

**Appendix 2 Table of excluded studies**

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Part I Osteoarthritis/Artros

Systematic reviews/Systematiska översikter

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/ Exklusionsorsak
National Institute for Clinical Excellence. Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis (Structured abstract). London: National Institute for Clinical Excellence (NICE). Technology Appraisal Guidance 27. 2001.	Wrong study design - Guideline
COX-2 inhibitor demonstrates lower incidence of adverse cardiorenal events compared with nonselective NSAIDs. <i>Formulary</i> , 2006; 41 (8): 372.	Wrong publication type - Conference abstract
Argoff CE. Recent developments in the treatment of osteoarthritis with NSAIDs. <i>Curr Med Res Opin</i> 2011;27:1315-27.	Wrong study design - Review article
Avouac J, Gossec L, Dougados M. Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. <i>Osteoarthritis Cartilage</i> 2007;15:957-65.	More recent SR available
Bannuru RR, Dasi UR, McAlindon TE. Reassessing the role of acetaminophen in osteoarthritis: Systematic review and meta-analysis. <i>Osteoarthritis Cartilage</i> 2010;18:S250.	Wrong publication type - Conference abstract
Bannuru RR, McAlindon TE, Wong JB, Kent D, Schmid C. Comparative effectiveness of pharmacological interventions for knee osteoarthritis: A network meta-analysis. <i>Arthritis Rheum</i> 2013;65:S915-S916.	Wrong publication type - Conference abstract
Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. <i>Ann Intern Med</i> 2015;162:46-54.	More recent SR available
Bjordal JM, Klovning A, Ljunggren AE, Slordal L. Short-term efficacy of pharmacotherapeutic interventions in osteoarthritic knee pain: A meta-analysis of randomised placebo-controlled trials. <i>Eur J Pain</i> 2007;11:125-38.	More recent SR available
Bruyère O, Curtis E, Honvo G, Fuggle N, Reginster JY, Cooper C. Reassessment of the safety of anti-osteoarthritis medications. <i>Osteoporos Int</i> 2018;29:S336-S337.	Wrong publication type - Conference abstract
Cadth. Celecoxib versus non-selective non-steroidal anti-inflammatory drugs and proton pump inhibitors: clinical effectiveness, safety, and cost-effectiveness (Structured abstract). Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH). 2011.	Research question too narrow - celecoxib only
Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. <i>Cochrane Database Syst Rev</i> 2006:Cd005522.	More recent SR available
Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis: A systematic review and metaanalysis. <i>J Rheumatol</i> 2007;34:543-55.	Double publication
Chen LC, Ashcroft DM. Risk of myocardial infarction associated with selective COX-2 inhibitors: Meta-analysis of randomised controlled trials. <i>Pharmacoepidemiol Drug Saf</i> 2007;16:762-72.	Research question too narrow - cox-2-inhibitors only
Chou R, Helfand M, Peterson K, Dana T, Roberts C. Comparative effectiveness and safety of analgesics for osteoarthritis (Structured abstract). <i>Health Technology Assessment Database</i> , 2006; (4): 125.	More recent SR available - Updated version available
Chou R, McDonagh M, Nakamoto E, Griffin J. Analgesics for osteoarthritis: an update of the 2006 comparative effectiveness review (Structured abstract). Rockville (MD): Agency for Healthcare Research and Quality (US). (Comparative Effectiveness Reviews, No. 38.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK65646/ .	More recent SR available
da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Juni P, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain	Wrong publication type - Retracted article

in knee and hip osteoarthritis: a network meta-analysis. <i>Lancet</i> , 2016; 387 (10033): 2093-105.	
Derry S, Wiffen PJ, Kalso EA, Bell RF, Aldington D, Phillips T, et al. Topical analgesics for acute and chronic pain in adults - an overview of Cochrane Reviews. <i>Cochrane Database of Systematic Reviews</i> , 2017; (5).	Wrong population – mixed population chronic pain
Feng X, Tian M, Zhang W, Mei H. Gastrointestinal safety of etoricoxib in osteoarthritis and rheumatoid arthritis: A meta-analysis. <i>PLoS ONE [Electronic Resource]</i> , 2018; 13 (1): e0190798.	Research question too narrow - etoricoxib only
Fuggle N, Curtis E, Shaw S, Spooner L, Bruyere O, Ntani G, et al. Safety of Opioids in Osteoarthritis: Outcomes of a Systematic Review and Meta-Analysis. <i>Drugs Aging</i> 2019;36:129-43.	Research question too narrow - opioid safety only
Germain H, Elizabeth C, Nicholas F, Sarah S, Camille P, Georgia N, et al. Adverse events of opioid analgesics in the management of osteoarthritis: a systematic review and meta-analysis of randomised, placebo-controlled trials. PROSPERO, 2017, CRD42017068249. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017068249	Wrong publication type - Prospero protocol
Germain H, Elizabeth C, Nicholas F, Sarah S, Camille P, Georgia N, et al. Adverse events of oral Selective Cyclooxygenase-2 (COX-2) inhibitors in osteoarthritis: a systematic review and meta-analysis of randomised, placebo-controlled trials (protocol). PROSPERO 2017 CRD42017068278. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017068278	Wrong publication type - Prospero protocol
Germain H, Véronique R, Anton G, Jean-Yves R, Cyrus C, Olivier B. Adverse events associated with symptomatic slow-acting drugs in osteoarthritis (SYSADOAs): a systematic review and stratified meta-analysis of randomised, placebo-controlled trials (protocol). PROSPERO 2017 CRD42017069875, Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017069875	Wrong publication type - Prospero protocol
Germain H, Victoria L, Charlotte B, Véronique R, Anton G, Jean-Yves R, et al. Side effects of topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in osteoarthritis: a systematic review and meta-analysis of randomised, placebo-controlled Trials. PROSPERO 2017 CRD4201705850.9 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017058509	Wrong publication type - Prospero protocol
Gilmer B, Hulkower S, Wilson CG, Macdonald B, Pozner J, Stigleman S. Which oral nonopioid agents are most effective for OA pain? <i>J Fam Pract</i> 2019;68:417-8.	Wrong study design
González-Pérez A, García Rodríguez LA. Upper gastrointestinal complications among users of paracetamol. <i>Basic Clin Pharmacol Toxicol</i> 2006;98:297-303.	Research question too narrow - paracetamol and upper GI-events
Gotzsche PC. NSAIDs. <i>Clin Evid</i> 2007;1:01.	Wrong study design - Review article
Gotzsche PC. NSAIDs. <i>Clin Evid</i> 2010;28:28.	Wrong population – Mixed population
Gregori D, Giacobelli G, Minto C, Barbetta B, Gualtieri F, Azzolina D, et al. A systematic review and network meta-analysis of long-term trials of pharmacological treatments in knee osteoarthritis. <i>Arthritis Rheumatol</i> 2016;68:369-70.	Wrong publication type - Conference abstract
Gregori D, Giacobelli G, Minto C, Barbetta B, Gualtieri F, Azzolina D, et al. Association of Pharmacological Treatments with Long-term Pain Control in Patients with Knee Osteoarthritis: A Systematic Review and Meta-analysis. <i>JAMA</i> 2018;320:2564-79.	Research question too narrow
Guanghua L, Chao Z, Jie W, Monica SMP, Aliya S, Michael D, et al. Relative efficacy and safety of topical non-steroidal anti-inflammatory drugs for osteoarthritis: a systematic review and network meta-analysis of randomized controlled trials and observational studies. PROSPERO 2017 CRD42017073057. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017073057	Wrong publication type - Prospero protocol

Gustavo M, Paulo F, Chris M, David H, Richard D, Marina P, et al. Safety and efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) for spinal pain and osteoarthritis: systematic review with meta-analysis of randomised placebo-controlled trials. PROSPERO 2015 CRD42015023746. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42015023746	Wrong publication type - Prospero protocol
Gustavo M, Paulo F, Chris M, Marina M, Chung-Wei Christine L, Richard D, et al. Efficacy and safety of paracetamol (acetaminophen) for spinal pain and osteoarthritis: a systematic review and meta-analysis of randomised, placebo-controlled trials. PROSPERO 2013 CRD42013006367. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD4201300636	Wrong publication type - Prospero protocol
Hitzeman N, Athale N. Opioids for osteoarthritis of the knee or Hip. Am Fam Physician 2010;81:1094-6.	Wrong study design - Report of a systematic review
Honvo G, Leclercq V, Geerinck A, Rabenda V, Beudart C, Cooper C, et al. Adverse events associated with topical nonsteroidal anti-inflammatory drugs (NSAIDs) in osteoarthritis: A systematic review and metaanalysis of randomised, placebo-controlled trials. Osteoporos Int 2018;29:S562.	Wrong publication type - conference abstract
Honvo G, Leclercq V, Geerinck A, Thomas T, Veronese N, Charles A, et al. Safety of Topical Non-steroidal Anti-Inflammatory Drugs in Osteoarthritis: Outcomes of a Systematic Review and Meta-Analysis. Drugs Aging 2019;36:45-64.	Research question too narrow . Safety only
Jaspreet K, Burak K, Michael D, Abishek A, Gwen F. To determine safety of oral paracetamol for osteoarthritis - a systematic review and meta-analysis. PROSPERO 2017 CRD42017079645. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017079645	Wrong publication type - Prospero protocol
Jaspreet K, Burak K, Weiya Z, Michael D, Abhishek A, Gwen F. Safety of topical non-steroidal anti-inflammatory drugs (NSAIDs) for osteoarthritis: a systematic review with meta-analysis. PROSPERO 2017 CRD42017078426. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017078426	Wrong publication type - Prospero protocol
Kaur J, Kundaki B, Nakafero G, Abhishek A, Doherty M, Zhang W. A systematic review and meta-analysis assessing gastrointestinal, liver, renal and cardiovascular adverse events of paracetamol. Ann Rheum Dis 2019;78:76.	Research question too narrow - safety paracetamol only
Laine L, White WB, Rostom A, Hochberg M. COX-2 Selective Inhibitors in the Treatment of Osteoarthritis. Semin Arthritis Rheum 2008;38:165-87.	Wrong study design - Review article
Lee C, Straus WL, Balshaw R, Barlas S, Vogel S, Schnitzer TJ. A comparison of the efficacy and safety of nonsteroidal antiinflammatory agents versus acetaminophen in the treatment of osteoarthritis: a meta-analysis. Arthritis Rheum 2004;51:746-54.	More recent SR available
Leopoldino AO, Machado GC, Ferreira PH, Pinheiro MB, Day RO, McLachlan AJ, et al. Efficacy and safety of paracetamol compared to placebo for knee and hip osteoarthritis: A cochrane systematic review. Osteoarthritis Cartilage 2016;24:S44.	Wrong publication type - Conference abstract
Machado GC, Maher CG, Ferreira PH, Pinheiro MB, Lin CW, Day RO, et al. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. BMJ, 2015; 350:h1225.	More recent SR available
Makris UE, Kohler MJ, Fraenkel L. Adverse effects of topical nonsteroidal antiinflammatory drugs in older adults with osteoarthritis: A systematic literature review. J Rheumatol 2010;37:1236-43.	More recent SR available
Mallen SR, Essex MN, Zhang R. Gastrointestinal tolerability of NSAIDs in elderly patients: a pooled analysis of 21 randomized clinical trials with celecoxib and nonselective NSAIDs. Curr Med Res Opin 2011;27:1359-66.	Wrong study design - Pooled analysis
Moga C, Harstall C, Tang Z. Celecoxib for the treatment of pain in osteoarthritis and rheumatoid arthritis (Structured abstract). Health Technology Assessment Database 2005.	Research question too narrow - celecoxib only

