trial, article, article in press - Publication dates: 2016-2022 - **Final Results: 2005**
Medline, OVID (1947-):	- Critical Care - NSAIDs - Pain/Pain management - Limits: English language - Publication Dates: 2016-Current - **Final Results: 47**
Scopus, Elsevier (xxxx-2021)	- Critical Care - NSAIDs - Publication dates: 2016-2021 - Limits: English language - **Final Results: 81**

APPENDIX B: Type of IRB Approval Required

IRB Approval was not required for the research project as it is a scoping review.

APPENDIX C: Data Collection Forms/Data Dictionary

Study Abstract Screening Tool
[Title of study]

Unique Identifier: _____ Reviewer Initials: _____
Study Citation: _____ Review Date: _____

Review the abstract and answer the following questions for inclusion.
(If unable to determine the answers from the abstract or no abstract is available, use the full text article for review.)

1. Is the study a randomized controlled trial, either parallel or crossover?
   ☐Yes ☐No
2. Did the control group receive a placebo or a NSAID-related product?
   ☐Yes ☐No
3. Is the study population in a critical care setting?
   ☐Yes ☐No
4. Is the study trial duration ≥ 14 days?
   ☐Yes ☐No
5. Are outcomes related to NSAID reported?
   ☐Yes ☐No

If "yes" to all questions, review for additional exclusion criteria below.

Note any additional reason(s) for exclusion below. (Check all that apply):

☐ Editorial/Letter ☐ Other _____
☐ Commentary
☐ Case study
☐ Emergency Room Patients
☐ Not English language
☐ Review
☐ Date out of range

Date of review team meeting: _____
Decision: ☐ Include ☐ Exclude ☐ Arbitration Needed

Date of arbitration meeting: _____
Decision: ☐ Include ☐ Exclude

APPENDIX D: **Data Extraction Tool**

Source Used: https://www.acpjournals.org/doi/10.7326/M18-0850

Database:
- ☐ PubMed
- ☐ Embase
- ☐ AccessPharmacy
- ☐ Stat!Ref
- ☐ Other:

Type of Article:
- ☐ Randomized control trial
- ☐ Case series
- ☐ Retrospective study

Country of Publication:
- ☐ United States
- ☐ United Kingdom
- ☐ Other:

Year of Publication:

Department:
- ☐ Intensive care unit
- ☐ Surgical Intensive care unit

Opioid Use:
- ☐ Yes
- ☐ No

NSAID used:
- ☐ Ibuprofen
- ☐ Ketorolac
- ☐ Celecoxib

Type of Adverse effect:
- ☐ GI bleeding or ulcerations
- ☐ Acute kidney injury
- ☐ Other:

SUPPLEMENTAL SEARCH STRATEGY

1) Medline/PubMed, National Library of Medicine (1940 – 2021)
Search conducted: 12/17/21
Concept: Critical Care
("Critical Care"[Mesh] OR "critical care"[ALL] OR "Critical Illness"[Mesh] OR "critical illness" OR "critical illnesses" OR "Intensive Care Units"[Mesh:NoExp] OR "intensive care"[ALL] OR "ICU"[ALL] OR "Trauma Centers"[Mesh] OR "Wounds and Injuries"[Mesh] OR "trauma"[ALL])
AND
Concept: NSAIDs
("anti inflammatory agents, non steroidal"[MeSH Terms] OR "anti inflammatory agents non steroidal"[Pharmacological Action] OR "anti inflammatory analgesic"[All Fields] OR "anti inflammatory analgesic*"[All Fields] OR "antiinflammatory analgesic"[All Fields] OR "antiinflammatory analgesic*"[All Fields] OR "anti inflammatory analgesia"[All Fields] OR "anti inflammatory analgesia*"[All Fields] OR "aspirin like agent"[All Fields] OR "aspirin like agent*"[All Fields] OR "non steroid anti inflammatory"[All Fields] OR "nonsteroid antiinflammatory"[All Fields] OR "non steroid antiinflammatory"[All Fields] OR "nonsteroid anti inflammatory"[All Fields] OR "non-steroidal anti-inflammatory"[All Fields] OR "non-steroidal anti-inflammatory"[All Fields] OR "non-steroidal anti-inflammatory agent"[All Fields] OR "non-steroidal anti-inflammatory agents"[All Fields] OR "nonsteroidal antiinflammatory"[All Fields] OR "non steroidal antiinflammatory"[All Fields] OR "nonsteroidal anti inflammatory"[All Fields] OR "non steroid anti rheumatic"[All Fields] OR "nonsteroid antirheumatic"[All Fields] OR "non steroid antirheumatic"[All Fields] OR "non steroidal anti rheumatic"[All Fields] OR "nonsteroidal antirheumatic"[All Fields] OR "non steroidal antirheumatic"[All Fields] OR "nonsteroidal anti rheumatic"[All Fields] OR "nsaid"[All Fields] OR "nsaid*"[All Fields] OR "Aspirin"[MeSH Terms] OR ("Aspirin"[MeSH Terms] OR "Aspirin"[All Fields] OR "aspirins"[All Fields] OR "aspirin s"[All Fields] OR "aspirine"[All Fields]) OR "Diflunisal"[MeSH Terms] OR ("Diflunisal"[MeSH Terms] OR "Diflunisal"[All Fields]) OR "Choline magnesium trisalicylate"[Supplementary Concept] OR "Choline magnesium trisalicylate"[All Fields] OR "Trilisate"[ALL] OR "salicylsalicylic acid"[Supplementary Concept] OR ("salicylsalicylic acid"[Supplementary Concept] OR "salicylsalicylic acid"[All Fields] OR "salsalate"[All Fields]) OR "Naproxen"[MeSH Terms] OR ("Naproxen"[MeSH Terms] OR "Naproxen"[All Fields] OR "naproxene"[All Fields]) OR "Ibuprofen"[MeSH Terms] OR ("Ibuprofen"[MeSH Terms] OR "Ibuprofen"[All Fields] OR "ibuprofen s"[All Fields] OR "ibuprofens"[All Fields]) OR "Ketoprofen"[MeSH Terms] OR ("Ketoprofen"[MeSH Terms] OR "Ketoprofen"[All Fields] OR "ketoprofens"[All Fields] OR "ketoprofene"[All Fields]) OR "Flurbiprofen"[MeSH Terms] OR ("Flurbiprofen"[MeSH Terms] OR "Flurbiprofen"[All Fields]) OR "Oxaprozin"[MeSH Terms] OR ("Oxaprozin"[MeSH Terms] OR "Oxaprozin"[All Fields]) OR "Diclofenac"[MeSH Terms] OR ("Diclofenac"[MeSH Terms] OR "Diclofenac"[All Fields]) OR "Etodolac"[MeSH Terms] OR ("Etodolac"[MeSH Terms] OR "Etodolac"[All Fields]) OR "Ketorolac"[MeSH Terms] OR ("Ketorolac"[MeSH Terms] OR "Ketorolac"[All Fields]) OR "Indomethacin"[MeSH Terms] OR ("Indomethacin"[MeSH Terms] OR "Indomethacin"[All Fields] OR "indometacin"[All Fields] OR "indomethacine"[All Fields]) OR "Tolmetin"[MeSH Terms] OR ("Tolmetin"[MeSH Terms] OR "Tolmetin"[All Fields]) OR "Sulindac"[MeSH Terms] OR ("Sulindac"[MeSH Terms] OR "Sulindac"[All Fields]) OR "Meloxicam"[MeSH Terms] OR ("Meloxicam"[MeSH Terms] OR "Meloxicam"[All Fields]) OR "Piroxicam"[MeSH Terms] OR ("Piroxicam"[MeSH Terms] OR "Piroxicam"[All Fields]) OR

"Meclofenamic Acid"[MeSH Terms] OR ("Meclofenamic Acid"[MeSH Terms] OR ("meclofenamic"[All Fields] AND "acid"[All Fields]) OR "Meclofenamic Acid"[All Fields] OR "meclofenamate"[All Fields] OR "meclofenamic"[All Fields]) OR "mefenamic acid"[MeSH Terms] OR "mefenamic acid"[All Fields] OR "Nabumetone"[MeSH Terms] OR ("Nabumetone"[MeSH Terms] OR "Nabumetone"[All Fields] OR "nabumeton"[All Fields]) OR "Celecoxib"[MeSH Terms] OR ("Celecoxib"[MeSH Terms] OR "Celecoxib"[All Fields] OR "celecoxib s"[All Fields]) OR "Etoricoxib"[MeSH Terms] OR ("Etoricoxib"[MeSH Terms] OR "Etoricoxib"[All Fields]) OR "Analgesia"[MeSH Terms:noexp] OR "Analgesia"[All Fields] OR "analgesia*"[All Fields] OR "analgesic"[All Fields] OR "analgesic*"[All Fields])
AND
Concept: Pain
("Pain"[MeSH Terms] OR ("Pain"[MeSH Terms] OR "Pain"[All Fields]) OR "acute pain"[All Fields] OR "pain management"[All Fields])
AND
Concept: Adjuvant
("adjuvants, pharmaceutic"[MeSH Terms] OR "adjuvant"[All Fields] OR "adjuvants"[All Fields])

