Bilaga 1–6

Läkemedelsbehandling av vanliga smärttillstånd hos äldre personer/ Pharmacological treatment of common pain conditions in the elderly, rapport 315 (2020)

SBU Statens beredning för medicinsk och social utvärdering • www.sbu.se
Telefon 08-412 32 00 • **Fax** 08-411 32 60 • **Organisationsnummer** 202100-4417
Besöksadress S:t Eriksgatan 117, Stockholm • **Postadress** Box 6183, 102 33 Stockholm

Bilaga 1

Läkemedelsbehandling av vanliga smärttillstånd hos äldre personer/ Pharmacological treatment of common pain conditions in the elderly, rapport 315 (2020)

Appendix 1/Bilaga 1 Search strategies/Sökstrategier

Table of contents/Innehållsförteckning

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Part I Osteoarthritis/Artros

Systematic reviews/Systematiska översikter

Cochrane Library via Wiley 8 January 2020
Title: Osteoarthritis – drug therapy (Paracetamol, NSAIDs, Opioides). Systematic reviews

Search terms		Items found
Population: Osteoarthritis		
	MeSH descriptor: [Osteoarthritis] explode all trees	6680
	osteoarthr* or degenerative next arthrit* or "degenerative joint disease":ti,ab,kw (Word variations have been searched)	16569
	1 or 2	*16569*
Intervention: Paracetamol		
	MeSH descriptor: [Acetaminophen] explode all trees	2992
	acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl:ti,ab,kw (Word variations have been searched)	10109
	4 or 5	*10109*
Intervention: NSAID		
	MeSH descriptor: [Aspirin] explode all trees	5540
	MeSH descriptor: [Diclofenac] explode all trees	1852
	MeSH descriptor: [Piroxicam] explode all trees	649
	MeSH descriptor: [Ibuprofen] explode all trees	1830
	MeSH descriptor: [Naproxen] explode all trees	1094
	MeSH descriptor: [Ketoprofen] explode all trees	542
	MeSH descriptor: [Celecoxib] explode all trees	871
	MeSH descriptor: [Ketorolac] explode all trees	805
	MeSH descriptor: [Meloxicam] explode all trees	214
	("acetylsalicylic acid" or "2-(Acetyloxy)benzoic Acid" or aspirin or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or diclophenac or dicrofenac or dichlofenal or "diclonate P" or feloran or voltarol or novapirina or orthofen or ortofen or orthophen or voltaren or diclofenac or piroxicam or feldene or reutenox or artriunic or "Novo-Tenoxicam" or mobiflex or tilcotil or "Apo-Tenoxicam" or tenoxicam or reumoxicam or miloxicam or movalis or uticox or mobic or mobicox or mobec or masflex or movicox or parocin or meloxicam or ibumetin or ibuprofen or motrin or nuprin or rufen or salprofen or "Trauma-Dolgit Gel" or "Trauma Dolgit Gel" or "TraumaDolgit Gel" or brufen or methoxypropiocin or anaprox or naproxen or aleve or proxen or synflex or naprosin or naprosyn or "naproxenate sodium" or "benzoylhydratropic acid" or "2-(3-Benzoylphenyl)propionic Acid" or profenid or alrheumum or orudis or alrheumat or dexibuprofen or s-ibuprofen or "S ibuprofen" or badyket or ketesse or sympal or quiralam or quirgel or adolquir or enangel or keral or enantyum or ketoprofen or dexketoprofen or celcoxib or celebrex or etoricoxib or arcoxia or nabumetone or arthraxan or "Gen-Nabumetone" or listran or relafen or relif or relifex or mebutan or "Rhoxal-nabumetone" or "Apo-Nabumetone" or celecoxib or nabucox) :ti,ab,kw (Word variations have been searched)	30873
	7-16 (OR)	*31559*
Intervention: Opioides		
	MeSH descriptor: [Buprenorphine] explode all trees	1044
	MeSH descriptor: [Buprenorphine, Naloxone Drug Combination] explode all trees	11
	MeSH descriptor: [Codeine] explode all trees	1606
	MeSH descriptor: [Hydrocodone] explode all trees	202
	MeSH descriptor: [Oxycodone] explode all trees	845
	MeSH descriptor: [Hydromorphone] explode all trees	342

	MeSH descriptor: [Morphine] explode all trees	4749
	MeSH descriptor: [Meperidine] explode all trees	1138
	MeSH descriptor: [Fentanyl] explode all trees	5289
	MeSH descriptor: [Tramadol] explode all trees	1070
	MeSH descriptor: [Methadone] explode all trees	1189
	MeSH descriptor: [Tapentadol] explode all trees	60
	morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict:ti,ab,kw (Word variations have been searched)	39300
	18-30 (OR)	*40374*
Limits: publication year		
	1990-2020	
Combined sets[1]		
	3 AND 6 AND 32	**1337 CDSR/83 Protocols /15 DARE/5 HTA/0**
	3 AND 17 AND 32	**1918 CDSR/18 Protocols /0 DARE/10 HTA/7**
	3 AND 31 AND 32	**622 CDSR/7 Protocols /0 DARE/3 HTA/0**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

[1] Databaserna DARE och HTA ingår inte längre i Cochrane Library och ingick inte i uppdateringssökningen i Cochrane Library.

CDSR = Cochrane Database of Systematic Review
Protocols= Protocols for Cochrane Reviews
DARE = Database Abstracts of Reviews of Effects, "other reviews"
HTA = Health Technology Assessments

PROSPERO via University of York, Centre for reviews and dissemination 12 December 2018
Title: Osteoarthritis – drug therapy (Paracetamol, NSAIDSs, Opioides). Systematic reviews

Search terms	Items found
Population: Osteoarthritis	
(osteoarthritis):TI,HA,KW	**293**

The search result, usually found at the end of the documentation, forms the list of abstracts.

TI = title
HA = health area
KW = keywords

Embase via Elsevier 20 December 2019
Title: Osteoarthritis – drug therapy (Paracetamol, NSAIDs, Opioides). Systematic reviews

Search terms	Items found
Population: Osteoarthritis	
'osteoarthritis'/exp	127,379
'osteoarthritis therapy'/exp	143
'osteoarthritis pain'/exp	30
osteoarthr*:ab,ti,de,kw OR 'degenerative arthrit*':ab,ti,de,kw OR 'degenerative joint disease':ab,ti,de,kw	146,518
1-4 (OR)	*153,829*
Intervention: Paracetamol	
'paracetamol'/exp	88,23
'cocodamol'/exp	1,603
'oxycodone plus paracetamol'/exp	1,516
'hydrocodone bitartrate plus paracetamol'/exp	1,374
'dextropropoxyphene plus paracetamol'/exp	964
(acetaminophen:ab,ti,kw,de OR paracetamol:ab,ti,kw,de OR acetominophen:ab,ti,kw,de OR hydroxyacetanilide:ab,ti,kw,de OR apap:ab,ti,kw,de OR 'p acetamidophenol':ab,ti,kw,de OR 'p hydroxyacetanilide':ab,ti,kw,de OR 'n-(4-hydroxyphenyl)acetanilide':ab,ti,kw,de OR acetamidophenol:ab,ti,kw,de OR 'n-acetyl-p-aminophenol':ab,ti,kw,de OR 'n-acetyl-para-aminophenol':ab,ti,kw,de OR acephen:ab,ti,kw,de OR acetaco:ab,ti,kw,de OR tylenol:ab,ti,kw,de OR 'anacin 3':ab,ti,kw,de OR anacin3:ab,ti,kw,de OR datril:ab,ti,kw,de OR panadol:ab,ti,kw,de OR acamol:ab,ti,kw,de OR algotropyl):ab,ti,kw,de	95,672
6–11 (OR)	*85,719*
Intervention: NSAIDs	
'acetylsalicylic acid'/exp/mj	59,819
'diclofenac'/exp/mj	10,537
'diclofenac potassium'/exp/mj	229
'diclofenac plus misoprostol'/exp/mj	44
'piroxicam'/exp/mj	3,933
'piroxicam beta cyclodextrin'/exp/mj	76
'cinnoxicam'/exp/mj	47
'ibuprofen'/exp/mj	13,190
'naproxen'/exp/mj	7,371
'ketoprofen'/exp/mj	4,340
'ketoprofen lysine'/exp/mj	68
'celecoxib'/exp/mj	4,753