Monica P, Yu F, Archan B, Siew Li G, Marienke van M, Sita B-Z, et al. Relative efficacy of topical non-steroidal anti-inflammatory drugs and topical capsaicin in osteoarthritis: an individual patient data meta-analysis. PROSPERO 2016 CRD42016035254. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42016035254	Wrong publication type - Prospero protocol
Myers J, Wielage RC, Han B, Price K, Gahn J, Paget MA, et al. The efficacy of duloxetine, non-steroidal anti-inflammatory drugs, and opioids in osteoarthritis: a systematic literature review and meta-analysis. BMC Musculoskelet Disord 2014;15:76-76.	Wrong drug - duloxetine
National Institute for Clinical Excellence. Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis (Structured abstract). London: National Institute for Clinical Excellence (NICE). Technology Appraisal Guidance 27. 2001.	Wrong study design - Guideline
Nüesch E, Rutjes AWS, Husni E, Welch V, Jüni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. Sao Paulo Med J 2009;127:388.	Wrong study design - Report of a systematic review
Pavelka K. A comparison of the therapeutic efficacy of diclofenac in osteoarthritis: a systematic review of randomised controlled trials. Curr Med Res Opin 2012;28:163-78.	Research question too narrow – diclofenac only
Persson M, Stocks J, Sarmanova A, Fernandes G, Varadi G, Hashempur MH, et al. The relative efficacy of topical nonsteroidal anti-inflammatory drugs and capsaicin in osteoarthritis: Moving from average treatment effects to individual treatment preferences. Ann Rheum Dis 2019;78:513-4.	Wrong comparison (capsaicin)
Puljak L, Marin A, Vrdoljak D, Markotic F, Utrobicic A, Tugwell P. Celecoxib for osteoarthritis. Cochrane Database of Systematic Reviews 2017.	Research question too narrow - etoricoxib only
Rajbir B, Kamal M, Jeffrey KA, Nia R. A pragmatic systematic review to evaluate the treatment harms caused by the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) in older adults with osteoarthritis. PROSPERO 2017 CRD42017073280. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017073280	Wrong publication type - Prospero protocol
Roberts E, Delgado Nunes V, Buckner S, Latchem S, Constanti M, Miller P, et al. Paracetamol: not as safe as we thought? A systematic literature review of observational studies. Ann Rheum Dis 2016;75:552-9.	Research question too narrow - only safety on paracetamol from observational studies
Rostom A, Goldkind L, Laine L. Nonsteroidal anti-inflammatory drugs and hepatic toxicity: a systematic review of randomized controlled trials in arthritis patients. Clin Gastroenterol Hepatol 2005;3:489-98.	Research question too narrow - NSAID and hepatic toxicity
Rostom A, Muir K, Dubé C, Jolicoeur E, Boucher M, Joyce J, et al. Gastrointestinal Safety of Cyclooxygenase-2 Inhibitors: A Cochrane Collaboration Systematic Review. Clin Gastroenterol Hepatol 2007;5:818-828.e5.	Research question too narrow - Cox-2 inhibitors only
Rovati LC. The need for evidence-based assessment of the long-term efficacy of medications in knee osteoarthritis: A new systematic review and network meta-analysis. Osteoporos Int 2017;28:S637-S638.	Wrong publication type - Conference abstract
Rovati LC, Giacobelli G, Minto C, Barbetta B, Gualtieri F, Azzolina D, et al. A new systematic review and network meta-analysis of long-term trials of pharmacological treatments in knee osteoarthritis. Osteoporos Int 2017;28:S54-S55.	Wrong publication type - Conference abstract
Salpeter SR, Gregor P, Ormiston TM, Whitlock R, Raina P, Thabane L, et al. Meta-Analysis: Cardiovascular Events Associated with Nonsteroidal Anti-inflammatory Drugs. Am J Med 2006;119:552-9.	Research question too narrow - NSAID och CV events
Samson D, Grant M, Ratko T, Bonnell C, Ziegler K, Aronson N. Treatment of primary and secondary osteoarthritis of the knee (Structured abstract). Health Technology Assessment Database 2007.	Wrong drug

Santos J, Alarcão J, Fareleira F, Vaz-Carneiro A, Costa J. Tapentadol for chronic musculoskeletal pain in adults. Cochrane Database of Systematic Reviews 2015.	Research question too narrow - tapentadol only
Sardana V, Burzynski J, Zalzal P. Safety and efficacy of topical ketoprofen in transfersome gel in knee osteoarthritis: A systematic review. Musculoskeletal Care 2017;15:114-21.	Research question too narrow - etoricoxib only
Sarzi-Puttini P, Atzeni F, Lanata L, Bagnasco M. Efficacy of ketoprofen vs. ibuprofen and diclofenac: A systematic review of the literature and meta-analysis. Clin Exp Rheumatol 2013;31:731-8.	Wrong population
Sarzi-Puttini P, Atzeni F, Lanata L, Egan CG, Bagnasco M. Safety of ketoprofen compared with ibuprofen and diclofenac: A systematic review and meta-analysis. Trends in Medicine, 2014; 14 (2): 17-26.	Wrong population
Schaffer D, Florin T, Eagle C, Marschner I, Singh G, Grobler M, et al. Risk of serious NSAID-related gastrointestinal events during long-term exposure: A systematic review. Med J Aust 2006;185:501-6.	Research question too narrow - NSAID and GI events only (not elderly)
Smith SR, Deshpande BR, Collins JE, Katz JN, Losina E. Comparative efficacy of oral non-steroidal antiinflammatory drugs and opioids for osteoarthritis: Systematic review and meta-analysis. Osteoarthritis Cartilage 2015;23:A355-A356.	Wrong publication type - Conference abstract
Stam W, Jansen J, Taylor S. Efficacy of etoricoxib, celecoxib, lumiracoxib, non-selective NSAIDs, and acetaminophen in osteoarthritis: a mixed treatment comparison. Open Rheumatol J 2012;6:6-20.	More recent SR available
Surasak S, Tatsanee S, Krithanon R, Norramon J, Ubolwan S. Efficacy and safety of oral pharmacologic interventions comparable with curcumin for knee osteoarthritis: a systematic review and network meta-analysis. PROSPERO 2015 CRD42015026890. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42015026890	Wrong comparison
Towheed T, Hochberg MC, Shea B, Wells GA. Analgesia and non-aspirin, non-steroidal anti-inflammatory drugs for osteoarthritis of the hip. Cochrane Database of Systematic Reviews 2006.	More recent SR available
Towheed T, Maxwell L, Judd M, Catton M, Hochberg MC, Wells GA. Acetaminophen for osteoarthritis. Cochrane Database of Systematic Reviews 2006.	More recent SR available
Towheed TE, Judd MJ, Hochberg MC, Wells G. Acetaminophen for osteoarthritis. Cochrane Database of Systematic Reviews 2003:CD004257.	More recent SR available. Updated version available
van Walsem A, Pandhi S, Nixon RM, Guyot P, Karabis A, Moore RA. Relative benefit-risk comparing diclofenac to other traditional non-steroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors in patients with osteoarthritis or rheumatoid arthritis: A network meta-analysis. Arthritis Res Ther 2015:1-18.	Research question too narrow - diclofenac only
Watson M, Brookes ST, Faulkner A, Kirwan JJ. Non-aspirin, non-steroidal anti-inflammatory drugs for treating osteoarthritis of the knee. Cochrane Database of Systematic Reviews 2006.	More recent SR available
Verkleij SP, Luijsterburg PA, Bohnen AM, Koes BW, Bierma-Zeinstra SM. NSAIDs versus acetaminophen in knee and hip osteoarthritis: A systematic review regarding heterogeneity influencing the outcomes. Osteoarthritis Cartilage 2011;19:S136.	Wrong outcome
Vries C. Cox-II inhibitors versus non-steroidal anti-inflammatory drugs in rheumatoid and osteoarthritis patients: gastrointestinal effects (Structured abstract). Health Technology Assessment Database 2002.	Research question too narrow - NSAID and GI-events (not elderly)
Xue Y, Zhu X, Wang J, Ma K. Efficacy and safety of extended-release tramadol for osteoarthritis: A meta-analysis. Pharmacotherapy 2014;34:e296-e297.	Wrong publication type - Conference abstract
Zeng C, Wei J, Persson MSM, Sarmanova A, Doherty M, Xie D, et al. Relative efficacy and safety of topical non-steroidal anti-inflammatory drugs for osteoarthritis: a systematic review and network meta-analysis of randomised controlled trials and observational studies. Br J Sports Med 2018;52:642-50.	Wrong drug - majority of included drugs not available on Swedish market.

Zhu X, Wu D, Sang L, Wang Y, Shen Y, Zhuang X, et al. Comparative effectiveness of glucosamine, chondroitin, acetaminophen or celecoxib for the treatment of knee and/or hip osteoarthritis: a network meta-analysis. Clin Exp Rheumatol 2018;36:595-602.	More recent SR available RE paracetamol. Research question too narrow RE celecoxib. Other drugs not in PICO.
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Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Juni P, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis.[Republished from Lancet. 2016 May 21;387(10033):2093-2105; PMID: 26997557]. Lancet, 2017; 390 (10090): e21-e33.	High RoB - interpretation of findings
Gunter BR, Butler KA, Wallace RL, Smith SM, Harirforoosh S. Non-steroidal anti-inflammatory drug-induced cardiovascular adverse events: a meta-analysis. J Clin Pharm Ther 2017;42:27-38.	High RoB - no RoB assessment of included studies
Jevsevar DS, Shores PB, Mullen K, Schulte DM, Brown GA, Cummins DS. Mixed Treatment Comparisons for Nonsurgical Treatment of Knee Osteoarthritis: A Network Meta-analysis. J Am Acad Orthop Surg 2018;26:325-36.	High RoB - interpretation of findings
Jung SY, Jang EJ, Nam SW, Kwon HH, Im SG, Kim D, et al. Comparative effectiveness of oral pharmacologic interventions for knee osteoarthritis: A network meta-analysis. Mod Rheumatol 2018;28:1021-8.	High RoB - interpretation of findings
Megale RZ, Deveza LA, Blyth FM, Naganathan V, Ferreira PH, McLachlan AJ, et al. Efficacy and Safety of Oral and Transdermal Opioid Analgesics for Musculoskeletal Pain in Older Adults: A Systematic Review of Randomized, Placebo-Controlled Trials. J Pain 2018;19:475.e1-475.e24.	High RoB – Considerable different different interventions in one meta-analysis
O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. Am J Geriatr Pharmacother 2012;10:331-42.	High RoB - no RoB assessment of included studies
Smith SR, Deshpande BR, Collins JE, Katz JN, Losina E. Comparative pain reduction of oral non-steroidal anti-inflammatory drugs and opioids for knee osteoarthritis: systematic analytic review. Osteoarthritis Cartilage 2016;24:962-72.	High RoB - analysis not based on control adjusted results
Stewart M, Cibere J, Sayre EC, Kopec JA. Efficacy of commonly prescribed analgesics in the management of osteoarthritis: a systematic review and meta-analysis. Rheumatol Int 2018;38:1985-97.	High RoB – High RoB in search strategy

Primary studies/Primärstudier

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Altman R, Hochberg M, Gibofsky A, Jaros M, Young C. Efficacy and safety of low-dose SoluMatrix meloxicam in the	Wrong drug - formulation not available on Swedish market - not bioequivalent with

treatment of osteoarthritis pain: a 12-week, phase 3 study. <i>Curr Med Res Opin</i> 2015;31:2331-43.	formulations on Swedish market
Banerjee M, Mondal S, Sarkar R, Mondal H, Bhattacharya K. Comparative study of efficacy and safety of tapentadol versus etoricoxib in mild to moderate grades of chronic osteoarthritis of knee. <i>Indian J Rheumatol</i> 2016;11:21-5.	Wrong population - mean age <60
Baraf HS, Gloth FM, Barthel HR, Gold MS, Altman RD. Safety and efficacy of topical diclofenac sodium gel for knee osteoarthritis in elderly and younger patients: pooled data from three randomized, double-blind, parallel-group, placebo-controlled, multicentre trials. <i>Drugs Aging</i> 2011;28:27-40.	Wrong study design - pooled post hoc analysis
Baraf HS, Gold MS, Petruschke RA, Wieman MS. Tolerability of topical diclofenac sodium 1% gel for osteoarthritis in seniors and patients with comorbidities. <i>Am J Geriatr Pharmacother</i> 2012;10:47-60.	Wrong study design - pooled post hoc analysis
Bierma-Zeinstra SMA, Brew J, Stoner K, Wilson R, Kilbourn A, Conaghan PG. A new lipid formulation of low dose ibuprofen shows non-inferiority to high dose standard ibuprofen: the FLARE study (flaring arthralgia relief evaluation in episodic flaring knee pain) - a randomised double-blind study. <i>Osteoarthritis Cartilage</i> 2017;25:1942-51.	Wrong population - mean age <60
Biondi D, Xiang J, Etropolski M, Moskovitz B. A post-hoc pooled data analysis to evaluate the gastrointestinal tolerability profile of tapentadol extended release (ER) versus oxycodone controlled release (CR) in patients ≥ 75 years of age. <i>Pharmacotherapy</i> 2011;31:366e.	Wrong publication type - Conference abstract
Biondi DM, Xiang J, Etropolski M, Moskovitz B. Tolerability and efficacy of tapentadol extended release in elderly patients ≥ 75 years of age with chronic osteoarthritis knee or low back pain. <i>J Opioid Manag</i> 2015;11:393-403.	Wrong study design - pooled post hoc analysis
Chan FKL, Ching JYL, Tse YK, Lam K, Wong GLH, Ng SC, et al. Gastrointestinal safety of celecoxib versus naproxen in patients with cardiothrombotic diseases and arthritis after upper gastrointestinal bleeding (CONCERN): an industry-independent, double-blind, double-dummy, randomised trial. <i>Lancet</i> 2017;389:2375-82.	Wrong outcome – Specific AE (35 % of population < 60 years, not pertinent to NSAID risk of PUB PICO either)
Cryer B, Li C, Simon LS, Singh G, Stillman MJ, Berger MF. GI-REASONS: a novel 6-month, prospective, randomized, open-label, blinded endpoint (PROBE) trial. <i>Am J Gastroenterol</i> 2013;108:392-400.	Wrong outcome - Specific AE
de Abajo FJ, Gil MJ, Garcia Poza P, Bryant V, Oliva B, Timoner J, et al. Risk of nonfatal acute myocardial infarction associated with non-steroidal antiinflammatory drugs, non-narcotic analgesics and other drugs used in osteoarthritis: a nested case-control study. <i>Pharmacoepidemiol Drug Saf</i> 2014;23:1128-38.	Wrong study design - non randomised study, not pertinent in efficacy evaluation
Domanski A, Bair M, Balk R, Brandt C, Brody A, Dismore R, et al. Evaluating the agreement between self-reported and documented analgesic use in older veterans with osteoarthritis. <i>J Am Geriatr Soc</i> 2017;65:S250.	Wrong publication type - Conference abstract
Essex MN, Brown PB, Sands GH. The efficacy of continuous versus intermittent celecoxib treatment in osteoarthritis patients aged <60 and ≥ 60 years. <i>Int J Clin Rheumatol</i> 2014;9:13-20.	Wrong study design - subgroup analysis on intermittent/continuous dosage