Whole search strategy from PubMed/Medline
((("critical care"[All Fields] OR "critical illness"[All Fields] OR "critical illnesses"[All Fields] OR "critically ill"[All Fields] OR "intensive care"[All Fields] OR "Intensive Care Units"[MeSH Terms:noexp] OR "ICU"[All Fields] OR "Trauma Centers"[MeSH Terms] OR "Wounds and Injuries"[MeSH Terms] OR "trauma"[All Fields]) AND ("anti inflammatory agents, non steroidal"[MeSH Terms] OR "anti inflammatory agents non steroidal"[Pharmacological Action] OR "anti inflammatory analgesic"[All Fields] OR "anti inflammatory analgesic*"[All Fields] OR "antiinflammatory analgesic"[All Fields] OR "antiinflammatory analgesic*"[All Fields] OR "anti inflammatory analgesia"[All Fields] OR "anti inflammatory analgesia*"[All Fields] OR "aspirin like agent"[All Fields] OR "aspirin like agent*"[All Fields] OR "non steroid anti inflammatory"[All Fields] OR "nonsteroid antiinflammatory"[All Fields] OR "non steroid antiinflammatory"[All Fields] OR "nonsteroid anti inflammatory"[All Fields] OR "non-steroidal anti-inflammatory"[All Fields] OR "non-steroidal anti-inflammatory"[All Fields] OR "non-steroidal anti-inflammatory agent"[All Fields] OR "non-steroidal anti-inflammatory agents"[All Fields] OR "nonsteroidal antiinflammatory"[All Fields] OR "non steroidal antiinflammatory"[All Fields] OR "nonsteroidal anti inflammatory"[All Fields] OR "non steroid anti rheumatic"[All Fields] OR "nonsteroid antirheumatic"[All Fields] OR "non steroid antirheumatic"[All Fields] OR "non steroidal anti rheumatic"[All Fields] OR "nonsteroidal antirheumatic"[All Fields] OR "non steroidal antirheumatic"[All Fields] OR "nonsteroidal anti rheumatic"[All Fields] OR "nsaid"[All Fields] OR "nsaid*"[All Fields] OR "Aspirin"[MeSH Terms] OR ("Aspirin"[MeSH Terms] OR "Aspirin"[All Fields] OR "aspirins"[All Fields] OR "aspirin s"[All Fields] OR "aspirine"[All Fields]) OR "Diflunisal"[MeSH Terms] OR ("Diflunisal"[MeSH Terms] OR "Diflunisal"[All Fields]) OR "Choline magnesium trisalicylate"[Supplementary Concept] OR "Choline magnesium trisalicylate"[All Fields] OR "Trilisate"[ALL] OR "salicylsalicylic acid"[Supplementary Concept] OR ("salicylsalicylic acid"[Supplementary Concept] OR "salicylsalicylic acid"[All Fields] OR "salsalate"[All Fields]) OR "Naproxen"[MeSH Terms] OR ("Naproxen"[MeSH Terms] OR "Naproxen"[All Fields] OR "naproxene"[All Fields]) OR "Ibuprofen"[MeSH Terms] OR ("Ibuprofen"[MeSH Terms] OR "Ibuprofen"[All Fields] OR