	'ketorolac'/exp/mj	1,885
	'tenoxicam'/exp/mj	635
	'meloxicam'/exp/mj OR 'florfenicol plus meloxicam'/exp/mj	1,530
	'ketorolac trometamol plus phenylephrine'/exp/mj OR 'ketorolac trometamol'/exp/mj	805
	'dexibuprofen'/exp/mj	106
	'dexketoprofen'/exp/mj OR 'dexketoprofen plus tramadol'/exp/mj	282
	'parecoxib'/exp/mj	511
	'etoricoxib'/exp/mj	653
	'nabumetone'/exp/mj	473
	'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	137,966
	13-34 (OR)	*170,180*
Intervention: Opioides		
	'buprenorphine'/exp/mj	6,425
	'buprenorphine plus naloxone'/exp/mj	582
	'codeine'/exp/mj	6,686
	'cocodamol'/exp/mj	156
	'hydrocodone'/exp/mj	719
	'hydrocodone bitartrate plus paracetamol'/exp/mj	89
	'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
	'oxycodone'/exp/mj	3,068
	'oxycodone plus paracetamol'/exp/mj	183
	'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
	'hydromorphone'/exp/mj	1,845
	'pethidine'/exp/mj	10,015
	'fentanyl'/exp/mj	17,310
	'tramadol'/exp/mj	4,304
	'paracetamol plus tramadol'/exp/mj	102
	'methadone'/exp/mj	14,055

	'codeine phosphate'/exp/mj	390
	'hydromorphone plus naloxone'/exp/mj	1
	'morphine'/exp/mj	46,853
	'ketobemidone'/exp/mj	207
	'tapentadol'/exp/mj	611
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	129,134
	36-57 (OR)	*155,896*
Study types: systematic reviews, meta analysis		
	'systematic review'/de	227,094
	'meta analysis'/de	175,332
	[cochrane review]/lim	20,928
	'review'/exp AND [1990-2007]/py	1,125,802
	(systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* OR metaanaly*):ti,ab	340,232
	59-63 (OR)	*1,511,138*
	64 NOT ('editorial'/it OR 'erratum'/it OR 'letter'/it OR 'note'/it)	1,491,462
Limits: language, publication year		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
Combined sets		
	5 AND 12 AND 65 AND 66	**731**
	5 AND 35 AND 65 AND 66	**588**
	5 AND 58 AND 65 AND 66	**137**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic

:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
“ ” = Citation Marks; searches for an exact phrase

Medline via OvidSP 19 December 2019
Title: Osteoarthritis – drug therapy (Paracetamol, NSAIDs, Opioides). Systematic reviews

Search terms		Items found
Population: Osteoarthritis		
	exp osteoarthritis/	61005
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,kw,ti.	72829
	1 OR 2	*92638*
Intervention: Paracetamol		
	exp Acetaminophen/	17743
	(acetaminophen OR paracetamol OR tylenol OR acetominophen OR hydroxyacetanilide OR APAP OR p-acetamidophenol OR p-hydroxyacetanilide OR "N-(4-Hydroxyphenyl)acetanilide" OR acetamidophenol OR "N-Acetyl-p-aminophenol" OR "N-acetyl-para-aminophenol" OR Acephen OR Acetaco OR Tylenol OR Anacin-3 OR "Anacin 3" OR Anacin3 OR Datril OR Panadol OR Acamol OR Algotropyl).ab,kf,kw,ti.	24946
	4 OR 5	*27776*
Intervention: NSAIDs		
	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/ OR exp Ketorolac/ OR exp Meloxicam/	72693
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	91929
	7 OR 8	*110609*
Intervention: Opioides		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/ or exp Tapentadol/	78261
	(morphia OR morphine OR pentahydrate OR "MS Contin" OR "Oramorph SR" OR duramorph OR dihydromorphinone OR hydromorphon OR palladone OR laudacon OR dilaudid OR hydromorphone OR dihydrone OR oxycone OR dihydrohydroxycodeinone OR oxycodeinon OR eucodal OR theocodin OR oxycodone OR oxycontin OR pancodine OR dinarkon OR oxiconum OR cetobemidon OR ketobemidone OR pethidine OR fentanyl OR isonipecain OR dolsin OR dolosal OR dolin OR "operidine EPJ-I" OR "operidine EPJ I" OR dolantin OR dolargan OR meperidine OR lidol OR lydol OR demerol OR dolcontral OR burenorphine OR codeine OR tramadol OR tapentadol OR methadone OR tramundin OR biodalgic OR jutadol OR nobligan OR prontofort OR zytram OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR	94329

	biokanol OR tramabeta OR tramadin OR tramadolratiopharm OR tramadoc OR ranitidin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR adolonta OR contramal OR amadol OR phentanyl OR fentanest OR dentanyl OR sublimaze OR duragesic OR durogesic OR fentora OR buprenex OR prefin OR subutex OR buprex OR temgesic OR buprenorphine OR N-Methylmorphine OR Isocodeine OR Codeine OR Ardinex OR Biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict).ab,kf,kw,ti.	
	10 OR 11	*111715*
Study types: systematic reviews, meta analysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	3 AND 6 AND 13 AND 14	**52**
	3 AND 9 AND 13 AND 14	**118**
	3 AND 12 AND 13 AND 14	**18**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Primary studies/Primärstudier

Cochrane Library via Wiley 8 January 2020 (CENTRAL)
Title: Osteoarthritis – drug therapy (NSAID)