Fujii T, Takana K, Orita S, Inoue G, Ochiai N, Kuniyoshi K, et al. Progressive change in joint degeneration in patients with knee or hip osteoarthritis treated with fentanyl in a randomized trial. <i>Yonsei Med J</i> 2014;55:1379-85.	Wrong drug - Formulation tramadol/paracetamol not available on Swedish market
Gibofsky A, Hochberg MC, Jaros MJ, Young CL. Efficacy and safety of low-dose submicron diclofenac for the treatment of osteoarthritis pain: a 12 week, phase 3 study. <i>Curr Med Res Opin</i> 2014;30:1883-93.	Wrong drug - formulation not available on Swedish market - not bioequivalent with formulations on Swedish market
Gualtierotti R, Zoppi A, Mugellini A, Derosa G, D'Angelo A, Fogari R. Effect of naproxen and acetaminophen on blood pressure lowering by ramipril, valsartan and aliskiren in hypertensive patients. <i>Expert Opin Pharmacother</i> 2013;14:1875-84.	Wrong population - mean age <60
Hirayama A, Tanahashi N, Daida H, Ishiguro N, Chachin M, Sugioka T, et al. Assessing the cardiovascular risk between celecoxib and nonselective nonsteroidal antiinflammatory drugs in patients with rheumatoid arthritis and osteoarthritis. <i>Circ J</i> 2014;78:194-205.	Wrong study design - non randomised study, not pertinent in efficacy evaluation
Karlsson J, Soderstrom A, Augustini BG, Berggren AC. Is buprenorphine transdermal patch equally safe and effective in younger and elderly patients with osteoarthritis-related pain? Results of an age-group controlled study. <i>Curr Med Res Opin</i> 2014;30:575-87.	Wrong comparison - no control group
Kellner H, Essex M, Li C. Safety and efficacy of nsais in elderly arthritis patients: A subgroup analysis. <i>Osteoarthritis Cartilage</i> 2011;19:S144.	Wrong publication type - Conference abstract
Kellner HL, Li C, Essex MN. Efficacy and safety of celecoxib versus diclofenac and omeprazole in elderly arthritis patients: a subgroup analysis of the CONDOR trial. <i>Curr Med Res Opin</i> 2012;28:1537-45.	Wrong drug - formulation not available on Swedish market - not bioequivalent with formulations on Swedish market
Kellner HL, Li C, Essex MN. Celecoxib and Diclofenac Plus Omeprazole are Similarly Effective in the Treatment of Arthritis in Patients at High GI Risk in the CONDOR Trial. <i>Open Rheumatol J</i> 2013;7:96-100.	Wrong study design - subanalysis on GI-bleeding risk
Kim S, Ryou J, Hur J. Comparison of Effectiveness and Safety of Tramadol/Acetaminophen and Non-steroidal Anti-inflammatory Drugs (NSAIDs) for Treatment of Knee Osteoarthritis in Elderly Patients. <i>Journal of rheumatic diseases</i> 2012;19:25-9.	Wrong language
Krebs EE, Gravely A, Nugent S, Jensen AC, DeRonne B, Goldsmith ES, et al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: the SPACE Randomized Clinical Trial. <i>JAMA</i> 2018;319:872-82.	Wrong population - mean age 58
Kushner P, Patel B, Garas SY. Minimal clinically important improvement (MCI) in knee osteoarthritis: a post hoc analysis of a prospective, randomized clinical trial of diclofenac sodium gel (DSG) 1%. <i>J Gen Intern Med</i> 2019;34:S286-.	Wrong publication type - conference abstract
Leng X, Li Z, Lv H, Zheng Y, Liu Y, Dai K, et al. Effectiveness and Safety of Transdermal Buprenorphine Versus Sustained-release Tramadol in Patients With Moderate to Severe Musculoskeletal Pain: An 8-Week, Randomized, Double-Blind,	Wrong population - mean age <60

Double-Dummy, Multicenter, Active-controlled, Noninferiority Study. Clin J Pain 2015;31:612-20.	
MacDonald TM, Hawkey CJ, Ford I, McMurray JJV, Scheiman JM, Hallas J, et al. Randomized trial of switching from prescribed non-selective non-steroidal anti-inflammatory drugs to prescribed celecoxib: the Standard care vs. Celecoxib Outcome Trial (SCOT).[Erratum appears in Eur Heart J. 2016 Dec 24; PMID: 28025195]. Eur Heart J 2017;38:1843-50.	Wrong outcome
Mallen SR, Essex MN, Zhang R. Gastrointestinal tolerability of NSAIDs in elderly patients: a pooled analysis of 21 randomized clinical trials with celecoxib and nonselective NSAIDs. Curr Med Res Opin 2011;27:1359-66.	Wrong study design - pooled analysis
Matsushita T, Hasebe M, Nishimura A. Phase III clinical study of tramadol hydrochloride/acetaminophen combination tablet in patients with chronic osteoarthritis pain or chronic low back pain - A randomized withdrawal, double-blind, parallelgroup, placebo-controlled study. Osteoporos Int 2012;23:S85.	Wrong publication type - Conference abstract
Nissen SE, Yeomans ND, Solomon DH, Luscher TF, Libby P, Husni ME, et al. Cardiovascular Safety of Celecoxib, Naproxen, or Ibuprofen for Arthritis. N Engl J Med 2016;375:2519-29.	Wrong outcome
Noyes Essex M, Zhang R, Mallen SR. Pooled safety data from elderly arthritis patients in 21 clinical trials. Ann Rheum Dis 2013;71.	Wrong publication type - Conference abstract
Obeid S, Libby P, Husni ME, Pfeffer MA, Wisniewski LM, Wolski KE, et al. Cardiorenal risks of celecoxib, naproxen or ibuprofen in arthritis patients: A sub-anaylsis from the precision trial. Circulation 2017;136.	Wrong publication type - Conference abstract
Park KS, Choi JJ, Kim WU, Min JK, Park SH, Cho CS. The efficacy of tramadol/acetaminophen combination tablets (Ultracet) as add-on and maintenance therapy in knee osteoarthritis pain inadequately controlled by nonsteroidal anti-inflammatory drug (NSAID). Clinical Rheumatology 2012;31:317-23.	Wrong intervention - Formulation not available on Swedish market
Peniston JH, Gold MS, Wieman MS, Alwine LK. Age analysis of long-term safety of diclofenac sodium 1% gel for patients with osteoarthritis of the knee. J Am Geriatr Soc 2012;60:S28.	Wrong publication type - Conference abstract
Pergolizzi JV, Raffa RB, Marcum Z, Colucci S, Ripa SR. Safety of buprenorphine transdermal system in the management of pain in older adults. Postgrad Med 2017;129:92-101.	Wrong population - mostly back pain
Rauk R, Rapoport R, Thippawong J. Results of a double-blind, placebo-controlled, fixed-dose assessment of once-daily OROS hydromorphone ER in patients with moderate to severe pain associated with chronic osteoarthritis. Pain Practice 2013;13:18-29.	Wrong drug - Formulation not available on Swedish market
Reed K, Collaku A, Moreira S. Efficacy and safety of twice daily sustained-release paracetamol formulation for osteoarthritis pain of the knee or hip: a randomized, double-blind, placebo-controlled, twelve-week study. Curr Med Res Opin 2018:1-11.	Wrong intervention - Formulation not available on Swedish market
Roberto G, Simonetti M, Piccinni C, Lora Aprile P, Cricelli I, Fanelli A, et al. Risk of Acute Cerebrovascular and Cardiovascular Events Among Users of Acetaminophen or an Acetaminophen-Codeine Combination in a Cohort of Patients	Wrong study design - non randomised study, not pertinent in efficacy evaluation

with Osteoarthritis: A Nested Case-Control Study. <i>Pharmacotherapy</i> 2015;35:899-909.	
Roth SH, Fuller P. Pooled safety analysis of diclofenac sodium topical solution 1.5% (w/w) in the treatment of osteoarthritis in patients aged 75 years or older. <i>Clin Interv Aging</i> 2012;7:127-37.	Wrong publication type - Conference abstract
Roth SH, Fuller P. Safety of diclofenac sodium topical solution compared with oral diclofenac for osteoarthritis of the knee in patients aged 65 years: Pooled analysis from 2 controlled trials. <i>Arthritis Rheum</i> 2011;63.	Wrong intervention - Formulation not available on swedish market
Ruschitzka F, Borer JS, Krum H, Flammer AJ, Yeomans ND, Libby P, et al. Differential blood pressure effects of ibuprofen, naproxen, and celecoxib in patients with arthritis: the PRECISION-ABPM (Prospective Randomized Evaluation of Celecoxib Integrated Safety Versus Ibuprofen or Naproxen Ambulatory Blood Pressure Measurement) Trial. <i>Eur Heart J</i> 2017;38:3282-92.	Wrong outcome
Sands GH, Brown PB, Essex MN. The Efficacy of Continuous Versus Intermittent Celecoxib Treatment in Osteoarthritis Patients with Body Mass Index ≥ 30 and < 30 kg/m ² . <i>Open Rheumatol J</i> 2013;7:32-7.	Wrong population - mean age < 60
Setnik B, Pixton GC, Webster LR. Safety profile of extended-release morphine sulfate with sequestered naltrexone hydrochloride in older patients: Pooled analysis of three clinical trials. <i>Curr Med Res Opin</i> 2016;32:563-72.	Wrong intervention - Formulation not available on swedish market
Simon LS, Cryer B, Singh G, Li C, Essex MN. Effect of advancing age on the gastrointestinal safety of celecoxib versus nonselective nonsteroidal anti-inflammatory drugs: A post HOC analysis of GI-reasons. <i>Arthritis Rheum</i> 2012;64:S113-S114.	Wrong publication type - Conference abstract
Solomon DH, Husni ME, Libby PA, Yeomans ND, Lincoff AM, Luscher TF, et al. The Risk of Major NSAID Toxicity with Celecoxib, Ibuprofen, or Naproxen: A Secondary Analysis of the PRECISION Trial. <i>Am J Med</i> 2017;130:1415-1422.e4.	Double publication
Solomon DH, Husni ME, Wolski KE, Wisniewski LM, Borer JS, Graham DY, et al. Differences in Safety of Nonsteroidal Antiinflammatory Drugs in Patients With Osteoarthritis and Patients With Rheumatoid Arthritis: a Randomized Clinical Trial. <i>Arthritis Rheumatol</i> 2018;70:537-46.	Wrong outcome - Specific AE
Solomon DH, Husni ME, Wolski KE, Wisniewski LM, Borer JS, Graham DY, et al. Differences in Safety of Non-Steroidal Anti-Inflammatory Drugs in Patients with Osteoarthritis and Rheumatoid Arthritis: A Randomized Clinical Trial. <i>Arthritis Rheumatol</i> 2017;20:20.	Double publication
Sostres C, Carrera-Lasfuentes P, Lanás A. Non-steroidal anti-inflammatory drug related upper gastrointestinal bleeding: types of drug use and patient profiles in real clinical practice. <i>Curr Med Res Opin</i> 2017;33:1815-20.	Wrong outcome - Specific AE
Strand V, Bergman M, Parenti D, Nezzar J, Young C. A phase 3 randomized controlled trial of lower-dose diclofenac capsules in patients with osteoarthritis pain: Impact on patient-reported outcomes. <i>Osteoarthritis Cartilage</i> 2014;22:S392-S393	Wrong publication type - Conference abstract
Strand V, Bergman M, Singh JA, Gibofsky A, Kivitz A, Young C. Low-dose SoluMatrix diclofenac in patients with	Wrong intervention - Formulation not available on swedish market

osteoarthritis pain: impact on quality of life in a controlled trial. <i>Clinical Rheumatology</i> 2017;36:1357-67.	
Vorsanger G, Xiang J, Biondi D, Upmalis D, Delfgaauw J, Allard R, et al. Post hoc analyses of data from a 90-day clinical trial evaluating the tolerability and efficacy of tapentadol immediate release and oxycodone immediate release for the relief of moderate to severe pain in elderly and nonelderly patients. <i>Pain Res Manag</i> 2011;16:245-51.	Wrong population - no information of how many with osteoarthritis and back pain, respectively
Young C, Hochberg MC. Safety of lower-dose diclofenac submicron particle capsules dosed up to 12 weeks in patients with osteoarthritis. <i>Arthritis Rheum</i> 2013;65:S915.	Wrong publication type - Conference abstract
Yu Z, Zhao L, Yu C, Bi J, Yu X. Clinical therapeutic effect and safety of celecoxib in treating knee osteoarthritis. <i>Pak J Pharm Sci</i> 2018;31:1629-32.	Wrong intervention – both groups received IA hyaluronic acid
Zamani O, Bottcher E, Rieger JD, Mitterhuber J, Hawel R, Stallinger S, et al. Comparison of safety, efficacy and tolerability of dexibuprofen and ibuprofen in the treatment of osteoarthritis of the hip or knee. <i>Wien Klin Wochenschr</i> 2014;126:368-75.	Wrong intervention - Formulation not available on Swedish market
Zavodovsky B, Sivordova L, Polyakova Y, Akhverdyan Y, Kuznetsova M, Zborovskaya I. The efficacy and safety of etoricoxib versus meloxicam in the treatment of patients with gonarthrosis. <i>Ter Arkh</i> 2016;88:78-81.	Wrong language

Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
Moss P, Benson HAE, Will R, Wright A. Fourteen days of etoricoxib 60 mg improves pain, hyperalgesia and physical function in individuals with knee osteoarthritis: a randomized controlled trial. <i>Osteoarthritis Cartilage</i> 2017;25:1781-91.	High RoB – High risk of Reporting bias

Part II Diabetic polyneuropathy/Diabetesneuropati

Systematic reviews/Systematiska översikter

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Adriaensen H, Plaghki L, Mathieu C, Joffroy A, Vissers K. Critical review of oral drug treatments for diabetic neuropathic pain - Clinical outcomes based on efficacy and safety data from placebo-controlled and direct comparative studies. <i>Diabetes Metab Res Rev</i> 2005;21:231-40.	Research question too narrow
Bansal D, Asrar MM. Efficacy and safety of interventions used for management of diabetic neuropathy pain: A frequentist network meta-analysis. <i>Pharmacoepidemiol Drug Saf</i> 2019;28:131.	Wrong publication typ - conference abstract
Blair HA. Capsaicin 8% Dermal Patch: A Review in Peripheral Neuropathic Pain. <i>Drugs</i> 2018;78:1489-500.	Research question too narrow
Buksnys T, Armstrong N, Worthy G, Sabatschus I, Boesl I, Buchheister B, et al. Systematic review and network meta-analysis of the efficacy and safety of lidocaine 700 mg medicated plaster vs. pregabalin. <i>Curr Med Res Opin</i> 2019;36:101-15.	Research question too narrow

Carroll DG, Kline KM, Malnar KF. Role of topiramate for the treatment of painful diabetic peripheral neuropathy. <i>Pharmacotherapy</i> 2004;24:1186-93.	Research question too narrow - topiramate only
Chou R, Carson S, Chan BKS. Gabapentin versus tricyclic antidepressants for diabetic neuropathy and post-herpetic Neuralgia: Discrepancies between direct and indirect meta-analyses of randomized controlled trials. <i>J Gen Intern Med</i> 2009;24:178-88.	Research question too narrow - gabapentin only
Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. <i>Cochrane Database Syst Rev</i> 2019;1:CD007076.	Research question too narrow
Edelsberg J, Lord C, Oster G. Systematic review of data from randomized controlled trials on the efficacy, safety and tolerability of drugs used to treat painful diabetic neuropathy. <i>J Pain Manag</i> 2011;4:339-51.	Research question too narrow
Gutierrez-Alvarez AM, Beltran-Rodriguez J, Moreno CB. Antiepileptic drugs in treatment of pain caused by diabetic neuropathy. <i>J Pain Symptom Manage</i> 2007;34:201-8.	Research question too narrow - anticonvulsants only
Hossain SM, Hussain SM, Ekram AR. Duloxetine in Painful Diabetic Neuropathy: A Systematic Review. <i>Clin J Pain</i> 2016;32:1005-10.	Research question too narrow - duloxetine only
Hurley RW, Lesley MR, Adams MC, Brummett CM, Wu CL. Pregabalin as a treatment for painful diabetic peripheral neuropathy: a meta-analysis. <i>Reg Anesth Pain Med</i> 2008;33:389-94.	Research question too narrow - pregabalin only
Joss JD. Tricyclic antidepressant use in diabetic neuropathy. <i>Ann Pharmacother</i> 1999;33:996-1000.	Research question too narrow - TCA only
Quilici S, Chancellor J, Lothgren M, Simon D, Said G, Le TK, et al. Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. <i>BMC Neurol</i> 2009;9:6.	Research question too narrow - duloxetine only
Rudroju N, Bansal D, Teja Talakokkula S, Gudala K, Hota D, Bhansali A, et al. Comparative efficacy and safety of six antidepressants and anticonvulsants in painful diabetic neuropathy: A network meta-analysis. <i>Pain Physician</i> 2013;16:E705-E714.	Research question too narrow - six drugs only
Sommer C, Klose P, Welsch P, Petzke F, Häuser W. Opioids for chronic non-cancer neuropathic pain. An updated systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks duration. <i>Eur J Pain</i> 2019;24:3-18.	Research question too narrow
van Nooten F, Treur M, Pantiri K, Stoker M, Charokopou M. Capsaicin 8% Patch Versus Oral Neuropathic Pain Medications for the Treatment of Painful Diabetic Peripheral Neuropathy: A Systematic Literature Review and Network Meta-analysis. <i>Clin Ther</i> 2017;39:787-803.e18.	Research question too narrow - capsaicin only
Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine medicated plaster in painful diabetic peripheral neuropathy (DPN): a systematic review. <i>Swiss Med Wkly</i> 2010;140:297-306.	Research question too narrow - lidocaine only
Wong MC, Chung JWY, Wong TKS. Effects of treatments for symptoms of painful diabetic neuropathy: Systematic review. <i>BMJ (Int Ed)</i> 2007;335:87-90.	Research question too narrow
Zhang SS, Wu Z, Zhang LC, Zhang Z, Chen RP, Huang YH, et al. Efficacy and safety of pregabalin for treating painful diabetic	Research question too narrow - pregabalin only

peripheral neuropathy: a meta-analysis. Acta Anaesthesiol Scand 2015;59:147-59.	
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Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
Griebeler ML, Morey-Vargas OL, Brito JP, Tsapas A, Wang Z, Carranza Leon BG, et al. Pharmacologic interventions for painful diabetic neuropathy: An umbrella systematic review and comparative effectiveness network meta-analysis. Ann Intern Med 2014;161:639-49.	High RoB - high RoB in search strategy
Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Mehta S, Botteman M. Systematic review and meta-analysis of pharmacological therapies for painful diabetic peripheral neuropathy. Pain Pract 2014;14:167-84.	High RoB - high RoB in search strategy
Waldfoegel JM, Nesbit SA, Dy SM, Sharma R, Zhang A, Wilson LM, et al. Pharmacotherapy for diabetic peripheral neuropathy pain and quality of life. Neurology 2017;88:1958-67.	High RoB - high RoB in search strategy
Vilar S, Castillo JM, Martínez PVM, Reina M, Pabón M. Therapeutic alternatives in painful diabetic neuropathy: A meta-analysis of randomized controlled trials. Korean J Pain 2018;31:253-60.	High RoB - high RoB in search strategy

Primary studies/Primärstudier

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Agrawal RP, Goswami J, Jain S, Kochar DK. Management of diabetic neuropathy by sodium valproate and glyceryl trinitrate spray: A prospective double-blind randomized placebo-controlled study. Diabetes Res Clin Pract 2009;83:371-8.	Wrong population - Too few participants - n=20 in relevant comparison
Arezzo JC, Rosenstock J, LaMoreaux L, Pauer L. Efficacy and safety of pregabalin 600 mg/d for treating painful diabetic peripheral neuropathy: A double-blind placebo-controlled trial. BMC Neurol 2008;8:33.	Wrong population - mean age 58
Argoff CE, Galer BS, Jensen MP, Oleka N, Gammaitoni AR. Effectiveness of the lidocaine patch 5% on pain qualities in three chronic pain states: Assessment with the Neuropathic Pain Scale. Curr Med Res Opin 2004;20:S21-S28.	Wrong comparison - no control group
Arshad I, Zulfiqar H, Shafi B. To compare the efficacy of pregabalin and amitriptyline for pain relief in patients with diabetic peripheral neuropathy. Journal of pioneering medical sciences 2018;8:21-5.	Wrong population - mean age 45
Backonja M-M. Gabapentin monotherapy for the symptomatic treatment of painful neuropathy: a multicenter, double-blind, placebo-controlled trial in patients with diabetes mellitus. Epilepsia 1999;40:S57-9; discussion S73-4.	Double publication
Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA 1998;280:1831-6.	Wrong population - mean age 53

Bansal D, Bhansali A, Hota D, Chakrabarti A, Dutta P. Amitriptyline vs. pregabalin in painful diabetic neuropathy: A randomized double blind clinical trial. <i>Diabet Med</i> 2009;26:1019-26.	Wrong population - mean age 54
Baron R, Mayoral V, Leijon G, Binder A, Steigerwald I, Serpell M. Efficacy and safety of 5% lidocaine (lignocaine) medicated plaster in comparison with pregabalin in patients with postherpetic neuralgia and diabetic polyneuropathy: Interim analysis from an open-label, two-stage adaptive, randomized, controlled trial. <i>Clin Drug Investig</i> 2009;29:231-41.	Double publication – data set identical to Baron 2009 pregabalin vs lidocaine
Baron R, Mayoral V, Leijon G, Binder A, Steigerwald I, Serpell M. Efficacy and safety of combination therapy with 5% lidocaine medicated plaster and pregabalin in post-herpetic neuralgia and diabetic polyneuropathy. <i>Curr Med Res Opin</i> 2009;25:1677-87.	Wrong population - 70% DPN only
Baron R, Nell G, Steigerwald I, Rogers P. 5% lidocaine medicated plaster vs pregabalin in patients with painful diabetic polyneuropathy (DPN): efficacy and tolerability results from a randomized, controlled trial. <i>Diabetologia</i> 2009;52:S452.	Wrong study design - Conference abstract
Baron R, Rosa M, Steigerwald I, Serpell M. 5% Lidocaine-medicated plaster vs. pregabalin in patients with Post-Herpetic Neuralgia (PHN) and painful diabetic polyneuropathy (DPN): a randomized, controlled trial. <i>Eur J Pain</i> 2009;13:S161-s162.	Wrong study design - Conference abstract
Beydoun A, Kobetz SA, Carrazana EJ. Efficacy of Oxcarbazepine in the Treatment of Painful Diabetic Neuropathy. <i>Clin J Pain</i> 2004;20:174-8.	Wrong comparison - no control group
Beydoun S, Alarcon F, Mangat S, Wan Y. Long-term safety and tolerability of oxcarbazepine in painful diabetic neuropathy. <i>Acta Neurol Scand</i> 2007;115:284-8.	Wrong comparison - no control group
Block JP. Combined treatment with gabapentin and nortriptyline improves pain control in peripheral neuropathy more than either agent alone. <i>J Clin Outcomes Manag</i> 2009;16:544-5.	Wrong study design - editorial
Calkins A, Shurman J, Jaros M, Kim R, Shang G. Peripheral edema and weight gain in adult patients with painful diabetic peripheral neuropathy (DPN) receiving gabapentin enacarbil (GEN) or pregabalin enrolled in a randomized phase 2 trial. <i>PM R</i> 2014;6:S369.	Wrong study design - Conference abstract
Chad D, Aronin N, Lundstrom R, McKeon P, Ross D, Molitch M, et al. Does capsaicin relieve the pain of diabetic neuropathy? <i>Pain</i> 1990;42:387-8.	Wrong study design - editorial
Dailey IGE, Muchmore DP, Springer JW, Donofrio PD, Walker FO, Hunt VP, et al. Effect of treatment with capsaicin on daily activities of patients with painful diabetic neuropathy. <i>Diabetes Care</i> 1992;15:159-65.	Double publication
Daniel, Sr., Badyal D, Kaur J, Jacob J. Effect of amitriptyline and pregabalin sustained release on pain relief and quality of life in painful diabetic neuropathy. <i>Indian J Pharmacol</i> 2013;45:S148.	Wrong study design - Conference abstract
Dellemijn PL, van Duijn H, Vanneste JA. Prolonged treatment with transdermal fentanyl in neuropathic pain. <i>J Pain Symptom Manage</i> 1998;16:220-9.	Wrong population - not DPN
Devi P, Madhu K, Ganapathy B, Sarma GRK, John L, Kulkarni C. Evaluation of efficacy and safety of gabapentin, duloxetine,	Wrong population - mean age 57