"ibuprofen s"[All Fields] OR "ibuprofens"[All Fields]) OR "Ketoprofen"[MeSH Terms] OR ("Ketoprofen"[MeSH Terms] OR "Ketoprofen"[All Fields] OR "ketoprofens"[All Fields] OR "ketoprofene"[All Fields]) OR "Flurbiprofen"[MeSH Terms] OR ("Flurbiprofen"[MeSH Terms] OR "Flurbiprofen"[All Fields]) OR "Oxaprozin"[MeSH Terms] OR ("Oxaprozin"[MeSH Terms] OR "Oxaprozin"[All Fields]) OR "Diclofenac"[MeSH Terms] OR ("Diclofenac"[MeSH Terms] OR "Diclofenac"[All Fields]) OR "Etodolac"[MeSH Terms] OR ("Etodolac"[MeSH Terms] OR "Etodolac"[All Fields]) OR "Ketorolac"[MeSH Terms] OR ("Ketorolac"[MeSH Terms] OR "Ketorolac"[All Fields]) OR "Indomethacin"[MeSH Terms] OR ("Indomethacin"[MeSH Terms] OR "Indomethacin"[All Fields] OR "indometacin"[All Fields] OR "indomethacine"[All Fields]) OR "Tolmetin"[MeSH Terms] OR ("Tolmetin"[MeSH Terms] OR "Tolmetin"[All Fields]) OR "Sulindac"[MeSH Terms] OR ("Sulindac"[MeSH Terms] OR "Sulindac"[All Fields]) OR "Meloxicam"[MeSH Terms] OR ("Meloxicam"[MeSH Terms] OR "Meloxicam"[All Fields]) OR "Piroxicam"[MeSH Terms] OR ("Piroxicam"[MeSH Terms] OR "Piroxicam"[All Fields]) OR "Meclofenamic Acid"[MeSH Terms] OR ("Meclofenamic Acid"[MeSH Terms] OR ("meclofenamic"[All Fields] AND "acid"[All Fields]) OR "Meclofenamic Acid"[All Fields] OR "meclofenamate"[All Fields] OR "meclofenamic"[All Fields]) OR "mefenamic acid"[MeSH Terms] OR "mefenamic acid"[All Fields] OR "Nabumetone"[MeSH Terms] OR ("Nabumetone"[MeSH Terms] OR "Nabumetone"[All Fields] OR "nabumeton"[All Fields]) OR "Celecoxib"[MeSH Terms] OR ("Celecoxib"[MeSH Terms] OR "Celecoxib"[All Fields] OR "celecoxib s"[All Fields]) OR "Etoricoxib"[MeSH Terms] OR ("Etoricoxib"[MeSH Terms] OR "Etoricoxib"[All Fields]) OR "Analgesia"[MeSH Terms:noexp] OR "Analgesia"[All Fields] OR "analgesia*"[All Fields] OR "analgesic"[All Fields] OR "analgesic*"[All Fields]) AND ("Pain"[MeSH Terms] OR ("Pain"[MeSH Terms] OR "Pain"[All Fields]) OR "acute pain"[All Fields] OR "pain management"[All Fields]) AND ("adjuvants, pharmaceutic"[MeSH Terms] OR "adjuvant"[All Fields] OR "adjuvants"[All Fields]) AND ("humans"[MeSH Terms] AND "english"[Language] AND 2016/01/01:2021/12/31[Date - Publication])) NOT ("letter"[Publication Type] OR "editorial"[Publication Type]) AND ((humans[Filter]) AND (english[Filter]) AND (alladult[Filter])) Filters: Humans, English, Adult: 19+ years

Limits: English, Human, Adult 19+ years
Publication date: 2016-present
Final Results: 73
Imported to Endnote library: PubMed

2) Embase, Elsevier (1947 – 2021):
Search conducted: 12/17/21
'critical care' OR 'intensive care'/exp OR 'intensive care' OR 'intensive care unit'/exp OR 'critical illness'/exp OR 'critically ill patient'/exp OR 'critically ill' OR 'icu' OR 'emergency health service'/exp OR 'injury'/exp OR 'trauma center*' OR 'trauma'
AND
'antiinflammatory agent'/exp OR 'antiinflammatory agent' OR 'nonsteroid antiinflammatory agent' OR 'antiinflammatory activity'/exp OR 'antiinflammatory activity' OR 'analgesic, antiinflammatory, antirheumatic and antigout agents'/exp OR 'analgesic, antiinflammatory, antirheumatic and antigout agents' OR 'nonsteroid antiinflammatory agent'/exp OR 'anitinflammatory agent' OR 'nonsteroid antirheumatic' OR 'non steroid anti rheumatic' OR 'nonsteroid anti rheumatic' OR 'nsaid' OR 'acetylsalicylic acid'/exp OR 'acetylsalicylic acid' OR

