**eTable 1. Search strategies for all databases**

|  |
| --- |
| **CDSR & DARE (COCHRANE LIBRARY)** |
| #1 MeSH descriptor: [Pain] explode all trees |
| #2 pain:ti (Word variations have been searched) |
| #3 #1 or #2 |
| #4 MeSH descriptor: [Child, Preschool] explode all trees |
| #5 MeSH descriptor: [Child] explode all trees |
| #6 MeSH descriptor: [Adolescent] explode all trees or MeSH descriptor: [Infant] explode all trees |
| #7 (child\* or infant\* or baby or babies\* or boy\* or girl\* or adolescen\* or teen\* or toddler\* or preschooler\* or pre-schooler\*):ti (Word variations have been searched) |
| #8 #4 or #5 or #6 or #7 |
| #9 #3 and #8 |
| #10 MeSH descriptor: [Narcotics] this term only |
| #11 MeSH descriptor: [Analgesics, Opioid] this term only |
| #12 (morphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone):ti (Word variations have been searched) |
| #13 #10 or #11 or #12 |
| #14 MeSH descriptor: [Antidepressive Agents] explode all trees |
| #15 (amitriptyline or clomipramine or doxepin or imipramine or nortriptyline or trimipramine or mianserin or trazadone or citalopram or fluoxetine or fluvoxamine or sertraline):ti (Word variations have been searched) |
| #16 MeSH descriptor: [Anticonvulsants] explode all trees |
| #17 (carbamazepine or clobazam or clonazepam or ethosuximide or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or phenytoin or pregabalin or rufinamide or topiramate or valproate or vigabatrin or zonisamide):ti (Word variations have been searched) |
| #18 MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees |
| #19 NSAID\*:ti (Word variations have been searched) |
| #20 "non-steroidal anti-inflammatory drug\*":ti (Word variations have been searched) |
| #21 (ibuprofen or aspirin or naproxen or fenoprofen or ketoprofen or tiaprofenic acid or diclofenac or aceclofenac or etodolac or indometacin or mefenamic acid or meloxicam or nabumeton or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or parecoxib or celecoxib or etoricoxib):ti (Word variations have been searched) |
| #22 MeSH descriptor: [Acetaminophen] this term only |
| #23 (acetaminophen or paracetamol or Calpol or Panadol or Tylenol):ti (Word variations have been searched) |
| #24 #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 |
| #27 #9 and #24 |
|  |
|  |
| **MEDLINE (OVID)** |
| 1 exp PAIN/ (353922) |
| 2 pain.tw. (518812) |
| 3 1 or 2 (665398) |
| 4 exp Infant/ (1056001) |
| 5 adolescent/ or exp child/ (2754553) |
| 6 (child\* or infant\* or baby or babies\* or boy\* or girl\* or adolescen\* or teen\* or toddler\* or preschooler\* or pre-schooler\*).tw. (1710613) |
| 7 4 or 5 or 6 (3644325) |
| 8 3 and 7 (116375) |
| 9 NARCOTICS/ (15842) |
| 10 Analgesics, Opioid/ (36058) |
| 11 (morphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone).tw. (91576) |
| 12 9 or 10 or 11 (117345) |
| 13 exp Antidepressive Agents/ (134160) |
| 14 (amitriptyline or clomipramine or doxepin or imipramine or nortriptyline or trimipramine or mianserin or trazadone or citalopram or fluoxetine or fluvoxamine or sertraline).tw. (36037) |
| 15 exp ANTICONVULSANTS/ (130253) |
| 16 (carbamazepine or clobazam or clonazepam or ethosuximide or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or phenytoin or pregabalin or rufinamide or topiramate or valproate or vigabatrin or zonisamide).tw. (45933) |
| 17 exp Anti-Inflammatory Agents, Non-Steroidal/ (182886) |
| 18 NSAID\*.tw. (21705) |
| 19 "non-steroidal anti-inflammatory drug\*".tw. (12142) |
| 20 (ibuprofen or aspirin or naproxen or fenoprofen or ketoprofen or tiaprofenic acid or diclofenac or aceclofenac or etodolac or indometacin or mefenamic acid or meloxicam or nabumeton or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or parecoxib or celecoxib or etoricoxib).tw. (84132) |
| 21 ACETAMINOPHEN/ (16380) |
| 22 (acetaminophen or paracetamol or Calpol or Panadol or Tylenol).tw. (21443) |
| 23 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (610504) |
| 24 8 and 23 (11308) |
| 25 limit 24 to humans (10871) |
| 26 meta-analysis.pt. (85095) |
| 27 meta-analysis.sh. (85095) |
| 28 (meta-analys$ or meta analys$ or metaanalys$).tw,sh. (144406) |
| 29 (systematic$ adj5 review$).tw,sh. (121923) |
| 30 (systematic$ adj5 overview$).tw,sh. (1551) |
| 31 (quantitativ$ adj5 review$).tw,sh. (6343) |