and pregabalin in patients with painful diabetic peripheral neuropathy. <i>Indian J Pharmacol</i> 2012;44:51-6.	
Donofrio PD, Raskin P, Rosenthal NR, Hewitt DJ, Jordan DM, Xiang J, et al. Safety and effectiveness of topiramate for the management of painful diabetic peripheral neuropathy in an open-label extension study. <i>Clin Ther</i> 2005;27:1420-31.	Wrong comparison - no control group
Eisenberg E, Lurie Y, Braker C, Daoud D, Ishay A. Lamotrigine reduces painful diabetic neuropathy: A randomized, controlled study. <i>Neurology</i> 2001;57:505-9.	Wrong population - mean age 57
Freeman R, Raskin P, Hewitt DJ, Vorsanger GJ, Jordan DM, Xiang J, et al. Randomized study of tramadol/acetaminophen versus placebo in painful diabetic peripheral neuropathy. <i>Curr Med Res Opin</i> 2007;23:147-61.	Wrong population - mean age <60
Freyenhagen R, Busche P, Konrad C, Balkenohl M. Effectiveness and time to onset of pregabalin in patients with neuropathic pain. <i>Schmerz</i> 2006;20:285-92.	Wrong language
Gilron I, Bailey JM, Tu D, Holden RR, Weaver DF, Houlden RL. Morphine, gabapentin, or their combination for neuropathic pain. <i>N Engl J Med</i> 2005;352:1324-34.	Wrong population - Population too small
Gilron I, Wajsbrot D, Therrien F, Lemay J. Pregabalin for peripheral neuropathic pain: A multicenter, enriched enrollment randomized withdrawal placebo-controlled trial. <i>Clin J Pain</i> 2011;27:185-93.	Wrong population - only 58% DPN, no separate presentation of results
Gómez-Pérez FJ, Perez-Monteverde A, Nascimento O, Aschner P, Tagle M, Fichtner K, et al. Gabapentin for the treatment of painful diabetic neuropathy: Dosing to achieve optimal clinical response. <i>Br J Diabetes Vasc Dis</i> 2004;4:173-8.	Wrong population - mean age 56
Irving G, Tanenberg RJ, Raskin J, Risser RC, Malcolm S. Comparative safety and tolerability of duloxetine vs. pregabalin vs. duloxetine plus gabapentin in patients with diabetic peripheral neuropathic pain. <i>Int J Clin Pract</i> 2014;68:1130-40.	Double publication -relevant data in Tanenberg 2011
Jensen MP, Friedman M, Bonzo D, Richards P. The validity of the neuropathic pain scale for assessing diabetic neuropathic pain in a clinical trial. <i>Clin J Pain</i> 2006;22:97-103.	Double publication
Jia H-y, Li Q-f, Song D-p, Liu Y-p, Ran X-w. Effects of venlafaxine and carbamazepine for painful peripheral diabetic neuropathy: a randomized, double-blind and double-dummy, controlled multi-center trial. <i>Chinese journal of evidence-based medicine</i> 2006;6:321-7.	Wrong population - mean age 55
Joharchi K, Memari M, Azargashb E, Saadat N. Correction to: Efficacy and safety of duloxetine and Pregabalin in Iranian patients with diabetic peripheral neuropathic pain: a double-blind, randomized clinical trial (<i>Journal of Diabetes & Metabolic Disorders</i> , (2019), 10.1007/s40200-019-00427-w). <i>J Diabetes Metab Disord</i> 2019;18:583.	Wrong study design - errata
Joharchi K, Memari M, Azargashb E, Saadat N. Efficacy and safety of duloxetine and Pregabalin in Iranian patients with diabetic peripheral neuropathic pain: a double-blind, randomized clinical trial. <i>J Diabetes Metab Disord</i> 2019;18:575-82.	Wrong population - mean age 54
Jose VM, Bhansali A, Hota D, Pandhi P. Randomized double-blind study comparing the efficacy and safety of lamotrigine and amitriptyline in painful diabetic neuropathy. <i>Diabet Med</i> 2007;24:377-83.	Wrong population - mean age 56

Kardanpour N, Khorvash F, Khorvash F, Memarzadeh M. A comparative study on the effect of duloxetine hydrochloride, venlafaxine hydrochloride, and pregabalin on the sensory symptoms in patients with diabetic polyneuropathy. <i>Journal of Isfahan Medical School</i> 2018;35:1885-91.	Wrong language
Kaur H, Hota D, Bhansali A, Dutta P, Bansal D, Chakrabarti A. A comparative evaluation of amitriptyline and duloxetine in painful diabetic neuropathy: A randomized, double-blind, cross-over clinical trial. <i>Diabetes Care</i> 2011;34:818-22.	Wrong population - mean age 53
Kiani J, Nasrollahi SA, Esna-Ashari F, Fallah P, Sajedi F. Amitriptyline 2% cream vs. Capsaicin 0.75% cream in the treatment of painful diabetic neuropathy (double blind, randomized clinical trial of efficacy and safety). <i>Iran J Pharm Res</i> 2015;14:1263-8.	Wrong intervention – amitriptyline cream not available on Swedish market
Ko SH, Kwon HS, Yu JM, Baik SH, Park IB, Lee JH, et al. Comparison of the efficacy and safety of tramadol/acetaminophen combination therapy and gabapentin in the treatment of painful diabetic neuropathy. <i>Diabet Med</i> 2010;27:1033-40.	Wrong population - mean age 57/58
Kochar D, Jain N, Agarwal R, Srivastava T, Agarwal P, Gupta S. Sodium valproate in the management of painful neuropathy in type 2 diabetes - a randomized placebo controlled study. <i>J Peripher Nerv Syst</i> 2003;8:128.	Double publication
Kochar DK, Jain N, Agarwal RP, Srivastava T, Agarwal P, Gupta S. Sodium valproate in the management of painful neuropathy in type 2 diabetes - A randomized placebo controlled study. <i>Acta Neurol Scand</i> 2002;106:248-52.	Wrong population - mean age 54/58
Kochar DK, Rawat N, Agrawal RP, Vyas A, Beniwal R, Kochar SK, et al. Sodium valproate for painful diabetic neuropathy: a randomized double-blind placebo-controlled study. <i>QJM</i> 2004;97:33-8.	Wrong population - mean age 54/56
Kopsky DJ, Keppel Hesselink JM. Single-blind placebo-controlled response test with phenytoin 10% cream in neuropathic pain patients. <i>Pharmaceuticals (Basel)</i> 2018;11.	Wrong intervention – phenytoin cream not available on Swedish market
Kulkantrakorn K, Chomjit A, Sithinamsuwan P, Tharavanij T, Suwankanoknark J, Napunnaphat P. 0.075% capsaicin lotion for the treatment of painful diabetic neuropathy: A randomized, double-blind, crossover, placebo-controlled trial. <i>J Clin Neurosci</i> 2019;62:174-9.	Wrong population - 27 completed the study
Luria Y, Brecker C, Daoud D, Ishay A, Eisenberg E. Lamotrigine in the treatment of painful diabetic neuropathy: a randomized, placebo-controlled study. <i>Prog Pain Res Manag</i> 2000;16:857-62.	Double publication – identical data to Eisenberg 2001
Mahmood R, Jawed I, Khan MI, Mahmood I, Tariq T, Kamil A, et al. Comparative role of pregabalin and carbamazepine regarding efficacy in painful diabetic neuropathy. <i>Pak J Pharm Sci</i> 2017;30:1275-8.	Wrong population - mean age <60
Majdinasab N, Kaveyani H, Azizi M. A comparative double-blind randomized study on the effectiveness of Duloxetine and Gabapentin on painful diabetic peripheral polyneuropathy. <i>Drug Des Devel Ther</i> 2019;13:1985-92.	Wrong intervention - gabapentin 900 mg – too low dose for clinical relevance
McCleane G. 200 mg daily of lamotrigine has no analgesic effect in neuropathic pain: a randomised, double-blind, placebo controlled trial. <i>Pain</i> 1999;83:105-7.	Wrong population - mean age 46
Meier T, Wasner G, Faust M, Kuntzer T, Ochsner F, Hueppe M, et al. Efficacy of lidocaine patch 5% in the treatment of focal	Wrong population - not DPN

peripheral neuropathic pain syndromes: A randomized, double-blind, placebo-controlled study. <i>Pain</i> 2003;106:151-8.	
Moon DE, Lee DI, Lee SC, Song SO, Yoon DM, Yoon MH, et al. Efficacy and Tolerability of Pregabalin Using a Flexible, Optimized Dose Schedule in Korean Patients With Peripheral Neuropathic Pain: A 10-Week, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study. <i>Clin Ther</i> 2010;32:2370-85.	Wrong population - 8% DPN only
Morrison S, Parson H, Vinik A. Pregabalin positively affects subjective pain, falls risk, and gait in persons with diabetic peripheral neuropathy. <i>Diabetes</i> 2015:A164.	Wrong study design - Conference abstract
Perrot S, Ortega E, Vinik E, Pazdera L, Stoker M, Nooten F, et al. Efficacy, quality of life and treatment satisfaction with capsaicin 8% patch versus standard of care in painful diabetic peripheral neuropathy. <i>Diabetologia</i> 2015;58:S514.	Wrong study design - Conference abstract
Raskin J, Smith TR, Wong K, Pritchett YL, D'Souza DN, Iyengar S, et al. Duloxetine versus routine care in the long-term management of diabetic peripheral neuropathic pain. <i>J Palliat Med</i> 2006;9:29-40.	Wrong population - mean age 59
Raskin P, Donofrio PD, Rosenthal NR, Hewitt DJ, Jordan DM, Xiang J, et al. Topiramate vs placebo in painful diabetic neuropathy: analgesic and metabolic effects. <i>Neurology</i> 2004;63:865-73.	Wrong population - mean age 58
Raskin P, Huffman C, Toth C, Asmus MJ, Messig M, Sanchez RJ, et al. Pregabalin in patients with inadequately treated painful diabetic peripheral neuropathy: A randomized withdrawal trial. <i>Clin J Pain</i> 2014;30:379-90.	Wrong population - mean age 58
Rauck R, Makumi CW, Schwartz S, Graff O, Meno-Tetang G, Bell CF, et al. A Randomized, Controlled Trial of Gabapentin Enacarbil in Subjects with Neuropathic Pain Associated with Diabetic Peripheral Neuropathy. <i>Pain Pract</i> 2013;13:485-96.	Wrong intervention - gabapentin enacarbil not available on swedish market
Rauck RL, Shaibani A, Biton V, Simpson J, Koch B. Lacosamide in painful diabetic peripheral neuropathy: A phase 2 double-blind placebo-controlled study. <i>Clin J Pain</i> 2007;23:150-8.	Wrong population - mean age 54/55
Razazian N, Baziyar M, Moradian N, Afshari D, Bostani A, Mahmoodi M. Evaluation of the efficacy and safety of pregabalin, venlafaxine, and carbamazepine in patients with painful diabetic peripheral neuropathy: A randomized, double-blind trial. <i>Neurosciences (Riyadh)</i> 2014;19:192-8.	Wrong population - mean age 55/58 years
Richter RW, Portenoy R, Sharma U, Lamoreaux L, Bockbrader H, Knapp LE. Relief of painful diabetic peripheral neuropathy with pregabalin: a randomized, placebo-controlled trial. <i>J Pain</i> 2005;6:253-60.	Wrong population - mean age 56/57 years
Saeed T, Nasrullah M, Ghafoor A, Shahid R, Islam N, Khattak MU, et al. Efficacy and tolerability of carbamazepine for the treatment of painful diabetic neuropathy in adults: a 12-week, open-label, multicenter study. <i>Int J Gen Med</i> 2014;7:339-43.	Wrong comparison - no control group
Sandercock D, Cramer M, Biton V, Cowles VE. A gastroretentive gabapentin formulation for the treatment of painful diabetic peripheral neuropathy: Efficacy and tolerability in a double-blind, randomized, controlled clinical trial. <i>Diabetes Res Clin Pract</i> 2012;97:438-45.	Wrong intervention - gastroretentive gabapentin not available on Swedish market
Sandercock D, Cramer M, Wu J, Chiang Y-K, Biton V, Heritier M. Gabapentin extended release for the treatment of painful diabetic peripheral neuropathy: efficacy and tolerability in a	Wrong study design - letter to the editor

double-blind, randomized, controlled clinical trial. <i>Diabetes Care</i> 2009;32:e20.	
Satoh J, Yagihashi S, Baba M, Suzuki M, Arakawa A, Yoshiyama T. Efficacy and safety evaluation of pregabalin treatment over 52 weeks in patients with diabetic neuropathic pain extended after a double-blind placebo-controlled trial. <i>J Diabetes Investig</i> 2011;2:457-63.	Wrong comparison - no control group
Sekar P, Punngai K, David DC. Comparative study of safety and efficacy of gabapentin versus amitriptyline in patients with painful diabetic peripheral neuropathy, a randomized open label parallel group study. <i>Biomedical and Pharmacology Journal</i> 2017;10:1259-65.	Wrong population - age not specified
Semel D, Murphy TK, Zlateva G, Cheung R, Emir B. Evaluation of the safety and efficacy of pregabalin in older patients with neuropathic pain: results from a pooled analysis of 11 clinical studies. <i>BMC Fam Pract</i> 2010;11:85.	Wrong study design - pooled analysis
Shabbir B, Shafi F, Mahboob F. Amitriptyline vs pregabalin in painful diabetic neuropathy a randomised placebo-based study. <i>Pakistan Journal of Medical and Health Sciences</i> 2011;5:745-7.	Wrong population - age not specified
Silver M, Blum D, Grainger J, Hammer AE, Qessy S. Double-Blind, Placebo-Controlled Trial of Lamotrigine in Combination with Other Medications for Neuropathic Pain. <i>J Pain Symptom Manage</i> 2007;34:446-54.	Wrong population - DPN only 65 %
Simpson DA. Gabapentin and venlafaxine for the treatment of painful diabetic neuropathy. <i>J Clin Neuromuscul Dis</i> 2001;3:53-62.	Wrong population - mean age 48/50
Snijder R, Ortega E, Perrot S, Vinik E, Pazdera L, Jacobs H, et al. Capsaicin 8% patch versus standard of care in painful diabetic peripheral neuropathy: efficacy of seven consecutive treatments over 52 weeks versus SOC. <i>Diabetologia</i> 2015;58:S515.	Conference abstract
Stoker M, Katz N, Van J, Snijder R, Jacobs H, Long S, et al. Capsaicin 8% patch in painful diabetic peripheral neuropathy: a randomised, double-blind, placebo-controlled study. <i>Diabetologia</i> 2015;58:S32.	Conference abstract
Sun DH, Ji CM, Ma L, Jiang CL. Efficacy and safety of pregabalin in patients with diabetic painful neuropathy. <i>Chinese journal of new drugs</i> 2011;20:1302-4.	Wrong language - Chinese
Tanenberg R, Irving G, Risser R, Ahl J, Malcolm S. An open-label, randomized comparison of duloxetine, pregabalin, and the combination of duloxetine and gabapentin among patients with inadequate response to gabapentin for the management of diabetic peripheral neuropathic pain. 2010.	Conference abstract
Tanenberg R, Irving G, Risser R, Ahl J, Malcolm S. An open-label, randomized comparison of duloxetine, pregabalin, and the combination of duloxetine and gabapentin among patients with inadequate response to gabapentin for the management of diabetic peripheral neuropathic pain. <i>Pain Med</i> 2011;12:525.	Conference abstract
Tesfaye S, Wilhelm S, Lledo A, Schacht A, Tölle T, Bouhassira D, et al. Duloxetine and pregabalin: High-dose monotherapy or their combination? the "cOMBO-DN study" - A multinational, randomized, double-blind, parallel-group study in patients with diabetic peripheral neuropathic pain. <i>Pain</i> 2013;154:2616-25.	Wrong comparison – compares monotherapy with combination therapy