'aspirin' OR 'diflunisal'/exp OR 'diflunisal' OR 'choline magnesium trisalicylate'/exp OR 'choline magnesium trisalicylate' OR 'salsalate'/exp OR 'salsalate' OR 'salicylsalicylic acid' OR 'naproxen'/exp OR 'naproxen' OR 'ibuprofen'/exp OR 'ibuprofen' OR 'ketoprofen'/exp OR 'ketoprofen' OR 'flurbiprofen'/exp OR 'flurbiprofen' OR 'oxaprozin'/exp OR 'oxaprozin' OR 'diclofenac'/exp OR 'diclofenac' OR 'etodolac'/exp OR 'etodolac' OR 'ketorolac'/exp OR 'ketorolac' OR 'indometacin'/exp OR 'indometacin' OR 'tolmetin'/exp OR 'tolmetin' OR 'sulindac'/exp OR 'sulindac' OR 'meloxicam'/exp OR 'meloxicam' OR 'piroxicam'/exp OR 'piroxicam' OR 'meclofenamic acid'/exp OR 'meclofenamic acid' OR 'meclofenamate sodium'/exp OR 'meclofenamate sodium' OR 'meclofenamate' OR 'nabumetone'/exp OR 'nabumetone' OR 'celecoxib'/exp OR 'celecoxib' OR 'etoricoxib'/exp OR 'etoricoxib' OR 'analgesia'/exp OR 'analgesic agent'/exp OR 'analgesia' OR 'analgesic agent' OR 'analgesic'
AND
'pain'/exp OR 'pain' OR 'acute pain' OR 'pain management'
AND
'pharmaceutical vehicles and additives'/exp OR 'central depressant agent'/exp OR 'adjuvant*'
AND
[randomized controlled trial]/lim AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2016-2022]/py AND ([adult]/lim OR [aged]/lim)

Limits: Randomized controlled trial, article, article in press, humans, english, publication dates: 2016-2022, ages: adult and aged
Results: 2005

3) Cochrane Library, Wiley (1898 – 2021)
Search Conducted: 12/17/21

Search Name: critical care
Comment: NSAID 12.9.21

ID	Search	Hits
#1	MeSH descriptor: [Critical Care] explode all trees	2181
#2	MeSH descriptor: [Critical Illness] explode all trees	2509
#3	MeSH descriptor: [Intensive Care Units] this term only	2540
#4	MeSH descriptor: [Trauma Centers] explode all trees	192
#5	MeSH descriptor: [Intensive Care Units] explode all trees	3950
#6	"critical care" OR "critical illness" OR "critical illnesses" OR "intensive care" OR "ICU" OR "Trauma"	74324
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	74540
#8	MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees	7833
#9	MeSH descriptor: [Aspirin] explode all trees	6103
#10	MeSH descriptor: [Diflunisal] explode all trees	103
#11	MeSH descriptor: [Naproxen] explode all trees	1171
#12	MeSH descriptor: [Ibuprofen] explode all trees	2089
#13	MeSH descriptor: [Ketoprofen] explode all trees	579
#14	MeSH descriptor: [Flurbiprofen] explode all trees	458
#15	MeSH descriptor: [Oxaprozin] explode all trees	22
#16	MeSH descriptor: [Diclofenac] explode all trees	1980