Search terms		Items found
Population: Osteoarthritis		
	MeSH descriptor: [Osteoarthritis] explode all trees	6680
	osteoarthr* or degenerative next arthrit* or "degenerative joint disease" or coxarthr* or gonarthr*:ti,ab,kw or (heberdens or bochards) next (noduli):ti,ab,kw (Word variations have been searched)	16770
	1 OR 2	*16770*
Intervention: NSAIDs		
	MeSH descriptor: [Aspirin] explode all trees	5540
	MeSH descriptor: [Diclofenac] explode all trees	1852
	MeSH descriptor: [Piroxicam] explode all trees	649
	MeSH descriptor: [Ibuprofen] explode all trees	1830
	MeSH descriptor: [Naproxen] explode all trees	1094
	MeSH descriptor: [Ketoprofen] explode all trees	542
	MeSH descriptor: [Celecoxib] explode all trees	871
	MeSH descriptor: [Ketorolac] explode all trees	805
	MeSH descriptor: [Meloxicam] explode all trees	214
	("acetylsalicylic acid" or "2-(Acetyloxy)benzoic Acid" or aspirin or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or diclophenac or dicrofenac or dichlofenal or "diclonate P" or feloran or voltarol or novapirina or orthofen or ortofen or orthophen or voltaren or diclofenac or piroxicam or feldene or reutenox or artriunic or "Novo-Tenoxicam" or mobiflex or tilcotil or "Apo-Tenoxicam" or tenoxicam or reumoxicam or miloxicam or movalis or uticox or mobic or mobicox or mobec or masflex or movicox or parocin or meloxicam or ibumetin or ibuprofen or motrin or nuprin or rufen or salprofen or "Trauma-Dolgit Gel" or "Trauma Dolgit Gel" or "TraumaDolgit Gel" or brufen or methoxypropiocin or anaprox or naproxen or aleve or proxen or synflex or naprosin or naprosyn or "naproxenate sodium" or "benzoylhydratropic acid" or "2-(3-Benzoylphenyl)propionic Acid" or profenid or alrheumum or orudis or alrheumat or dexibuprofen or s-ibuprofen or "S ibuprofen" or badyket or ketesse or sympal or quiralam or quirgel or adolquir or enangel or keral or enantyum or ketoprofen or dexketoprofen or celcoxib or celebrex or etoricoxib or arcoxia or nabumetone or arthraxan or "Gen-Nabumetone" or listran or relafen or relif or relifex or mebutan or "Rhoxal-nabumetone" or "Apo-Nabumetone" or celecoxib or nabucox) :ti,ab,kw (Word variations have been searched)	30873
	4-13 (OR)	*31559*
Limits: publication year		
	From 2011-2020	
Combined sets		
	3 AND 14 AND 15	**Central/ 844**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 20 December 2019
Title: Osteoarthritis – drug therapy (NSAID)

Search terms	Items found
Population: Osteoarthritis	
'osteoarthritis'/exp	127,379
'osteoarthritis therapy'/exp	143
'osteoarthritis pain'/exp	30
osteoarthr*:ab,kw,ti,de OR 'degenerative arthrit*':ab,kw,ti,de OR 'degenerative joint disease':ab,kw,ti,de OR coxarthr*:ab,kw,ti,de OR gonarthr*:ab,kw,ti,de OR ((heberdens OR bochards) NEAR/1 noduli):ab,kw,ti,de	147,532
1-4 (OR)	*141,108*
Intervention: NSAID	
'acetylsalicylic acid'/exp/mj	59,819
'diclofenac'/exp/mj	10,537
'diclofenac potassium'/exp/mj	229
'diclofenac plus misoprostol'/exp/mj	44
'piroxicam'/exp/mj	3,933
'piroxicam beta cyclodextrin'/exp/mj	76
'cinnoxicam'/exp/mj	47
'ibuprofen'/exp/mj	13,190
'naproxen'/exp/mj	7,371
'ketoprofen'/exp/mj	4,340
'ketoprofen lysine'/exp/mj	68
'celecoxib'/exp/mj	4,753
'ketorolac'/exp/mj	1,885
'tenoxicam'/exp/mj	635
'meloxicam'/exp/mj OR 'florfenicol plus meloxicam'/exp/mj	1,530
'ketorolac trometamol plus phenylephrine'/exp/mj OR 'ketorolac trometamol'/exp/mj	805
'dexibuprofen'/exp/mj	106
'dexketoprofen'/exp/mj OR 'dexketoprofen plus tramadol'/exp/mj	282
'parecoxib'/exp/mj	511
'etoricoxib'/exp/mj	653
'nabumetone'/exp/mj	473
'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw	137,966

	OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	
	6-27 (OR)	*170,180*
Study types: randomised controlled trials[2]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,508,903
Limits: publication date, language, human studies		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
	'animal'/exp NOT 'human'/exp	5,371,991
Combined sets		
	(5 AND 28 AND 29 AND 30) NOT 31	**1780**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 19 December 2019
Title: Osteoarthritis- drug therapy (NSAID)

Search terms		Items found
Population: Osteoarthritis		
	exp osteoarthritis/	61005
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,kw,ti.	72829
	1 OR 2	*92638*
Intervention: NSAID		
	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/ OR exp Ketorolac/ OR exp Meloxicam/	72693
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR	91929

[2] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	
	4 OR 5	*110609*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2666163
Limits: publication year, language		
	(yr="2011 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**383**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 8 January 2020 (CENTRAL)
Title: Osteoarthritis – drug therapy (Opioides)

Search terms		Items found
Population: Osteoarthritis		
	MeSH descriptor: [Osteoarthritis] explode all trees	6680
	osteoarthr* or degenerative next arthrit* or "degenerative joint disease" or coxarthr* or gonarthr*:ti,ab,kw or (heberdens or bochards) next (noduli):ti,ab,kw (Word variations have been searched)	16569
	1 OR 2	*16569*
Intervention: Opioides		
	MeSH descriptor: [Buprenorphine] explode all trees	1044
	MeSH descriptor: [Buprenorphine, Naloxone Drug Combination] explode all trees	11
	MeSH descriptor: [Codeine] explode all trees	1606
	MeSH descriptor: [Hydrocodone] explode all trees	202
	MeSH descriptor: [Oxycodone] explode all trees	845
	MeSH descriptor: [Hydromorphone] explode all trees	342
	MeSH descriptor: [Morphine] explode all trees	4749
	MeSH descriptor: [Meperidine] explode all trees	1138
	MeSH descriptor: [Fentanyl] explode all trees	5289
	MeSH descriptor: [Tramadol] explode all trees	1070
	MeSH descriptor: [Methadone] explode all trees	1189
	MeSH descriptor: [Tapentadol] explode all trees	60
	morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or	39300

	lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict:ti,ab,kw (Word variations have been searched)	
	4-16 (OR)	*40374*
Limits: publication year		
	From 2011-2020	
Combined sets		
	3 AND 17 AND 18	**Central/ 348**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 9 February 2018
Title: Osteoarthritis – drug therapy (Opioides)

Search terms		Items found
Population: Osteoarthritis		
	'osteoarthritis'/exp	127,379
	'osteoarthritis therapy'/exp	143
	'osteoarthritis pain'/exp	30
	osteoarthr*:ab,kw,ti,de OR 'degenerative arthrit*':ab,kw,ti,de OR 'degenerative joint disease':ab,kw,ti,de OR coxarthr*:ab,kw,ti,de OR gonarthr*:ab,kw,ti,de OR ((heberdens OR bochards) NEAR/1 noduli):ab,kw,ti,de	147,532
	1-4 (OR)	*141,108*
Intervention: Opioides		
	'buprenorphine'/exp/mj	6,425
	'buprenorphine plus naloxone'/exp/mj	582
	'codeine'/exp/mj	6,686
	'cocodamol'/exp/mj	156
	'hydrocodone'/exp/mj	719
	'hydrocodone bitartrate plus paracetamol'/exp/mj	89
	'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
	'oxycodone'/exp/mj	3,068
	'oxycodone plus paracetamol'/exp/mj	183
	'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
	'hydromorphone'/exp/mj	1,845
	'pethidine'/exp/mj	10,015

	'fentanyl'/exp/mj	17,310
	'tramadol'/exp/mj	4,304
	'paracetamol plus tramadol'/exp/mj	102
	'methadone'/exp/mj	14,055
	'codeine phosphate'/exp/mj	390
	'hydromorphone plus naloxone'/exp/mj	1
	'morphine'/exp/mj	46,853
	'ketobemidone'/exp/mj	207
	'tapentadol'/exp/mj	611
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	129,134
	6-27 (OR)	*155,896*
Study types: randomised controlled trials[3]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,508,903
Limits: publication date, language, human studies		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
	'animal'/exp NOT 'human'/exp	5,371,991
Combined sets		
	(5 AND 28 AND 29 AND 30) NOT 31	**515**

The search result, usually found at the end of the documentation, forms the list of abstracts.