Watson CP, Moulin D, Watt-Watson J, Gordon A, Eisenhoffer J. Controlled-release oxycodone relieves neuropathic pain: a randomized controlled trial in painful diabetic neuropathy. <i>Pain</i> 2003;105:71-8.	Wrong population - Too few participants - n=36 evaluable patients
Webster LR, Peppin JF, Murphy FT, Tobias JK, Vanhove GF. Tolerability of NGX-4010, a capsaicin 8% patch, in conjunction with three topical anesthetic formulations for the treatment of neuropathic pain. <i>J Pain Res</i> 2012;5:7-13.	Wrong comparison - no control group
Wernicke JF, Raskin J, Rosen A, Pritchett YL, D'Souza DN, Iyengar S, et al. Duloxetine in the long-term management of diabetic peripheral neuropathic pain: An open-label, 52-week extension of a randomized controlled clinical trial. <i>Curr Ther Res Clin Exp</i> 2006;67:283-304.	Wrong population - mean age 59
Wernicke JF, Wang F, Pritchett YL, Smith TR, Raskin J, D'Souza DN, et al. An open-label 52-week clinical extension comparing duloxetine with routine care in patients with diabetic peripheral neuropathic pain. <i>Pain Med</i> 2007;8:503-13.	Wrong population - mean age 58
Vinik A, Perrot S, Vinik E, Pazdera L, Jacobs H, Stoker M, et al. Capsaicin 8% patch repeat treatment versus standard of care in painful diabetic peripheral neuropathy: a randomised, open-label, 52-week study. <i>Diabetologia</i> 2015;58:S514-s515.	Wrong study design - Conference abstract
Wymer JP, Simpson J, Sen D, Bongardt S. Efficacy and safety of lacosamide in diabetic neuropathic pain: An 18-week double-blind placebo-controlled trial of fixed-dose regimens. <i>Clin J Pain</i> 2009;25:376-85.	Wrong population - mean age 57/58
Yasuda H, Hotta N, Kasuga M, Kashiwagi A, Kawamori R, Yamada T, et al. Efficacy and safety of 40 mg or 60 mg duloxetine in Japanese adults with diabetic neuropathic pain: Results from a randomized, 52-week, open-label study. <i>J Diabetes Investig</i> 2016;7:100-8.	Wrong comparison - no control group
Yuen E, Gueorguieva I, Bueno-Burgos L, Iyengar S, Aarons L. Population pharmacokinetic/pharmacodynamic models for duloxetine in the treatment of diabetic peripheral neuropathic pain. <i>Eur J Pain</i> 2013;17:382-93.	Wrong study design - pooled analysis
Zakerkish M, Amiri F, Nasab NM, Ghorbani A. Comparative efficacy of duloxetine versus nortriptyline in patients with diabetic peripheral neuropathic pain: A double blind randomized controlled trial. <i>Iran Red Crescent Med J</i> 2017;19:e59995.	Wrong population - mean age <60
Ziegler D, Hidvegi T, Gurieva I, Bongardt S, Freynhagen R, Sen D, et al. Efficacy and safety of lacosamide in painful diabetic neuropathy. <i>Diabetes Care</i> 2010;33:839-41.	Wrong population - age not specified
Zin CS, Nissen LM, O'Callaghan JP, Duffull SB, Smith MT, Moore BJ. A randomized, controlled trial of oxycodone versus placebo in patients with postherpetic neuralgia and painful diabetic neuropathy treated with pregabalin. <i>J Pain</i> 2010;11:462-71.	Wrong population - too small population with DPN

Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
Gorson K, Schott C, Herman R, Ropper A, Rand W. Gabapentin in the treatment of painful diabetic neuropathy: a placebo controlled, double blind, crossover trial. <i>J Neurol Neurosurg Psychiatry</i> 1999;66:251-2.	High RoB

Scheffler NM, Sheitel PL, Lipton MN. Treatment of painful diabetic neuropathy with capsaicin 0.075%. J Am Podiatr Med Assoc 1991;81:288-93.	High RoB
Schwartz S, Etropolski M, Shapiro DY, Okamoto A, Lange R, Haeussler J, et al. Safety and efficacy of tapentadol ER in patients with painful diabetic peripheral neuropathy: results of a randomized-withdrawal, placebo-controlled trial. Curr Med Res Opin 2011;27:151-62.	High RoB - enrichment design
Shamsinejad S, Davati A, Roughani M, Ghasemlouie A, Afshinmajd S. Evaluation of topiramate efficacy on neuropathic pain in patients with diabetic polyneuropathy. Acta Med Iran 2018;56:764-8.	High risk of bias in 4 domains
Vinik AI, Shapiro DY, Rauschkolb C, Lange B, Karcher K, Pennett D, et al. A randomized withdrawal, placebo-controlled study evaluating the efficacy and tolerability of tapentadol extended release in patients with chronic painful diabetic peripheral neuropathy. Diabetes care 2014;37:2302-9.	High RoB enrichment design

Part III Pain Adverse effects/Biverkningar

Systematic reviews/Systematiska översikter

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Aguiar JP, Brito AM, Da Costa FA, Leufkens H, Martins AP. A systematic overview of potentially inappropriate medications (PIMS) with risk of major adverse cardiac and cerebrovascular events (MACCE). Int J Clin Pharm 2018;40:500-1.	Wrong publication type - Poster available only
Ashraf E, Cooper S, Kellstein D, Jayawardena S. Safety profile of nonprescription ibuprofen in the elderly osteoarthritis patient: A meta-analysis. Inflammopharmacology 2001;9:35-41.	Research question too narrow - nonprescription ibuprofen only
Bally M, Dendukuri N, Rich B, Nadeau L, Helin-Salmivaara A, Garbe E, et al. Risk of acute myocardial infarction with NSAIDs in real world use: Bayesian meta-analysis of individual patient data. BMJ 2017;357:j1909.	Wrong study design - literature review and primary study
Dart RC, Bailey E. Does therapeutic use of acetaminophen cause acute liver failure? Pharmacotherapy 2007;27:1219-30.	Wrong outcome
Els C, Jackson TD, Kunyk D, Lappi VG, Sonnenberg B, Hagtvedt R, et al. Adverse events associated with medium- and long-term use of opioids for chronic non-cancer pain: An overview of Cochrane Reviews. Cochrane Database Syst Rev 2017.	Wrong population - not elderly
Gurwitz JH, Avorn J. The ambiguous relation between aging and adverse drug reactions. Ann Intern Med 1991;114:956-66.	Wrong outcome
Kahan M, Wilson L, Mailis-Gagnon A, Srivastava A. Canadian guideline for safe and effective use of opioids for chronic noncancer pain - Clinical summary for family physicians. Part 2: Special populations. Can Fam Physician 2011;57:1269-76.	Wrong study design - guideline
Lewis SC, Langman MJS, Laporte JR, Matthews JNS, Rawlins MD, Wiholm BE. Dose-response relationships between individual nonaspirin nonsteroidal anti-inflammatory drugs (NNSAIDs) and serious upper gastrointestinal bleeding: A	Wrong population - not elderly

meta-analysis based on individual patient data. <i>Br J Clin Pharmacol</i> 2002;54:320-6.	
Lucenteforte E, Lombardi N, Vetrano DL, La Carpia D, Mitrova Z, Kirchmayer U, et al. Inappropriate pharmacological treatment in older adults affected by cardiovascular disease and other chronic comorbidities: A systematic literature review to identify potentially inappropriate prescription indicators. <i>Clin Interv Aging</i> 2017;12:1761-78.	Wrong outcome
MacLean CH, Pencharz JN, Saag KG. Quality indicators for the care of osteoarthritis in vulnerable elders. <i>J Am Geriatr Soc</i> 2007;55:S383-S391.	Wrong study design - Guideline
Maree RD, Marcum ZA, Saghabi E, Weiner DK, Karp JF. A Systematic Review of Opioid and Benzodiazepine Misuse in Older Adults. <i>Am J Geriatr Psychiatry</i> 2016;24:949-63.	Wrong outcome
Martin Arias LH, Martin Gonzalez A, Sanz Fadrique R, Salgueiro Vazquez E. Gastrointestinal safety of coxibs: systematic review and meta-analysis of observational studies on selective inhibitors of cyclo-oxygenase 2. <i>Fundam Clin Pharmacol</i> 2019;33:134-47.	Wrong population - not elderly
Megale RZ, Deveza LA, Blyth FM, Naganathan V, Ferreira PH, McLachlan AJ, et al. Efficacy and Safety of Oral and Transdermal Opioid Analgesics for Musculoskeletal Pain in Older Adults: A Systematic Review of Randomized, Placebo-Controlled Trials. <i>J Pain</i> 2018;19:475.e1-475.e24.	Wrong population - not elderly. No specific adverse events
Motter FR, Fritzen JS, Hilmer SN, Paniz É V, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. <i>Eur J Clin Pharmacol</i> 2018;74:679-700.	Wrong study design - review of PIM/guidelines
Nderitu P, Doos L, Jones PW, Davies SJ, Kadam UT. Non-steroidal anti-inflammatory drugs and chronic kidney disease progression: a systematic review. <i>Family Practice</i> 2013;30:247-55.	Wrong outcome - effect on chronic kidney disease
Pellicano R. Gastrointestinal damage by non-steroidal anti-inflammatory drugs: Updated clinical considerations. <i>Minerva Gastroenterol Dietol</i> 2014;60:255-61.	Wrong study design - review article
Ruxton K, Woodman RJ, Mangoni AA. Drugs with anticholinergic effects and cognitive impairment, falls and all-cause mortality in older adults: A systematic review and meta-analysis. <i>Br J Clin Pharmacol</i> 2015;80:209-20.	More recent SR available
Thorat MA, Cuzick J. Prophylactic use of aspirin: systematic review of harms and approaches to mitigation in the general population. <i>Eur J Epidemiol</i> 2015;30:5-18.	Wrong outcome - Baseline risk bleeding in different age groups
Woolcott JC, Richardson KJ, Wiens MO, Patel B, Marin J, Khan KM, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. <i>Arch Intern Med</i> 2009;169:1952-60.	More recent SR available
Yuhara H, Corley DA, Nakahara F, Nakajima T, Koike J, Igarashi M, et al. Aspirin and non-aspirin NSAIDs increase risk of colonic diverticular bleeding: A systematic review and meta-analysis. <i>J Gastroenterol</i> 2014;49:992-1000.	Wrong population - not elderly

Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
Chen Y, Zhu LL, Zhou Q. Effects of drug pharmacokinetic/pharmacodynamic properties, characteristics of medication use, and relevant pharmacological interventions on fall risk in elderly patients. <i>Ther Clin Risk Manag</i> 2014;10:437-48.	High RoB - no assessment of RoB of the included studies
Hegeman J, van den Bemt BJ, Duysens J, van Limbeek J. NSAIDs and the risk of accidental falls in the elderly: a systematic review. <i>Drug Saf</i> 2009;32:489-98.	High RoB - little info about search strategy, no synthesis made, conclusions do not consider limitations
Hernández-Díaz S, García Rodríguez LA. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation an overview of epidemiologic studies published in the 1990s. <i>Arch Intern Med</i> 2000;160:2093-9.	High RoB - little info about search strategy
Loke YK, Trivedi AN, Singh S. Meta-analysis: Gastrointestinal bleeding due to interaction between selective serotonin uptake inhibitors and non-steroidal anti-inflammatory drugs. <i>Aliment Pharmacol Ther</i> 2008;27:31-40.	High RoB - no assessment of RoB of the included studies
Loza E. [Systematic review: is the use of NSAIDs effective and safe in the elderly?]. <i>Reumatol Clin</i> 2008;4:172-82.	High RoB - little info about search strategy
Makris UE, Kohler MJ, Fraenkel L. Adverse effects of topical nonsteroidal antiinflammatory drugs in older adults with osteoarthritis: a systematic literature review. <i>J Rheumatol</i> 2010;37:1236-43.	High RoB - no assessment of RoB of the included studies
O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. <i>Am J Geriatr Pharmacother</i> 2012;10:331-42.	High RoB - no assessment of RoB of the included studies
Oka Y, Okamoto K, Kawashita N, Shirakuni Y, Takagi T. Meta-analysis of the risk of upper gastrointestinal hemorrhage with combination therapy of selective serotonin reuptake inhibitors and non-steroidal anti-inflammatory drugs. <i>Biol Pharm Bull</i> 2014;37:947-53.	High RoB - no assessment of RoB of the included studies
Papaleontiou M, Henderson Jr CR, Turner BJ, Moore AA, Olkhovskaya Y, Amanfo L, et al. Outcomes associated with opioid use in the treatment of chronic noncancer pain in older adults: A systematic review and meta-analysis. <i>J Am Geriatr Soc</i> 2010;58:1353-69.	High RoB: very little info on search strategy
Park H, Satoh H, Miki A, Urushihara H, Sawada Y. Medications associated with falls in older people: Systematic review of publications from a recent 5-year period. <i>Eur J Clin Pharmacol</i> 2015;71:1429-40.	High RoB - no assessment of RoB of the included studies