| 32 (quantitativ$ adj5 overview$).tw,sh. (266) |
| 33 (quantitativ$ adj5 synthesis$).tw,sh. (2062) |
| 34 (methodologic$ adj5 review$).tw,sh. (4951) |
| 35 (methodologic$ adj5 overview$).tw,sh. (330) |
| 36 (integrative research review$ or research integration).tw. (118) |
| 37 or/26-36 (225428) |
| 38 25 and 37 (271) |
|  |
| **EMBASE (OVID)** |
| 1 exp PAIN/ (1123664) |
| 2 pain.tw. (765050) |
| 3 1 or 2 (1344895) |
| 4 \*NARCOTIC AGENT/ (4160) |
| 5 \*Narcotic Analgesic Agent/ (6991) |
| 6 (morphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone).tw. (124203) |
| 7 4 or 5 or 6 (132140) |
| 8 exp \*Antidepressant Agent/ (190291) |
| 9 (amitriptyline or clomipramine or doxepin or imipramine or nortriptyline or trimipramine or mianserin or trazadone or citalopram or fluoxetine or fluvoxamine or sertraline).tw. (47626) |
| 10 exp \*ANTICONVULSIVE AGENT/ (153682) |
| 11 (carbamazepine or clobazam or clonazepam or ethosuximide or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or phenytoin or pregabalin or rufinamide or topiramate or valproate or vigabatrin or zonisamide).tw. (69681) |
| 12 exp \*nonsteroid antiinflammatory agent/ (234761) |
| 13 NSAID\*.tw. (37057) |
| 14 "non-steroidal anti-inflammatory drug\*".tw. (16827) |
| 15 (ibuprofen or aspirin or naproxen or fenoprofen or ketoprofen or tiaprofenic acid or diclofenac or aceclofenac or etodolac or indometacin or mefenamic acid or meloxicam or nabumeton or phenylbutazone or piroxicam or sulindac or tenoxicam or tolfenamic acid or ketorolac or parecoxib or celecoxib or etoricoxib).tw. (166661) |
| 16 \*paracetamol/ (23397) |
| 17 (acetaminophen or paracetamol or Calpol or Panadol or Tylenol).tw. (35301) |
| 18 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (830513) |
| 19 \*review/ (1793) |
| 20 (literature adj3 review$).ti,ab. (293221) |
| 21 \*meta analysis/ or \*network meta analysis\*/ (14769) |
| 22 \*Systematic Review/ (11979) |
| 23 (systematic$ adj2 (review$ or overview)).ti,ab. (154930) |
| 24 (meta?anal$ or meta anal$ or meta-anal$ or metaanal$ or metanal$).ti,ab. (162084) |
| 25 or/19-24 (516440) |
| 26 \*child/ or \*boy/ or \*girl/ or \*toddler/ (99119) |
| 27 \*preschool child/ (2674) |
| 28 \*infant/ or \*baby/ or \*high risk infant/ or \*hospitalized infant/ or \*newborn/ (62266) |
| 29 \*adolescent/ or \*hospitalized adolescent/ (29168) |
| 30 (child\* or infant\* or baby or babies\* or boy\* or girl\* or adolescen\* or teen\* or toddler\* or preschooler\* or pre-schooler\*).tw. (2162280) |
| 31 26 or 27 or 28 or 29 or 30 (2201713) |
| 32 3 and 18 and 25 and 31 (577) |
| 33 limit 32 to human (563) |
|  |

**eTable 2: Excluded review references and reasons**

|  |  |
| --- | --- |
| **Excluded review reference** | **Reason for exclusion** |
| Ahn, J. S., Lin, J., Ogawa, S., Yuan, C., O’Brien, T., Le, B. H., Bothwell, A. M., Moon, H., Hadjiat, Y., & Ganapathi, A. (2017). Transdermal buprenorphine and fentanyl patches in cancer pain: a network systematic review. *Journal of pain research*, *10*, 1963. | Review does not include children |
| Anonymous. (2006). Effective medications for juvenile idiopathic arthritis. *Journal of the National Medical Association, 98*(1), 101-102. | Review is not a full peer-reviewed systematic review |
| Davis, M. P. (2011). Fentanyl for breakthrough pain: a systematic review. *Expert Review of Neurotherapeutics, 11*(8), 1197-1216. doi: 10.1586/ern.11.63 | Review does not include chronic cancer or non-cancer pain |
| de Martino, M., & Chiarugi, A. (2015). Recent Advances in Pediatric Use of Oral Paracetamol in Fever and Pain Management. *Pain and Therapy, 4*(2), 149-168. doi: 10.1007/s40122-015-0040-z | Review does not include chronic cancer or non-cancer pain |
| Devulder, J., Richarz, U., & Nataraja, S. H. (2005). Impact of long-term use of opioids on quality of life in patients with chronic, non-malignant pain. *Current Medical Research & Opinion, 21*(10), 1555-1568. | Review does not include children |
| Dunlop, R., & Bennett Kyle, C. L. B. (2014). Pain management for sickle cell disease in children and adults. *Cochrane Database of Systematic Reviews*, Volume(4). doi:10.1002/14651858.CD003350.pub3 | Review does not include chronic cancer or non-cancer pain |