[3] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 19 December 2019
Title: Osteoarthritis – drug therapy (Opioides)

Search terms		Items found
Population: Osteoarthritis		
	exp osteoarthritis/	61005
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,kw,ti.	72829
	1 OR 2	*92638*
Intervention: Opioides		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/ OR exp Tapentadol/	78261
	(morphia OR morphine OR pentahydrate OR "MS Contin" OR "Oramorph SR" OR duramorph OR dihydromorphinone OR hydromorphon OR palladone OR laudacon OR dilaudid OR hydromorphone OR dihydrone OR oxycone OR dihydrohydroxycodeinone OR oxycodeinon OR eucodal OR theocodin OR oxycodone OR oxycontin OR pancodine OR dinarkon OR oxiconum OR cetobemidon OR ketobemidone OR pethidine OR fentanyl OR isonipecain OR dolsin OR dolosal OR dolin OR "operidine EPJ-I" OR "operidine EPJ I" OR dolantin OR dolargan OR meperidine OR lidol OR lydol OR demerol OR dolcontral OR burenorphine OR codeine OR tramadol OR tapentadol OR methadone OR tramundin OR biodalgic OR jutadol OR nobligan OR prontofort OR zytram OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR biokanol OR tramabeta OR tramadin OR tramadolratiopharm OR tramadoc OR ranitidin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR adolonta OR contramal OR amadol OR phentanyl OR fentanest OR dentanyl OR sublimaze OR duragesic OR durogesic OR fentora OR buprenex OR prefin OR subutex OR buprex OR temgesic OR buprenorphine OR N-Methylmorphine OR Isocodeine OR Codeine OR Ardinex OR Biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict).ab,kf,kw,ti.	94329
	4 OR 5	*111715*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2666163
Limits: publication year, language		
	(yr="2011- Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**148**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title

.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 8 January 2020 (CENTRAL)
Title: Osteoarthritis – drug therapy (Paracetamol)

Search terms		Items found
Population: Osteoarthritis		
	MeSH descriptor: [Osteoarthritis] explode all trees	6680
	osteoarthr* or degenerative next arthrit* or "degenerative joint disease" or coxarthr* or gonarthr*:ti,ab,kw or (heberdens or bochards) next (noduli):ti,ab,kw (Word variations have been searched)	16569
	1 OR 2	*16569*
Intervention: Paracetamol		
	MeSH descriptor: [Acetaminophen] explode all trees	2992
	acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl:ti,ab,kw (Word variations have been searched)	10109
	4 OR 5	*10109*
Limits: publication year		
	From 2011-2020	
Combined sets		
	3 AND 6 AND 7	**Central/ 1036**

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:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 20 December 2019
Title: Osteoarthritis – drug therapy (Paracetamol)

Search terms		Items found
Population: Osteoarthritis		
	'osteoarthritis'/exp	127,379
	'osteoarthritis therapy'/exp	143
	'osteoarthritis pain'/exp	30
	osteoarthr*:ab,kw,ti,de OR 'degenerative arthrit*':ab,kw,ti,de OR 'degenerative joint disease':ab,kw,ti,de OR coxarthr*:ab,kw,ti,de OR gonarthr*:ab,kw,ti,de OR ((heberdens OR bochards) NEAR/1 noduli):ab,kw,ti,de	147,532
	1-4 (OR)	*141,108*
Intervention: Paracetamol		
	'paracetamol'/exp	88,23
	'cocodamol'/exp	1,603

	'oxycodone plus paracetamol'/exp	1,516
	'hydrocodone bitartrate plus paracetamol'/exp	1,374
	'dextropropoxyphene plus paracetamol'/exp	964
	acetaminophen:ab,ti,kw,de OR paracetamol:ab,ti,kw,de OR acetominophen:ab,ti,kw,de OR hydroxyacetanilide:ab,ti,kw,de OR apap:ab,ti,kw,de OR 'p acetamidophenol':ab,ti,kw,de OR 'p hydroxyacetanilide':ab,ti,kw,de OR 'n-(4-hydroxyphenyl)acetanilide':ab,ti,kw,de OR acetamidophenol:ab,ti,kw,de OR 'n-acetyl-p-aminophenol':ab,ti,kw,de OR 'n-acetyl-para-aminophenol':ab,ti,kw,de OR acephen:ab,ti,kw,de OR acetaco:ab,ti,kw,de OR tylenol:ab,ti,kw,de OR 'anacin 3':ab,ti,kw,de OR anacin3:ab,ti,kw,de OR datril:ab,ti,kw,de OR panadol:ab,ti,kw,de OR acamol:ab,ti,kw,de OR algotropyl:ab,ti,kw,de	95,672
	6–11 (OR)	*85,719*
Study types: randomised controlled trials[4]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,508,903
Limits: publication date, language, human studies		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2011-2020]/py	
	'animal'/exp NOT 'human'/exp	5,371,991
Combined sets		
	(5 AND 12 AND 13 AND 14) NOT 15	**798**

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/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 19 December 2019
Title: Osteoarthritis – drug therapy (Paracetamol)

Search terms		Items found
Population: Osteoarthritis		
	exp osteoarthritis/	61005
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,kw,ti.	72829
	1 OR 2	*92638*
Intervention: Paracetamol		
	exp Acetaminophen/	17743
	(acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl).ab,kf,kw,ti.	24946
	4 OR 5	*27776*

[4] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2666163
Limits: publication year, language		
	(yr="2011 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**169**

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* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Part II Diabetic polyneuropathy/Diabetesneuropati

Systematic reviews/Systematiska översikter

Cochrane Library via Wiley 20 December 2017 (CDSR, DARE & CENTRAL)
Title: Diabetic neuropathies – drug therapy

Search terms		Items found
Population: Diabetic neuropathies		
	MeSH descriptor: [Diabetic Nephropathies] explode all trees	1195
	diabet* and neuropat* near/15 pain*:ti,ab,kw (Word variations have been searched)	729
Combined sets		
	1 OR 2	1917 **CDSR/45** **DARE/77** **HTA/5**

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:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Cochrane Library via Wiley 12 December 2019 (CDSR)
Title: Diabetic neuropathies – drug therapy (opioider)

Search terms		Items found
Population: Diabetic neuropathies		
	MeSH descriptor: [Diabetic Nephropathies] explode all trees	1864
	diabet* and neuropat* near/15 pain*:ti,ab,kw (Word variations have been searched)	1268
Combined sets		
	1 OR 2 From 1990 to 2019	2713 **CDSR/58**

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:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review