#17 MeSH descriptor: [Etodolac] explode all trees 110
#18 MeSH descriptor: [Ketorolac] explode all trees 924
#19 MeSH descriptor: [Indomethacin] explode all trees 2703
#20 MeSH descriptor: [Tolmetin] explode all trees 364
#21 MeSH descriptor: [Sulindac] explode all trees 170
#22 MeSH descriptor: [Meloxicam] explode all trees 239
#23 MeSH descriptor: [Piroxicam] explode all trees 664
#24 MeSH descriptor: [Meclofenamic Acid] explode all trees 49
#25 MeSH descriptor: [Mefenamic Acid] explode all trees 135
#26 MeSH descriptor: [Nabumetone] explode all trees 90
#27 MeSH descriptor: [Celecoxib] explode all trees 982
#28 MeSH descriptor: [Etoricoxib] explode all trees 239
#29 MeSH descriptor: [Analgesia] this term only 2163
#30 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 20521
#31 "anti inflammatory analgesic" OR "antiinflammatory analgesic" OR "anti inflammatory analgesia" OR "aspirin like agent" OR "non steroid anti inflammatory" OR "nonsteroid anti inflammatory" OR "non-steroidal anti-inflammatory" OR "non-steroidal anti-inflammatory agent" OR "non-steroidal anti-inflammatory agents" OR "nonsteroidal antiinflammatory" OR "non steroidal antiinflammatory" OR "non steroid anti rheumatic" OR "nonsteroid antirheumatic" OR "non steroid antirheumatic" OR "non steroidal anti rheumatic" OR "nonsteroidal antirheumatic" OR "non steroidal antirheumatic" OR "nonsteroidal anti rheumatic" OR "NSAID" OR "aspirins" OR "Diflunisal" OR "Choline magnesium trisalicylate" OR "Trilisate" OR "salicylsalicylic acid" OR "salsalate" OR "Naproxen" OR "naproxene" OR "Ibuprofen" OR "Ketoprofen" OR "Flurbiprofen" OR "Oxaprozin" OR "Diclofenac" OR "Etodolac" OR "Ketorolac" OR "Indomethacin" OR "Tolmetin" OR "Sulindac" OR "Meloxicam" OR "Piroxicam" OR "Meclofenamic Acid" OR "Nabumetone" OR "Celecoxib" OR "Etoricoxib" OR "analgesia" OR "analgesic" 82720
#32 #30 OR #31 89662
#33 MeSH descriptor: [Pain] explode all trees 53230
#34 MeSH descriptor: [Acute Pain] explode all trees 852
#35 MeSH descriptor: [Pain Management] explode all trees 4186
#36 #33 OR #34 OR #35 54414
#37 "pain" OR "acute pain" OR "pain management" 206166
#38 #36 OR #37 212506
#39 MeSH descriptor: [Adjuvants, Pharmaceutic] explode all trees 104
#40 "adjuvant" OR "adjuvants" 37981
#41 #39 OR #40 37981
#42 #7 AND #32 AND #38 AND #41 with Cochrane Library publication date Between Jan 2016 and Dec 2021

Results: 203

4) Medline, Ovid (1947 –):
Search conducted: 12/17/21

*Critical Care/ or Critical Illness/ or *Intensive Care Units/ or "Wounds and Injuries"/ or Trauma Centers/ or critical care.mp. or critical illness.mp. or critical illnesses.mp. or intensive care.mp. or ICU.mp. or trauma.mp.
OR

Anti-Inflammatory Agents/ or Anti-Inflammatory Agents, Non-Steroidal/ or non steroidal anti inflammatory agent.mp. or anti inflammatory analgesic.mp. or anti inflammatory analgesic.mp. or antiinflammatory analgesic.mp. or antiinflammatory analgesic.mp. or anti inflammatory analgesia.mp. or anti inflammatory analgesia.mp. or aspirin like agent.mp. or aspirin like agent.mp. or non steroid anti inflammatory.mp. or nonsteroid antiinflammatory.mp. or non steroid antiinflammatory.mp. or nonsteroid anti inflammatory.mp. or non-steroidal anti-inflammatory.mp. or non-steroidal anti-inflammatory.mp. or non-steroidal anti-inflammatory agent.mp. or non-steroidal anti-inflammatory agents.mp. or nonsteroidal antiinflammatory.mp. or non steroidal antiinflammatory.mp. or nonsteroidal anti inflammatory.mp. or non steroid anti rheumatic.mp. or nonsteroid antirheumatic.mp. or non steroid antirheumatic.mp. or non steroidal anti rheumatic.mp. or nonsteroidal antirheumatic.mp. or non steroidal antirheumatic.mp. or nonsteroidal anti rheumatic.mp. or nsaid.mp. or nsaid.mp. or Aspirin/ or Aspirin.mp. or aspirin*.mp. or aspirine.mp. or Diflunisal/ or choline magnesium trisalicylate.mp. or salsalate.mp. or Trilisate.mp. or salicylsalicylic acid.mp. or Naproxen/ or naproxene.mp. or Ibuprofen/ or ibuprofen*.mp. or Ketoprofen/ or ketoprofens.mp. or ketoprofene.mp. or Flurbiprofen/ or flurbiprofen.mp. or Oxaprozin/ or Oxaprozin.mp. or Diclofenac/ or Diclofenac.mp. or Etodolac/ or Etodolac.mp. or Ketorolac/ or Indomethacin/ or Indomethacin.mp. or indometacin.mp. or indomethacine.mp. or Tolmetin/ or Tolmetin.mp. or Sulindac/ or Sulindac.mp. or Meloxicam/ or Meloxicam.mp. or Piroxicam/ or Piroxicam.mp. or Meclofenamic Acid/ or Meclofenamic Acid.mp. or meclofenamate.mp. or meclofenamic.mp. or Nabumetone/ or nabumeton.mp. or Celecoxib/ or Celecoxib*.mp. or Etoricoxib/ or Etoricoxib.mp. or Analgesia/ or analgesia*.mp. or analgesic.mp. or analgesic*.mp.
OR