| Egunsola, O., Choonara, I., & Sammons, H. M. (2015). Safety of lamotrigine in paediatrics: a systematic review. *BMJ Open, 5*(6), e007711. doi:https://dx.doi.org/10.1136/bmjopen-2015-007711 | Review does not include chronic cancer or non-cancer pain |
| Fedorowicz, Z., Nasser, M., Jagannath, V. A., Beaman, J. H., Ejaz, K., & van Zuuren, E. J. (2012). Beta2-adrenoceptor agonists for dysmenorrhoea. *Cochrane Database of Systematic Reviews*(5), CD008585. doi:10.1002/14651858.CD008585.pub2 | Review does not include children |
| Foisy, M., Ali, S., Geist, R., Weinstein, M., Michail, S., & Thakkar, K. (2011). The Cochrane Library and the treatment of chronic abdominal pain in children and adolescents: an overview of reviews. *Evidence Based Child Health: A Cochrane Review Journal*, *6*(4), 1027-1043. | Review is not a full peer-reviewed systematic review |
| Frampton, J. E., & Keating, G. M. (2007). Celecoxib: A review of its use in the management of arthritis and acute pain. Drugs, 67(16), 2433-2472. | Review is not a full peer-reviewed systematic review |
| Goldstein, L. H., Berlin, M., Berkovitch, M., & Kozer, E. (2008). Effectiveness of oral vs rectal acetaminophen: a meta-analysis. *Archives of Pediatrics & Adolescent Medicine, 162*(11), 1042-1046. doi: 10.1001/archpedi.162.11.1042 | Review is not include chronic cancer or non-cancer pain |
| Huber, A. M., Tomlinson, G. A., Koren, G., & Feldman, B. M. (2007). Amitriptyline to relieve pain in juvenile idiopathic arthritis: a pilot study using Bayesian metaanalysis of multiple N-of-1 clinical trials. *Journal of Rheumatology, 34*(5), 1125-1132. | Review is not a full peer-reviewed systematic review |
| Huertas-Ceballos, A., Logan, S., Bennett, C., & Macarthur, C. (2008). Pharmacological interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. *Cochrane Database of Systematic Reviews*(1), CD003017. doi: 10.1002/14651858.CD003017.pub2 | Cochrane review that has been updated |
| Kahan, M., Wilson, L., Mailis-Gagnon, A., & Srivastava, A. (2011). Canadian guideline for safe and effective use of opioids for chronic noncancer pain. *Canadian Family Physician*, *57*(11), 1269-1276. | Review is not a full peer-reviewed systematic review |
| Lang, B. C., Yang, C.-S., Zhang, L.-L., Zhang, W.-S., & Fu, Y.-Z. (2017). Efficacy of lidocaine on preventing incidence and severity of pain associated with propofol using in pediatric patients: A PRISMA-compliant meta-analysis of randomized controlled trials. *Medicine, 96*(11), e6320. doi: 10.1097/MD.0000000000006320 | Review does not include chronic cancer or non-cancer pain |
| Marjoribanks, J., Proctor, M., Farquhar, C., & Derks, R. S. (2010). Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane*  *Database of Systematic Reviews* Issue 1. Art. No.: CD001751. DOI: 10.1002/14651858.CD001751.pub2. | Review does not include children |
| Meremikwu, M. M., & Okomo, U. (2011). Sickle cell disease. *Clinical Evidence,* 14, 14. | Review does not include chronic cancer or non-cancer pain |
| Meremikwu, M. M. (2009). Sickle cell disease. *Clinical Evidence,* 27, 27. | Review does not include chronic cancer or non-cancer pain |
| Mudd, S. (2011). Intranasal fentanyl for pain management in children: a systematic review of the literature. *Journal of Pediatric Health Care, 25*(5), 316-322. doi: 10.1016/j.pedhc.2010.04.011 | Review does not include chronic cancer or non-cancer pain |
| Nuesch, E., Hauser, W., Bernardy, K., Barth, J., & Juni, P. (2013). Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. *Annals of the Rheumatic Diseases, 72*(6), 955-962. doi: 10.1136/annrheumdis-2011-201249 | Review does not include children |
| Persad, R., Harvey, K., & Becker, L. (2009). The Cochrane Library and Recurrent Abdominal Pain in Children: An Overview of Reviews. *Evidence Based Child Health: A Cochrane Review Journal*, *4*(1), 4-14. | Review is not a full peer-reviewed systematic review |
| Pierce, C. A., & Voss, B. (2010). Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. *Annals of Pharmacotherapy, 44*(3), 489-506. doi:https://dx.doi.org/10.1345/aph.1M332 | Review does not include chronic cancer or non-cancer pain |
| Porzio, F. (1993). Meta-analysis of two double-blind comparative studies with the sustained-release form of etodolac in rheumatoid arthritis. *Rheumatology International, 13*(2 Suppl), S25-30. | Review does not include children |