Embase via Elsevier 11 December 2019
Title: Diabetic neuropathy – drug therapy

Search terms	Items found
Population: Diabetic neuropathy	
'diabetic neuropathy'/exp OR 'diabetic neuropathic pain'/exp	24,304
((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland":ab,ti	18,334
1 OR 2	*29,905*
Intervention: Drug therapy (Tricyclic antidepressants)	
'amitriptyline'/exp OR 'amitriptyline plus perphenazine'/exp OR 'amitriptyline plus chlordiazepoxide'/exp OR 'nortriptyline'/exp OR 'maprotiline'/exp OR 'clomipramine'/exp	57,423
amineurin:ti,ab OR amitrip:ti,ab OR amitriptylin:ti,ab OR amitriptyline:ti,ab OR amitrol:ti,ab OR anapsique:ti,ab OR 'apo amitriptyline':ti,ab OR damilen:ti,ab OR domical:ti,ab OR elavil:ti,ab OR endep:ti,ab OR laroxyl:ti,ab OR lentizol:ti,ab OR novoprotect:ti,ab OR saroten:ti,ab OR sarotex:ti,ab OR syneudon:ti,ab OR triptafen:ti,ab OR tryptanol:ti,ab OR tryptine:ti,ab OR tryptizol:ti,ab OR allegron:ti,ab OR 'apo nortriptyline':ti,ab OR aventyl:ti,ab OR desitriptyline:ti,ab OR desmethylamitriptylin:ti,ab OR 'gen nortriptyline':ti,ab OR norfenazin:ti,ab OR nortrilen:ti,ab OR nortriptylin:ti,ab OR nortriptyline:ti,ab OR 'novo nortriptyline':ti,ab OR 'nu nortriptyline':ti,ab OR pamelor:ti,ab OR paxtibi:ti,ab OR 'pms nortriptyline':ti,ab OR 'ratio nortriptyline':ti,ab OR deprilept:ti,ab OR dibencycladine:ti,ab OR ludiomil:ti,ab OR maprolu:ti,ab OR maprotilin:ti,ab OR maprotiline:ti,ab OR mirpan:ti,ab OR 'novo maprotiline':ti,ab OR psymion:ti,ab OR 'ba34,276':ti,ab OR 'ba-34,276':ti,ab OR 'n-methyl-9,10-ethanoanthracene-9(10h)-propylamine':ti,ab OR anafranil:ti,ab OR chlomipramin:ti,ab OR chlomipramine:ti,ab OR chlorimipramine:ti,ab OR hydiphen:ti,ab	12,803
4 OR 5	*58,397*
Intervention: Drug therapy (SNRI)	
'venlafaxine'/exp OR 'duloxetine'/exp	27,105
dobupal:ab,ti OR efexor:ab,ti OR effexor:ab,ti OR 'sila venlafaxine':ab,ti OR trevilor:ab,ti OR vandral:ab,ti OR venlafaxin:ab,ti OR venlafaxine:ab,ti OR 'wy 45030':ab,ti OR '1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl':ab,ti OR 'cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride':ab,ti OR cymbalta:ab,ti OR 'duloxetine':ab,ti OR duloxetine:ab,ti OR 'ly 227942':ab,ti OR 'ly 248686':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide':ab,ti	9,520
7 OR 8	*27,586*
Intervention: Drug therapy (antiepileptic drugs)	
'gabapentin'/exp OR 'pregabalin'/exp OR 'etiracetam'/exp OR 'lamotrigine'/exp OR 'lacosamide'/exp OR 'carbamazepine'/exp OR 'oxcarbazepine'/exp OR 'topiramate'/exp OR 'phentermine plus topiramate'/exp OR 'valproic acid'/exp OR 'zonisamide'/exp	148,636
convalis:ab,ti OR gabapentin:ab,ti OR gabapentine:ab,ti OR 'pms gabapentin':ab,ti OR neurontin:ab,ti OR 'novo gabapentin':ab,ti OR 'apo gabapentin':ab,ti OR lyrica:ab,ti OR pregabalin:ab,ti OR pregabaline:ab,ti OR etiracetam:ab,ti OR etiracetame:ab,ti OR keppra:ab,ti OR levetiracetam:ab,ti OR levetiracetame:ab,ti OR risomet:ab,ti OR labileno:ab,ti OR lamictal:ab,ti OR lamiktal:ab,ti OR lamotrigin:ab,ti OR lamotrigine:ab,ti OR lacosamid:ab,ti OR lacosamide:ab,ti OR vimpat:ab,ti OR mizepine:ab,ti OR carbamazepin:ab,ti OR carbamazepine:ab,ti OR carbazepin:ab,ti OR epitol:ab,ti OR finlepsin:ab,ti OR neurotol:ab,ti OR tegretol:ab,ti OR oxcarbazepin:ab,ti OR oxcarbazepine:ab,ti OR timox:ab,ti OR trileptal:ab,ti OR epitomax:ab,ti OR topamax:ab,ti OR topiramat:ab,ti OR topiramate:ab,ti OR convulsofin:ab,ti OR depakene:ab,ti OR depakine:ab,ti OR depakote:ab,ti OR divalproex:ab,ti OR ergenyl:ab,ti OR 'propylisopropylacetic acid':ab,ti OR valproat:ab,ti OR valproate:ab,ti OR 'valproic acid':ab,ti OR vupral:ab,ti OR zonisamid:ab,ti OR zonisamide:ab,ti OR zonegran:ab,ti	67,953
10 OR 11	*152,818*
Intervention: Drug therapy (topical treatment)	
'lidocaine'/exp OR 'capsaicin'/exp	91,816

	dalcaine:ab,ti OR lidocain:ab,ti OR lidocaine:ab,ti OR lignocaine:ab,ti OR octocaine:ab,ti OR xylesthesin:ab,ti OR xylocaine:ab,ti OR xylocitin:ab,ti OR xyloneural:ab,ti OR '2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide':ab,ti OR '2-2etn-2mephacn':ab,ti OR instillagel:ab,ti OR cophenylcaine:ab,ti OR aurobin:ab,ti OR 'neo lidocaton':ab,ti OR axsain:ab,ti OR capsaicin:ab,ti OR capsaicine:ab,ti OR capsicum:ab,ti OR capsidol:ab,ti OR capsin:ab,ti OR capzasin:ab,ti OR gelcen:ab,ti OR katrum:ab,ti OR zacin:ab,ti OR zostrix:ab,ti OR 'ngx4010':ab,ti OR '8-methyl-n-vanillyl-6-nonenamide':ab,ti	52,049
	13 OR 14	*100,776*
Intervention: Opioides		
	'buprenorphine'/exp/mj	6,412
	'buprenorphine plus naloxone'/exp/mj	578
	'codeine'/exp/mj	6,685
	'cocodamol'/exp/mj	156
	'hydrocodone'/exp/mj	713
	'hydrocodone bitartrate plus paracetamol'/exp/mj	89
	'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
	'oxycodone'/exp/mj	3,059
	'oxycodone plus paracetamol'/exp/mj	182
	'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
	'hydromorphone'/exp/mj	1,845
	'pethidine'/exp/mj	10,015
	'fentanyl'/exp/mj	17,299
	'tramadol'/exp/mj	4,300
	'paracetamol plus tramadol'/exp/mj	102
	'methadone'/exp/mj	14,041
	'codeine phosphate'/exp/mj	390
	'hydromorphone plus naloxone'/exp/mj	1
	'morphine'/exp/mj	46,830
	'ketobemidone'/exp/mj	207
	'tapentadol'/exp/mj	609
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti	128,959

	OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	
	16-38 (OR)	*155,714*
Study types: systematic reviews, meta analysis		
	'systematic review'/de	225,484
	'meta analysis'/de	174,508
	[cochrane review]/lim	20,872
	'review'/exp AND [1990-2007]/py	1,125,800
	(systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab	338,515
	39-43 (OR)	1,509,020
	44 NOT ('editorial'/it OR 'erratum'/it OR 'letter'/it OR 'note'/it)	1,489,125
Limits: language, publication year		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
Combined sets		
	3 AND (6 OR 9 OR 12 OR 15 OR 38) AND 45 AND 46	**647**