Pain/ or Pain.mp. or Acute Pain/ or acute pain.mp. or Pain Management/ or Pain management.mp.

Limits: 2016 – current, English language

Results: 47

5) Scopus, Elsevier (xxxx - 2021):

Search conducted: 12/17/21
(TITLE-ABS-KEY (*{Critical Care}* OR *{critical care}* OR *{Critical Illness}* OR *{critical illnesses}* OR *{Intensive Care Units}* OR *{intensive care}* OR *{ICU}* OR *{Trauma Centers}* OR *{Wounds and Injuries}* OR *{trauma}*)) AND (TITLE-ABS-KEY (*{non steroidal anti inflammatory agent$}* OR *{anti inflammatory analgesic}* OR *{anti inflammatory analgesic$}* OR *{antiinflammatory analgesic}* OR *{antiinflammatory analgesic$}* OR *{anti inflammatory analgesia}* OR *{anti inflammatory analgesia$}* OR *{aspirin like agent}* OR *{aspirin like agent$}* OR *{non steroid anti inflammatory}* OR *{nonsteroid anti-*

inflammatory} OR *{non steroid anti-inflammatory}* OR *{nonsteroid anti inflammatory}* OR *{non-steroidal anti-inflammatory}* OR *{non-steroidal anti-inflammatory}* OR *{non-steroidal anti-inflammatory agent}* OR *{non-steroidal anti-inflammatory agent$}* OR *{nonsteroidal anti-inflammatory}* OR *{non steroidal anti-inflammatory}* OR *{nonsteroidal anti inflammatory}* OR *{non steroid anti rheumatic}* OR *{nonsteroid antirheumatic}* OR *{non steroid antirheumatic}* OR *{non steroidal anti rheumatic}* OR *{nonsteroidal antirheumatic}* OR *{non steroidal antirheumatic}* OR *{nonsteroidal anti rheumatic}* OR *nsaid* OR *nsaid$* OR *aspirin* OR *diflunisal* OR *{Choline magnesium trisalicylate}* OR *trilisate* OR *{salicylsalicylic acid}* OR *salsalate* OR *naproxen* OR *naproxene* OR *ibuprofen* OR *ibuprofen$* OR *ketoprofen* OR *ketoprofen$* OR *flurbiprofen* OR *oxaprozin* OR *diclofenac* OR *etodolac* OR *ketorolac* OR *indomethacin* OR *indometacin* OR *indomethacine* OR *tolmetin* OR *sulindac* OR *meloxicam* OR *piroxicam* OR *{Meclofenamic Acid}* OR *meclofenamate* OR *meclofenamic* OR *nabumetone* OR *nabumeton* OR *celecoxib* OR *celecoxib$* OR *etoricoxib* OR *analgesia* OR *analgesia$* OR *analgesic* OR *analgesic$*)) AND (TITLE-ABS-KEY (*pain* OR *{acute pain}* OR *{pain management}*)) AND (TITLE-ABS-KEY (*adjuvant$*)) AND (LIMIT-TO (PUBYEAR , *2021*) OR LIMIT-TO (PUBYEAR , *2020*) OR LIMIT-TO (PUBYEAR , *2019*) OR LIMIT-TO (PUBYEAR , *2018*) OR LIMIT-TO (PUBYEAR , *2017*) OR LIMIT-TO (PUBYEAR , *2016*)) AND (LIMIT-TO (DOCTYPE , *"ar"*) OR LIMIT-TO (DOCTYPE , *"re"*)) AND (LIMIT-TO (LANGUAGE , *"English"*))
Results: 81