Primary studies/Primärstudier

Risk of acute renal failure/Risk för akut njurpåverkan

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Alayed N, Alkhalifah B, Alharbi M, Alwohaibi N, Farooqui M. Adverse drug reaction (ADR) as a cause of hospitalization at a government hospital in Saudi Arabia: A prospective observational study. <i>Curr Drug Saf</i> 2019;14:192-8.	Wrong population - mean age 49
Cabassi A, Tedeschi S, Perlini S, Verzicco I, Volpi R, Gonzi G, et al. Non-steroidal anti-inflammatory drug effects on renal and cardiovascular function: from physiology to clinical practice. <i>Eur J Prev Cardiol</i> 2019.	Wrong publication type - Conference abstract
Cabré M, Elias L, García M, Palomera E, Serra-Prat M. Avoidable hospitalizations due to adverse drug reactions in an acute geriatric unit. Analysis of 3,292 patients. <i>Med Clin (Barc)</i> 2018;150:209-14.	Wrong comparison – examining prevalence, no control group
Caravaca-Fontan F, Villacorta J, Cordon A, Praga M, Fernández-Juárez G. Clinical determinants of renal outcomes in drug-induced acute interstitial nephritis. <i>Nephrol Dial Transplant</i> 2017;32:iii498.	Wrong publication type - Conference abstract
Chou CI, Shih CJ, Chen YT, Ou SM, Yang CY, Kuo SC, et al. Adverse Effects of Oral Nonselective and cyclooxygenase-2-Selective NSAIDs on Hospitalization for Acute Kidney Injury: A Nested Case-Control Cohort Study. <i>Medicine (Baltimore)</i> 2016;95:e2645.	Wrong population - mean age 67 (SD 20)
Davis-Ajami ML, Fink JC, Wu J. Nephrotoxic medication exposure in U.S. adults with predialysis chronic kidney disease: Health services utilization and cost outcomes. <i>J Manag Care Spec Pharm</i> 2016;22:959-68.	Wrong outcome - assessing exposure to NSAID in CKD patients
Douros A, Bronder E, Klimpel A, Erley C, Garbe E, Kreutz R. Drug-induced kidney injury: A large case series from the Berlin Case-Control Surveillance Study. <i>Clin Nephrol</i> 2018;89:18-26.	Wrong population - mean age 69
Ehrmann S, Helms J, Joret A, Martin-Lefevre L, Quenot JP, Herbrecht JE, et al. Nephrotoxic drug burden among 1001 critically ill patients: impact on acute kidney injury. <i>Ann Intensive Care</i> 2019;9.	Wrong population - mean age 65
Ernst R, Fischer K, de Godoi Rezende Costa Molino C, Orav EJ, Theiler R, Meyer U, et al. Polypharmacy and Kidney Function in Community-Dwelling Adults Age 60 Years and Older: A Prospective Observational Study. <i>J Am Med Dir Assoc</i> 2019.	Wrong outcome - not acute kidney impairment
Fassio V, Aspinall SL, Zhao X, Miller DR, Singh JA, Good CB, et al. Trends in opioid and nonsteroidal anti-inflammatory use and adverse events. <i>Am J Manag Care</i> 2018;24:e61-e72.	Wrong outcome
Hsiao KC, Huang JY, Lee CT, Hung TW, Liaw YP, Chang HR. Different impact of aspirin on renal progression in patients with predialysis advanced chronic kidney disease with or without previous stroke. <i>Eur J Intern Med</i> 2017;39:63-8.	Wrong population - mean age 64
Kaewput W, Disorn P, Satirapoj B. Selective cyclooxygenase-2 inhibitor use and progression of renal function in patients with chronic kidney disease: A single-center retrospective cohort study. <i>Int J Nephrol Renovasc Dis</i> 2016;9:273-8.	Wrong outcome
Kate RJ, Perez RM, Mazumdar D, Pasupathy KS, Nilakantan V. Prediction and detection models for acute kidney injury in hospitalized older adults. <i>BMC Med Inform Decis Mak</i> 2016;16:39.	Wrong outcome – evaluates model to predict AKI

Lai KM, Chen TL, Chang CC, Chen HH, Lee YW. Association between NSAID use and mortality risk in patients with end-stage renal disease: A population-based cohort study. <i>Clin Epidemiol</i> 2019;11:429-41.	Wrong outcome – evaluates mortality in existing condition
Lipworth L, Abdel-Kader K, Morse J, Stewart TG, Kabagambe EK, Parr SK, et al. High prevalence of non-steroidal anti-inflammatory drug use among acute kidney injury survivors in the southern community cohort study. <i>BMC Nephrol</i> 2016;17:1-9.	Wrong population - mean age 58
Mangoni AA, Kholmurodova F, Mayner L, Hakendorf P, Woodman RJ. The Concomitant Use of Diuretics, Non-Steroidal Anti-Inflammatory Drugs, and Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers (Triple Whammy), Extreme Heat, and In-Hospital Acute Kidney Injury in Older Medical Patients. <i>Adv Ther</i> 2017;34:2534-41.	Wrong comparison
Nishtala P, Chyou TY. Association rule analysis to evaluate frequent drug combinations associated with acute kidney injury in older adults. <i>Pharmacoepidemiol Drug Saf</i> 2019;28:425.	Wrong publication type - Conference abstract
Novick TK, Grams ME. Safely treating pain in older adults. <i>Nephrol Dial Transplant</i> 2019;34:1075-7.	Wrong study design - review article
Oliveira D, Silva S, Dias P, Feio J. Acute kidney failure due to anti-inflammatory drugs and antihypertensive drugs in elderly inpatients. <i>Eur Geriatr Med</i> 2016;7:S240.	Wrong publication type - Conference abstract
Patel M, Balwani M, Bendale K, Dighore P, Kute V. Clinical spectrum and outcome of acute kidney injury in elderly from western India. <i>Nephrol Dial Transplant</i> 2017;32:iii536.	Wrong publication type - Conference abstract
Pedrós C, Formiga F, Corbella X, Arnau JM. Adverse drug reactions leading to urgent hospital admission in an elderly population: Prevalence and main features. <i>Eur J Clin Pharmacol</i> 2016;72:219-26.	Wrong comparison
Perez Gutthann S, Garcia Rodriguez LA, Raiford DS, Duque Oliart A, Ris Romeu J. Nonsteroidal anti-inflammatory drugs and the risk of hospitalization for acute renal failure. <i>Arch Intern Med</i> 1996;156:2433-9.	Wrong drug - most NSAIDs not available on Swedish market
Radulescu D, Peride I, David C, Bogueanu C, Niculae A, Checherita IA. Factors affecting prognosis of acute kidney injury in elderly. <i>Nephrol Dial Transplant</i> 2017;32:iii537-iii538.	Wrong publication type - Conference abstract
Reed GW, Abdallah MS, Shao M, Wolski K, Wisniewski L, Yeomans N, et al. Effect of Aspirin Coadministration on the Safety of Celecoxib, Naproxen, or Ibuprofen. <i>J Am Coll Cardiol</i> 2018;71:1741-51.	Wrong population - mean age 63
Robert L, Ficheur G, Gautier S, Servais A, Luyckx M, Soula J, et al. Community-Acquired Acute Kidney Injury Induced By Drugs In Older Patients: A Multifactorial Event. <i>Clin Interv Aging</i> 2019;14:2105-13.	Wrong drug - examining combination of drugs
Rocchi RE, Rossi M, Bartolini F, Benedetti A, Costantini M, D'Arpino A, et al. Drug related renal failure. An observational, prospective, multicenter pharmacovigilance study performed in medicine and cardiology wards of the hospitals in Umbria. <i>Giornale italiano di farmacia clinica</i> 2017;31:23-34.	Wrong language - italian
Schmidt M, Mansfield KE, Bhaskaran K, Nitsch D, Sørensen HT, Smeeth L, et al. Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: Cohort study. <i>BMJ</i> 2017;356:j791.	Wrong drug
Solomon DH, Husni ME, Libby PA, Yeomans ND, Lincoff AM, Lüscher TF, et al. The Risk of Major NSAID Toxicity with	Wrong population – mean age 63

Celecoxib, Ibuprofen, or Naproxen: a Secondary Analysis of the PRECISION Trial. <i>Am J Med</i> 2017;130:1415-1422.e4.	
Solomon DH, Husni ME, Wolski KE, Wisniewski LM, Borer JS, Graham DY, et al. Differences in Safety of Nonsteroidal Antiinflammatory Drugs in Patients With Osteoarthritis and Patients With Rheumatoid Arthritis: a Randomized Clinical Trial. <i>Arthritis Rheumatol</i> 2018;70:537-46.	Wrong population - mean age 64

Studies with high risk of bias/Studier med hög risk för bias

Study/Studie	Reason for exclusion/Exklusionsorsak
Turgutalp K, Bardak S, Horoz M, Helvacı I, Demir S, Kiykim AA. Clinical outcomes of acute kidney injury developing outside the hospital in elderly. <i>Int Urol Nephrol</i> 2017;49:113-21.	High RoB – unacceptable high risk of confounding, no adjustment of data

Risk of gastrointestinal perforations, bleeds or ulcerations/Risk för PUB

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Chi T-Y, Zhu H-M, Zhang M. Risk factors associated with nonsteroidal anti-inflammatory drugs (NSAIDs)-induced gastrointestinal bleeding resulting on people over 60 years old in Beijing. <i>Medicine (Baltimore)</i> 2018;97:e0665.	Wrong comparison – comparison of treatments with different durations
Combe B, Swergold G, McLay J, McCarthy T, Zerbini C, Emery P, et al. Cardiovascular safety and gastrointestinal tolerability of etoricoxib vs diclofenac in a randomized controlled clinical trial (The MEDAL study). <i>Rheumatology</i> 2009;48:425-32.	Wrong population - mean age 64
Cryer B, Li C, Simon LS, Singh G, Stillman MJ, Berger MF. GI-REASONS: a novel 6-month, prospective, randomized, open-label, blinded endpoint (PROBE) trial. <i>Am J Gastroenterol</i> 2013;108:392-400.	Wrong population - mean age 63
De Vries F, Setakis E, Van Staa TP. Concomitant use of ibuprofen and paracetamol and the risk of major clinical safety outcomes. <i>Br J Clin Pharmacol</i> 2010;70:429-38.	Wrong population - mean age ca 55
García Rodríguez LA, Lanás A, Soriano-Gabarró M, Cea Soriano L. Low-dose aspirin and risk of upper/lower gastrointestinal bleeding by bleed severity: a cohort study with nested case-control analysis using primary care electronic health records from the United Kingdom. <i>Ann Med</i> 2019;51:182-92.	Wrong population - inclusion 40 years and older
Kellner HL, Li C, Essex MN. Efficacy and safety of celecoxib versus diclofenac and omeprazole in elderly arthritis patients: A subgroup analysis of the CONDOR trial. <i>Curr Med Res Opin</i> 2012;28:1537-45.	Wrong drug - slow release formulation not available on Swedish market
Kellner HL, Li C, Essex MN. Celecoxib and diclofenac plus omeprazole are similarly effective in the treatment of arthritis in patients at high gi risk in the CONDOR trial. <i>Open Rheumatol J</i> 2013;7:96-100.	Wrong outcome - efficacy
Kim J, Lee J, Shin CM, Lee DH, Park BJ. Risk of gastrointestinal bleeding and cardiovascular events due to NSAIDs in the diabetic elderly population. <i>BMJ Open Diabetes Res Care</i> 2015;3:e000133.	Wrong drug – NSAIDs not available on Swedish market
Kocoglu H, Oguz B, Dogan H, Okuturlar Y, Hursitoglu M, Harmankaya O, et al. Do NSAIDs and ASA Cause More Upper	Wrong comparison