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/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 11 December 2019
Title: Diabetic neuropathies – drug therapy

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	21931
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	13039
	1-2 (OR)	*26712*
Intervention: Drug therapy (Tricyclic antidepressants)		
	exp amitriptyline/ or exp nortriptyline/ OR exp Maprotiline/ OR exp Clomipramine/	11203
	(amineurin OR amitrip OR amitriptylin OR amitriptyline OR amitrol OR anapsique OR apo-amitriptyline OR damilen OR domical OR elavil OR endep OR laroxyl OR lentizol OR novoprotect OR saroten OR sarotex OR syneudon OR triptafen OR tryptanol OR tryptine OR tryptizol OR allegron OR apo-Nortriptyline OR aventyl OR desitriptyline OR desmethylamitriptylin OR gen-nortriptyline OR norfenazin OR nortrilen OR nortriptylin OR nortriptyline OR novo-nortriptyline OR nu-nortriptyline OR pamelor OR paxtibi OR PMS-nortriptyline OR ratio-nortriptyline OR deprilept OR dibencycladine OR ludiomil OR maprolu OR maprotilin OR maprotiline OR mirpan OR novo-maprotiline OR psymion OR "Ba34,276" OR "Ba-34,276" OR "N-Methyl-9,10-ethanoanthracene-9(10H)-propylamine" OR anafranil OR chlomipramin OR chlomipramine OR chlorimipramine OR hydiphen):ti,ab,kf	9623
	4 OR 5	*14808*
Intervention: Drug therapy (SNRI)		
	exp Venlafaxine Hydrochloride/ OR exp Duloxetine Hydrochloride/	3916
	Dobupal OR efexor OR effexor OR sila-venlafaxine OR trevilor OR vandral OR venlafaxin OR	5936

	venlafaxine OR "wy 45030" OR "1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl" OR "cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride" OR cymbalta OR duloxetin OR duloxetine OR "LY 227942" OR "LY 248686" OR "N-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine" OR "N-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide"	
	7 OR 8	*5853*
Intervention: Drug therapy (antiepileptic drugs)		
	exp Pregabalin/ OR exp Carbamazepine/ OR exp Valproic Acid OR exp Gabapentin/ OR exp Levetiracetam/ OR exp Lamotrigine/ OR exp Oxcarbazepine/ OR exp Topiramate/ OR exp Zonisamide/	32561
	convalis OR gabapentin OR gabapentine OR pms-gabapentin OR neurontin OR novo-gabapentin OR apo-gabapentin OR "1-(aminomethyl)cyclohexaneacetic acid" OR lyrica OR pregabalin OR pregabaline OR "(r-)-3-isobutyl gaba" OR "(s)-3-(aminomethyl)-5-methylhexanoic acid" OR "(s+)-3-isobutyl gaba" OR "1008, ci" OR "3-(aminomethyl)-5-methylhexanoic acid" OR "3-isobutyl gaba" OR "ci 1008"OR "ci1008" OR "gaba, 3-isobutyl" OR etiracetam OR etiracetame OR keppra OR levetiracetam OR levetiracetame OR "UCB 6474" OR "ucb L059" OR "ucb L060" OR "alpha-ethyl-2-oxo-1-pyrrolidineacetamide" OR crisomet OR labileno OR lamictal OR lamiktal OR lamotrigin OR lamotrigine OR "3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine" OR "3,5-diamino-6-(2,3-dichlorophenyl)-as-triazine" OR "bw-430c" OR lacosamid OR lacosamide OR vimpat OR "n-benzyl-2-acetamido-3-methoxypropionamide" OR "n-benzyl-acmeoprnh2" OR amizepine OR carbamazepin OR carbamazepine OR carbazepin OR epitol OR finlepsin OR neurotol OR tegretol OR oxcarbazepin OR oxcarbazepine OR timox OR trileptal OR "10,11-dihydro-10-oxo-5H-dibenz(b,f)azepine-5-carboxamide" OR "GP 47680" OR epitomax OR topamax OR topiramat OR topiramate OR usl255 OR "2,3-4,5-bis-o-(1-methylethylidene)-beta-d-fructopyranose sulfamate" OR "mcn 4853" OR convulsofin OR depakene OR depakine OR depakote OR divalproex OR "divalproex sodium" OR ergenyl OR "propylisopropylacetic acid" OR valproat OR valproate OR "valproic acid" OR vupral OR "2-propylpentanoic acid" OR zonisamid OR zonisamide OR zonegran OR "1,2-benzisoxazole-3-methanesulfonamide" OR "3-sulfamoylmethyl-1,2-benzisoxazole" OR "AD 810" OR "CI 912"	44891
	10 OR 11	*49691*
Intervention: Drug therapy (topical treatment)		
	exp Lidocaine/ OR exp Capsaicin/	34184
	dalcaine OR lidocain OR lidocaine OR lignocaine OR octocaine OR xylesthesin OR xylocaine OR xylocitin OR xyloneural OR "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " OR "2-2etn-2mephacn" OR instillagel OR cophenylcaine OR aurobin OR "neo lidocaton" OR axsain OR capsaicin OR capsaicine OR capsicum OR capsidol OR capsin OR capzasin OR gelcen OR katrum OR zacin OR zostrix OR "NGX4010 " OR "8-Methyl-N-Vanillyl-6-Nonenamide"	40786
	13 OR 14	*50016*
Intervention: Drug therapy (opioides)		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/ OR exp Tapentadol/	78115
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or	94130

	Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict).ab,kf,ti.	
	16 OR 17	*111455*
Study types: systematic reviews, metaanalysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	3 AND (6 OR 9 OR 12 OR 15 AND 18) AND 19 AND 20	**80**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Primary studies/Primärstudier

Cochrane Library via Wiley 4 October 2018 (CENTRAL)
Title: Diabetic neuropathies – drug therapy

Search terms		Items found
Population: Diabetic neuropathies		
	MeSH descriptor: [Diabetic Nephropathies] explode all trees	1719
	((diabetic) near/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ti,ab,kw (Word variations have been searched)	2589
	diabet* and neuropat* near/15 pain*:ti,ab,kw (Word variations have been searched)	894
	"Bruns-Garland":ti,ab,kw (Word variations have been searched)	1
	1-4 (OR)	*3287*
Intervention: Opioides		
	[mh Buprenorphine]	988
	[mh "buprenorphine, naloxone drug combination"]	96
	[mh Codeine]	1502
	[mh Hydrocodone]	183
	[mh Oxycodone]	756
	[mh Hydromorphone]	312
	[mh Morphine]	4533
	[mh Meperidine]	1124
	[mh Fentanyl]	5042
	[mh Tramadol]	1005
	[mh Methadone]	1152
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or	33807

	tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict):ti,ab,kw	
	6-17 (OR)	*34845*
Limits: publication year		
	with Publication Year from 1990 to 2018, in Trials	
Combined sets		
	5 AND 18 AND 19	**Central/ 86**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials

Cochrane Library via Wiley 16 December 2019 (CENTRAL)
Title: Diabetic neuropathies – drug therapy

Search terms		Items found
Population: Diabetic neuropathies		
	MeSH descriptor: [Diabetic Nephropathies] explode all trees	1397
	((diabetic) near/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ti,ab,kw (Word variations have been searched)	2248
	diabet* and neuropat* near/15 pain*:ti,ab,kw (Word variations have been searched)	536
	"Bruns-Garland":ti,ab,kw (Word variations have been searched)	1
	1-4 (OR)	*2758*
Limits: publication year		
	2016-2019	
Combined sets		
	5 AND 6	**Central/ 780**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials

Medline via OvidSP 20 Mars 2018
Title: Diabetic neuropathies – drug therapy

Search terms		Items found
Population: Diabetic neuropathies		
	Diabetic Neuropathies/	20181
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11769
	1-2 (OR)	*24319*
Intervention: Drug therapy (Tricyclic antidepressants)		
	exp amitriptyline/ or exp nortriptyline/ OR exp Maprotiline/ OR exp Clomipramine/	10984
	amineurin OR amitrip OR amitriptylin OR amitriptyline OR amitrol OR anapsique OR apo-amitriptyline OR damilen OR domical OR elavil OR endep OR laroxyl OR lentizol OR novoprotect OR saroten OR sarotex OR syneudon OR triptafen OR tryptanol OR tryptine OR tryptizol OR allegron OR apo-Nortriptyline OR aventyl OR desitriptyline OR desmethylamitriptylin OR gen-nortriptyline OR norfenazin OR nortrilen OR nortriptylin OR nortriptyline OR novo-nortriptyline OR nu-nortriptyline OR pamelor OR paxtibi OR PMS-nortriptyline OR ratio-nortriptyline OR deprilept OR dibencycladine OR ludiomil OR maprolu OR maprotilin OR maprotiline OR mirpan OR novo-maprotiline OR psymion OR "Ba34,276" OR "Ba-34,276" OR "N-Methyl-9,10-ethanoanthracene-9(10H)-propylamine" OR anafranil OR chlomipramin OR chlomipramine OR chlorimipramine OR hydiphen	9259
	4 OR 5	*14367*
Intervention: Drug therapy (SNRI)		
	exp Venlafaxine Hydrochloride/ OR exp Duloxetine Hydrochloride/	3610
	Dobupal OR efexor OR effexor OR sila-venlafaxine OR trevilor OR vandral OR venlafaxin OR venlafaxine OR "wy 45030" OR "1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl" OR "cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride" OR cymbalta OR duloxetin OR duloxetine OR "LY 227942" OR "LY 248686" OR "N-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine" OR "N-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide"	5352
	7 OR 8	*5853*
Intervention: Drug therapy (antiepileptic drugs)		
	exp Pregabalin/ OR exp Carbamazepine/ OR exp Valproic Acid	21873
	convalis OR gabapentin OR gabapentine OR pms-gabapentin OR neurontin OR novo-gabapentin OR apo-gabapentin OR "1-(aminomethyl)cyclohexaneacetic acid" OR lyrica OR pregabalin OR pregabaline OR "(r-)-3-isobutyl gaba" OR "(s)-3-(aminomethyl)-5-methylhexanoic acid" OR "(s+)-3-isobutyl gaba" OR "1008, ci" OR "3-(aminomethyl)-5-methylhexanoic acid" OR "3-isobutyl gaba" OR "ci 1008"OR "ci1008" OR "gaba, 3-isobutyl" OR etiracetam OR etiracetame OR keppra OR levetiracetam OR levetiracetame OR "UCB 6474" OR "ucb L059" OR "ucb L060" OR "alpha-ethyl-2-oxo-1-pyrrolidineacetamide" OR crisomet OR labileno OR lamictal OR lamiktal OR lamotrigin OR lamotrigine OR "3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine" OR "3,5-diamino-6-(2,3-dichlorophenyl)-as-triazine" OR "bw-430c" OR lacosamid OR lacosamide OR vimpat OR "n-benzyl-2-acetamido-3-methoxypropionamide" OR "n-benzyl-acmeoprnh2" OR amizepine OR carbamazepin OR carbamazepine OR carbazepin OR epitol OR finlepsin OR neurotol OR tegretol OR oxcarbazepin OR oxcarbazepine OR timox OR trileptal OR "10,11-dihydro-10-oxo-5H-dibenz(b,f)azepine-5-carboxamide" OR "GP 47680" OR epitomax OR topamax OR topiramat OR topiramate OR usl255 OR "2,3-4,5-bis-o-(1-methylethylidene)-beta-d-fructopyranose sulfamate" OR "mcn 4853" OR convulsofin OR depakene OR depakine OR depakote OR divalproex OR "divalproex sodium" OR ergenyl OR "propylisopropylacetic acid" OR valproat OR valproate OR "valproic acid" OR vupral OR "2-propylpentanoic acid" OR zonisamid OR zonisamide OR zonegran OR "1,2-benzisoxazole-3-methanesulfonamide" OR "3-sulfamoylmethyl-1,2-benzisoxazole" OR "AD 810" OR "CI 912"	40935
	10 OR 11	*44637*
Intervention: Drug therapy (topical treatment)		
	exp Lidocaine/ OR exp Capsaicin/ OR exp Lidocaine/ OR exp Capsaicin/	32786
	dalcaine OR lidocain OR lidocaine OR lignocaine OR octocaine OR xylesthesin OR xylocaine OR xylocitin OR xyloneural OR "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " OR "2-2etn-2mephacn" OR instillagel OR cophenylcaine OR aurobin OR "neo lidocaton" OR axsain	38074

	OR capsaicin OR capsaicine OR capsicum OR capsidol OR capsin OR capzasin OR gelcen OR katrum OR zacin OR zostrix OR "NGX4010 " OR "8-Methyl-N-Vanillyl-6-Nonenamide"	
	13 OR 14	*47030*
Study types: systematic reviews, metaanalysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - 2018") and (danish or english or norwegian or swedish)	
Combined sets		
	3 AND (6 OR 9 OR 12 OR 15) AND 16 AND 17	**118**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Embase via Elsevier 16 December 2019
Title: Diabetic neuropathies – drug therapy (Antiepileptic drugs)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp OR 'diabetic neuropathic pain'/exp	24,304
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland".ab,ti	18,334
	1 OR 2	*29,905*
Intervention: Drug therapy (antiepileptic drugs)		
	'gabapentin'/exp OR 'pregabalin'/exp OR 'etiracetam'/exp OR 'lamotrigine'/exp OR 'lacosamide'/exp OR 'carbamazepine'/exp OR 'oxcarbazepine'/exp OR 'topiramate'/exp OR 'phentermine plus topiramate'/exp OR 'valproic acid'/exp OR 'zonisamide'/exp	148,636
	convalis:ab,ti OR gabapentin:ab,ti OR gabapentine:ab,ti OR 'pms gabapentin':ab,ti OR neurontin:ab,ti OR 'novo gabapentin':ab,ti OR 'apo gabapentin':ab,ti OR lyrica:ab,ti OR pregabalin:ab,ti OR pregabaline:ab,ti OR etiracetam:ab,ti OR etiracetame:ab,ti OR keppra:ab,ti OR levetiracetam:ab,ti OR levetiracetame:ab,ti OR risomet:ab,ti OR labileno:ab,ti OR lamictal:ab,ti OR lamiktal:ab,ti OR lamotrigin:ab,ti OR lamotrigine:ab,ti OR lacosamid:ab,ti OR lacosamide:ab,ti OR vimpat:ab,ti OR mizepine:ab,ti OR carbamazepin:ab,ti OR carbamazepine:ab,ti OR carbazepin:ab,ti OR epitol:ab,ti OR finlepsin:ab,ti OR neurotol:ab,ti OR tegretol:ab,ti OR oxcarbazepin:ab,ti OR oxcarbazepine:ab,ti OR timox:ab,ti OR trileptal:ab,ti OR epitomax:ab,ti OR topamax:ab,ti OR topiramat:ab,ti OR topiramate:ab,ti OR convulsofin:ab,ti OR depakene:ab,ti OR depakine:ab,ti OR depakote:ab,ti OR divalproex:ab,ti OR ergenyl:ab,ti OR 'propylisopropylacetic acid':ab,ti OR valproat:ab,ti OR valproate:ab,ti OR 'valproic acid':ab,ti OR vupral:ab,ti OR zonisamid:ab,ti OR zonisamide:ab,ti OR zonegran:ab,ti	67,953
	4 OR 5	*152,818*