| Quigley, C. (2002). Hydromorphone for acute and chronic pain. *Cochrane Database of Systematic Reviews*(1), CD003447. | Cochrane review that has been updated |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **AMSTAR-2 item** | | | | | | | |
|  | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** |
| Bao, 20165 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Beecham, 20156 | Yes | Yes | Yes | Partial yes | Yes | Yes | Yes | Yes |
| Cooper, 201714 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Cooper, 201715 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Cooper, 201713 | Yes | Yes | Yes | Yes | Yes | N/A | Yes | N/A |
| Cooper, 201712 | Yes | Yes | Yes | Yes | Yes | N/A | Yes | N/A |
| Cooper, 201711 | Yes | Yes | Yes | Yes | Yes | N/A | Yes | N/A |
| Eccleston, 201722 | Yes | Yes | Yes | Yes | Yes | N/A | Yes | Yes |
| Hadley, 201335 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Heintjes, 200437 | Yes | Yes | Yes | Partial yes | Yes | Yes | Yes | Yes |
| Kaminski, 201144 | Yes | Yes | Yes | Partial yes | Yes | Yes | Yes | Partial yes |
| Korterink, 201551 | Yes | No | No | No | Yes | No | No | Yes |
| Martin, 201756 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Nicholson, 201765 | Yes | Partial yes | Yes | Yes | Yes | No | Yes | Partial yes |
| Quigley, 200370 | Yes | No | No | Partial Yes | No | No | No | Yes |
| Saps, 201576 | Yes | No | No | No | Yes | Yes | No | No |
| Schmidt-Hanswen, 201679 | Yes | Yes | Yes | Partial Yes | Yes | Yes | No | Yes |
| Straube, 201483 | Yes | Yes | Yes | Partial Yes | Yes | Yes | Yes | Partial yes |
| Weydert, 200390 | No | No | No | No | No | No | No | Partial yes |
| Wiffen, 201791 | Yes | Yes | Yes | Yes | Yes | N/A | Yes | N/A |
| Wiffen, 201697 | Yes | No | Yes | Partial Yes | No | Yes | Yes | Yes |
| Wiffen, 201795 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial yes |
| Wiffen, 201793 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial yes |

**eTable 3: Quality ratings for included reviews**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Review ID** | **AMSTAR-2 item** | | | | | | | |
| **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** |
| Bao, 20165 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Beecham, 20156 | Yes | Yes | No meta-analysis | No meta-analysis | No | Yes | No meta-analysis | No |
| Cooper, 201714 | Yes | Yes | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Cooper, 201715 | Yes | Yes | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | No |
| Cooper, 201713 | N/A | N/A | No meta-analysis | No meta-analysis | N/A | N/A | No meta-analysis | Yes |
| Cooper, 201712 | N/A | N/A | No meta-analysis | No meta-analysis | N/A | N/A | No meta-analysis | Yes |
| Cooper, 201711 | N/A | N/A | No meta-analysis | No meta-analysis | N/A | N/A | No meta-analysis | Yes |
| Eccleston, 201722 | Yes | Yes | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Hadley, 201335 | Yes | No | Yes | No | Yes | Yes | No | No |
| Heintjes, 200437 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Kaminski, 201144 | Yes | Yes | No meta-analysis | No meta-analysis | No | No | No meta-analysis | Yes |
| Korterink, 201551 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Martin, 201756 | Yes | Yes | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Nicholson, 201765 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Quigley, 200370 | No | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | No |
| **Review ID** | **AMSTAR-2 item** | | | | | | | |
| **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** |
| Saps, 201576 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Schmidt-Hanswen, 201679 | Yes | Yes | No meta-analysis | No meta-analysis | Yes | No | No meta-analysis | Yes |
| Straube, 201483 | Partial yes | Yes | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Weydert, 200390 | No | No | No meta-analysis | No meta-analysis | No | No | No meta-analysis | No |
| Wiffen, 201791 | N/A | N/A | No meta-analysis | No meta-analysis | N/A | N/A | No meta-analysis | Yes |
| Wiffen, 201697 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Wiffen, 201795 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |
| Wiffen, 201793 | Yes | No | No meta-analysis | No meta-analysis | Yes | Yes | No meta-analysis | Yes |