Gastrointestinal Bleeding in Elderly than Adults? Gastroenterol Res Pract 2016;2016:8419304.	
Lanas A, Carrera-Lasfuentes P, Arguedas Y, Garcia S, Bujanda L, Calvet X, et al. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. Clin Gastroenterol Hepatol 2015;13:906-12.e2.	Wrong population - mean age 66
Lenti MV, Pasina L, Cococcia S, Cortesi L, Miceli E, Caccia Dominioni C, et al. Mortality rate and risk factors for gastrointestinal bleeding in elderly patients. United European Gastroenterol J 2018;6:A295.	Wrong outcome
Lin X-H, Lin C-C, Wang Y-J, Luo J-C, Young S-H, Chen P-H, et al. Risk factors of the peptic ulcer bleeding in aging uremia patients under regular hemodialysis. J Chin Med Assoc 2018;81:1027-32.	Wrong comparison
Lin X-H, Young S-H, Luo J-C, Peng Y-L, Chen P-H, Lin C-C, et al. Risk Factors for Upper Gastrointestinal Bleeding in Patients Taking Selective COX-2 Inhibitors: A Nationwide Population-Based Cohort Study. Pain Med 2018;19:225-31.	Wrong population - mean age 67
Mahady S, Woods R, Polekhina G, Chan A, Wolfe R, Lockery J, et al. Factors associated with aspirin-related upper gastrointestinal bleeding in the elderly: Data from a randomized controlled trial of 19 114 people. J Gastroenterol Hepatol 2019;34:176.	Wrong publication type - Conference abstract
Masclee GMC, Valkhoff VE, Coloma PM, De Ridder M, Romio S, Schuemie MJ, et al. Risk of upper gastrointestinal bleeding from different drug combinations. Gastroenterology 2014;147:784-792.e9.	Wrong population
Matei D, Groza I, Pasca S, Negrutiu D, Furnea B, Bocsan C, et al. Peptic ulcer bleeding in the elderly: Clinical outcomes and in-hospital mortality. United European Gastroenterol J 2017;5:A784.	Wrong publication type - Conference abstract
McDonald DD. Predictors of gastrointestinal bleeding in older persons taking nonsteroidal anti-inflammatory drugs: Results from the FDA adverse events reporting system. J Am Assoc Nurse Pract 2019;31:206-13.	Wrong comparison
Sigurgísladóttir S, Hreinsson JP, Björnsson E. Gastrointestinal bleeding in patients 80 years and older: Incidence, association with drugs and prognosis. Gastroenterology 2016;150:S887-S888.	Wrong publication type - Conference abstract
Solomon DH, Husni ME, Wolski KE, Wisniewski LM, Borer JS, Graham DY, et al. Differences in Safety of Nonsteroidal Antiinflammatory Drugs in Patients With Osteoarthritis and Patients With Rheumatoid Arthritis: a Randomized Clinical Trial. Arthritis Rheumatol 2018;70:537-46.	Wrong population – mean age 64
Van Der Linden MW, Van Der Bij S, Welsing P, Kuipers EJ, Herings RMC. The balance between severe cardiovascular and gastrointestinal events among users of selective and non-selective non-steroidal anti-inflammatory drugs. Ann Rheum Dis 2009;68:668-73.	Wrong population - mean age 67
Yang YJ, Bang CS, Shin SP, Park TY, Suk KT, Baik GH, et al. Clinical characteristics of peptic ulcer perforation in Korea. World J Gastroenterol 2017;23:2566-74.	Wrong comparison

Opioids and the risk of falls/Risk för fall vid opioidbehandling

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Recent opioid use associated with increased risk of falls in older people. Drug Ther Bull 2018;56:74.	Wrong publication type - editorial abstract
Alshehri M, Alqahtani B, Alenazi A, Waitman L, Kluding P. Comorbidities and Medications Associated With Falls in Older Adults With Osteoarthritis: A Retrospective Study. Arch Phys Med Rehabil 2019;100:e55.	Wrong publication type - Conference abstract
Axmon A, Sandberg M, Ahlström G, Midlöv P. Fall-risk-increasing drugs and falls requiring health care among older people with intellectual disability in comparison with the general population: A register study. PLoS One 2018;13.	Wrong population - median age 57
Bambina E, Mestivier E, Berod T. Falls and medication-related risk factors in the elderly: Contribution of medication-related work-up at admission. Pharmacie Hospitalier et Clinicien 2017;52:21-25.	Wrong language
Beunza-Sola M, Hidalgo-Ovejero Á M, Martí-Ayerdi J, Sánchez-Hernández JG, Menéndez-García M, García-Mata S. Study of fall risk-increasing drugs in elderly patients before and after a bone fracture. Postgrad Med J 2018;94:76-80.	Wrong outcome
Daoust R, Paquet J, Moore L, Gosselin S, Gélinas C, Rouleau DM, et al. Incidence and risk factors of long-term opioid use in elderly trauma patients. Ann Surg 2018;268:985-91.	Wrong outcome
Delgado-Silveira E, Kinnear A, Parro-Martin A, Gramage-Caro T, Velez-Diaz-Pallarés M, Bermejo-Vicedo T. Pharmacological and non-pharmacological conditions and falls in elderly people as a cause of hospital admission. Eur J Hosp Pharm 2016;23:A227-A228.	Wrong publication type – conference poster
Hamza SA, Adly NN, Abdelrahman EE, Fouad IM. The relation between falls and medication use among elderly in assisted living facilities. Pharmacoepidemiol Drug Saf 2019.	Wrong population - age range ca 55 - 85
Hart LA, Marcum ZA, Gray SL, Walker RL, Crane PK, Larson EB. The Association Between Central Nervous System-Active Medication Use and Fall-Related Injury in Community-Dwelling Older Adults with Dementia. Pharmacotherapy 2019;39:530-43.	Wrong drug - cns active medication as group, not specifically opioids
Kim TW, Walley AY, Ventura AS, Patts GJ, Heeren TC, Lerner GB, et al. Polypharmacy and risk of falls and fractures for patients with HIV infection and substance dependence. AIDS Care 2018;30:150-9.	Wrong population - median age 50
Lo-Ciganic WH, Floden L, Lee JK, Ashbeck EL, Zhou L, Chinthammit C, et al. Analgesic use and risk of recurrent falls in participants with or at risk of knee osteoarthritis: data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2017;25:1390-8.	Wrong population - mean age 60
Machado-Duque ME, Castaño-Montoya JP, Medina-Morales DA, Castro-Rodríguez A, González-Montoya A, Machado-Alba JE. Association between the use of benzodiazepines and opioids with the risk of falls and hip fractures in older adults. Int Psychogeriatr 2018;30:941-6.	Wrong comparison
Musich S, Wang SS, Slindee LB, Ruiz J, Yeh CS. Concurrent Use of Opioids with Other Central Nervous System-Active Medications Among Older Adults. Popul Health Manag 2019.	Wrong drug - investigating opioids plus cns active medication

Park H, Satoh H, Miki A, Maki H, Asai K, Shiraishi A, et al. Medications and fall risk: a case-control study in nursing home residents in Japan. <i>Aging Clin Exp Res</i> 2019.	Wrong comparison - adjusted data not compared to non-opioid use
Ryan-Atwood TE, Hutchinson-Kern M, Ilomäki J, Dooley MJ, Poole SG, Kirkpatrick CM, et al. Medication Use and Fall-Related Hospital Admissions from Long-Term Care Facilities: A Hospital-Based Case-Control Study. <i>Drugs Aging</i> 2017;34:625-33.	Wrong drug - opioid data not presented separately
Schwarzer A, Kaisler M, Kipping K, Seybold D, Rausch V, Maier C, et al. Opioid intake prior to admission is not increased in elderly patients with low-energy fractures: A case-control study in a German hospital population. <i>Eur J Pain</i> 2018;22:1651-61.	Wrong population
Tormo V, Xiang Q, Kirby T, Passik S, Camper S. Efficacy and tolerability of buprenorphine buccal film in older adults with chronic pain requiring around-the-clock therapy. <i>Postgraduate Medicine</i> 2016;128:92.	Wrong publication type - abstract
Zia A, Kamaruzzaman SB, Tan MP. The consumption of two or more fall risk-increasing drugs rather than polypharmacy is associated with falls. <i>Geriatr Gerontol Int</i> 2017;17:463-70.	Wrong drug

Part IV Experiences of encounters between elderly with pain and health care staff/Upplevelser av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer

Primary studies/Primärstudier

Studies considered not relevant/Studier som bedömts som inte relevanta

Study/Studie	Reason for exclusion/Exklusionsorsak
Allvin R, Fjordkvist E, Blomberg K. Struggling to be seen and understood as a person - Chronic back pain patients' experiences of encounters in health care: An interview study. <i>Nurs Open</i> 2019;6:1047-54.	Wrong population - median age 66
Baird CL, Yehle KS, Schmeiser D. Experiences of women with osteoarthritis in assisted living facilities. <i>Clin Nurse Spec</i> 2007;21:276-84; quiz 285-6.	Wrong study question
Ballantyne PJ, Gignac MA, Hawker GA. A patient-centered perspective on surgery avoidance for hip or knee arthritis: lessons for the future. <i>Arthritis Rheum</i> 2007;57:27-34.	Wrong study question
Blomqvist K, Hallberg IR. Managing pain in older persons who receive home-help for their daily living. Perceptions by older persons and care providers. <i>Scand J Caring Sci</i> 2002;16:319-28.	Design
Darlow B, Brown M, Thompson B, Hudson B, Grainger R, McKinlay E, et al. Living with osteoarthritis is a balancing act: an exploration of patients' beliefs about knee pain. <i>BMC Rheumatol</i> 2018;2:15.	Wrong population
de Luca K, Parkinson L, Hunter S, Byles JE. Qualitative insights into the experience of pain in older Australian women with arthritis. <i>Australas J Ageing</i> 2018;37:210-6.	Wrong population - mean age 64
Driscoll MA, Knobf MT, Higgins DM, Heapy A, Lee A, Haskell S. Patient Experiences Navigating Chronic Pain Management in	Wrong population - mean age 60

an Integrated Health Care System: A Qualitative Investigation of Women and Men. <i>Pain Med</i> 2018;19:S19-S29.	
Franklin ZC, Smith NC, Fowler NE. A qualitative investigation of factors that matter to individuals in the pain management process. <i>Disabil Rehabil</i> 2016;38:1934-42.	Wrong population
Gran SV, Festvag LS, Landmark BT. 'Alone with my pain - it can't be explained, it has to be experienced'. A Norwegian in-depth interview study of pain in nursing home residents. <i>Int J Older People Nurs</i> 2010;5:25-33.	Wrong study question
Grime J, Richardson JC, Ong BN. Perceptions of joint pain and feeling well in older people who reported being healthy: a qualitative study. <i>Br J Gen Pract</i> 2010;60:597-603.	Wrong study question
Halifax E. How certified nursing assistants understand their residents' pain: University of California, San Francisco; 2013.	Wrong study question
Harding G, Parsons S, Rahman A, Underwood M. "It struck me that they didn't understand pain": the specialist pain clinic experience of patients with chronic musculoskeletal pain. <i>Arthritis Rheum</i> 2005;53:691-6.	Wrong population
Harmon J, Summons P, Higgins I. Experiences of the older hospitalised person on nursing pain care: An ethnographic insight. <i>J Clin Nurs</i> 2019;28:4447-59.	Wrong study question
Jones KR, Fink RM, Clark L, Hutt E, Vojir CP, Mellis BK. Nursing home resident barriers to effective pain management: Why nursing home residents may not seek pain medication. <i>J Am Med Dir Assoc</i> 2005;6:10-7.	Wrong study design
Karlsson C, Sidenvall B, Bergh I, Ernsth-Bravell M. Registered Nurses' View of Performing Pain Assessment among Persons with Dementia as Consultant Advisors. <i>Open Nurs J</i> 2012;6:62-70.	Wrong study question
Karlsson C, Sidenvall B, Bergh I, Ernsth-Bravell M. Certified nursing assistants' perception of pain in people with dementia: a hermeneutic enquiry in dementia care practice. <i>J Clin Nurs</i> 2013;22:1880-9.	Wrong study question
Karlsson CE, Ernsth Bravell M, Ek K, Bergh I. Home healthcare teams' assessments of pain in care recipients living with dementia: a Swedish exploratory study. <i>Int J Older People Nurs</i> 2015;10:190-200.	Wrong study question
Kemper JA. Pain management of older adults after discharge from outpatient surgery. <i>Pain Manag Nurs</i> 2002;3:141-53.	Wrong population
Kennedy MC, Cousins G, Henman MC. Analgesic use by ageing and elderly patients with chronic non-malignant pain: a qualitative study. <i>Int J Clin Pharm</i> 2017;39:798-807.	Wrong study design
Mackichan F, Adamson J, Gooberman-Hill R. 'Living within your limits': activity restriction in older people experiencing chronic pain. <i>Age Ageing</i> 2013;42:702-8.	Wrong study question
Manias E. Complexities of pain assessment and management in hospitalised older people: a qualitative observation and interview study. <i>Int J Nurs Stud</i> 2012;49:1243-54.	Wrong study question
Markotic F, Cerni Obrdalj E, Zalihic A, Pehar R, Hadziosmanovic Z, Pivic G, et al. Adherence to pharmacological treatment of chronic nonmalignant pain in individuals aged 65 and older. <i>Pain Med</i> 2013;14:247-56.	Wrong study design
Nielsen M, Foster M, Henman P, Strong J. 'Talk to us like we're people, not an X-ray': the experience of receiving care for chronic pain. <i>Aust J Prim Health</i> 2013;19:138-43.	Wrong population

Paier GS. Specter of the crone: the experience of vertebral fracture. <i>ANS Adv Nurs Sci</i> 1996;18:27-36.	Wrong population
Pouli N, Das Nair R, Lincoln NB, Walsh D. The experience of living with knee osteoarthritis: exploring illness and treatment beliefs through thematic analysis. <i>Disabil Rehabil</i> 2014;36:600-7.	Wrong population
Ryan S, Lillie K, Thwaites C, Adams J. 'What I want clinicians to know'-experiences of people with arthritis. <i>Br J Nurs</i> 2013;22:808-12.	Wrong publication type
Schofield P. Pain management. Pain management of older people in care homes: a pilot study. <i>Br J Nurs</i> 2006;15:509-14.	Wrong study question
Webster F, Perruccio AV, Jenkinson R, Jaglal S, Schemitsch E, Waddell JP, et al. Where is the patient in models of patient-centred care: a grounded theory study of total joint replacement patients. <i>BMC Health Serv Res</i> 2013;13:531.	Wrong population
Zamanzadeh V, Ahmadi F, Foolady M, Behshid M, Irajpoor A. The Health Seeking Behaviors and Perceptions of Iranian Patient with Osteoarthritis about Pain Management: A Qualitative Study. <i>J Caring Sci</i> 2017;6:81-93.	Wrong population