Study types: randomised controlled trials[5]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,505,088
	'animal'/exp NOT 'human'/exp	5,368,733
	7 NOT 8	*2,260,725*
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2016-2020]/py	
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**67**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 13 December 2019
Title: Diabetic neuropathies – drug therapy (Antiepileptic drugs)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	20290
	((diabetic) adj3 (neuropath* OR neuralg* OR polyneuropath* OR mononeuropath* OR amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11843
	1 OR 2	*24459*
Intervention: Drug therapy (antiepileptic drugs)		
	exp Pregabalin/ OR exp Carbamazepine/ OR exp Valproic Acid OR exp Gabapentin/ OR exp Levetiracetam/ OR exp Lamotrigine/ OR exp Oxcarbazepine/ OR exp Topiramate/ OR exp Zonisamide/	32580
	convalis OR gabapentin OR gabapentine OR pms-gabapentin OR neurontin OR novo-gabapentin OR apo-gabapentin OR "1-(aminomethyl)cyclohexaneacetic acid" OR lyrica OR pregabalin OR pregabaline OR "(r-)-3-isobutyl gaba" OR "(s)-3-(aminomethyl)-5-methylhexanoic acid" OR "(s+)-3-isobutyl gaba" OR "1008, ci" OR "3-(aminomethyl)-5-methylhexanoic acid" OR "3-isobutyl gaba" OR "ci 1008"OR "ci1008" OR "gaba, 3-isobutyl" OR etiracetam OR etiracetame OR keppra OR levetiracetam OR levetiracetame OR "UCB 6474" OR "ucb L059" OR "ucb L060" OR "alpha-ethyl-2-oxo-1-pyrrolidineacetamide" OR crisomet OR labileno OR lamictal OR lamiktal OR lamotrigin OR lamotrigine OR "3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine" OR "3,5-diamino-6-(2,3-dichlorophenyl)-as-triazine" OR "bw-430c" OR lacosamid OR lacosamide OR vimpat OR "n-benzyl-2-acetamido-3-methoxypropionamide" OR "n-benzyl-acmeoprnh2" OR amizepine OR carbamazepin OR	44929

[5] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	carbamazepine OR carbazepin OR epitol OR finlepsin OR neurotol OR tegretol OR oxcarbazepin OR oxcarbazepine OR timox OR trileptal OR "10,11-dihydro-10-oxo-5H-dibenz(b,f)azepine-5-carboxamide" OR "GP 47680" OR epitomax OR topamax OR topiramat OR topiramate OR usl255 OR "2,3-4,5-bis-o-(1-methylethylidene)-beta-d-fructopyranose sulfamate" OR "mcn 4853" OR convulsofin OR depakene OR depakine OR depakote OR divalproex OR "divalproex sodium" OR ergenyl OR "propylisopropylacetic acid" OR valproat OR valproate OR "valproic acid" OR vupral OR "2-propylpentanoic acid" OR zonisamid OR zonisamide OR zonegran OR "1,2-benzisoxazole-3-methanesulfonamide" OR "3-sulfamoylmethyl-1,2-benzisoxazole" OR "AD 810" OR "CI 912"	
	4 OR 5	*49730*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized OR randomised OR placebo OR randomly OR trial OR groups).ab. OR exp controlled clinical trial/ OR exp randomized controlled trial/ OR exp pragmatic clinical trial/ OR exp Clinical Trials as Topic/ OR drug therapy/) not (exp animals/ not humans.sh.)	2659118
Limits: publication year, language		
	(yr="2011 - Current" and (danish OR english OR norwegian OR swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**156**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract OR title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* OR $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 8 May 2018 (CENTRAL)
Title: Diabetic neuropathies – drug therapy (Lidocaine) studies 2009-2016

Search terms		Items found
Population: Diabetic neuropathies		
	MeSH descriptor: [Diabetic Nephropathies] explode all trees	1212
	((diabetic) near/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ti,ab,kw (Word variations have been searched)	2244
	diabet* and neuropat* near/15 pain*:ti,ab,kw (Word variations have been searched)	743
	"Bruns-Garland":ti,ab,kw (Word variations have been searched)	1
	1-4 (OR)	*3421*
Intervention: Lidocaine		
	MeSH descriptor: [Lidocaine] explode all trees	4375
	(dalcaine or lidocain or lidocaine or lignocaine or octocaine or xylesthesin or xylocaine or xylocitin or xyloneural or "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " or "2-2etn-2mephacn" or instillagel or cophenylcaine or aurobin or "neo lidocaton"):ti,ab,kw (Word variations have been searched)	9170
	6 OR 7	*9170*
Limits: publication year		
	2009-2018	
Combined sets		
	5 AND 8 AND 9	**Central/ 17**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials

Embase via Elsevier 8 May 2018
Title: Diabetic neuropathies – drug therapy (Lidocaine) studies 2009-2016

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp	21,943
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland".ab,ti	16,455
	1 OR 2	*27,201*
Intervention: Lidocaine		
	'lidocaine'/exp	69,073
	dalcaine:ti,ab OR lidocain:ti,ab OR lidocaine:ti,ab OR lignocaine:ti,ab OR octocaine:ti,ab OR xylesthesin:ti,ab OR xylocaine:ti,ab OR xylocitin:ti,ab OR xyloneural:ti,ab OR '2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide':ab,ti OR '2-2etn-2mephacn':ti,ab OR instillagel:ti,ab OR cophenylcaine:ti,ab OR aurobin:ti,ab OR 'neo lidocaton':ti,ab	30,959
	4 OR 5	*73,020*
Study types: randomised controlled trials[6]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,230,620
	'animal'/exp NOT 'human'/exp	5,035,633
	7 NOT 8	*2,013,820*
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND ([1-1-2009]/sd NOT [1-1-2019]/sd)	
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**46**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary

[6] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 9 May 2018
Title: Diabetic neuropathies – drug therapy (Lidocaine) studies 2009-2016

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	20345
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11873
	1-2 (OR)	*24530*
Intervention: Lidocaine		
	exp Lidocaine/	23280
	(dalcaine or lidocain or lidocaine or lignocaine or octocaine or xylesthesin or xylocaine or xylocitin or xyloneural or "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " or "2-2etn-2mephacn" or instillagel or cophenylcaine or aurobin or "neo lidocaton").ab,kf,ti.	23871
	4-5 (OR)	*31701*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not exp humans/)	2405194
Limits: Publication year, language		
	(yr="2009 - 2019" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**24**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Embase via Elsevier 13 December 2019
Title: Diabetic neuropathies – drug therapy(opioides)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp	24,304
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR	18,334

	"Bruns-Garland".ab,ti	
	1 OR 2	*29,905*
Intervention: Opioides		
	'buprenorphine'/exp/mj	6,414
	'buprenorphine plus naloxone'/exp/mj	579
	'codeine'/exp/mj	6,685
	'cocodamol'/exp/mj	156
	'hydrocodone'/exp/mj	715
	'hydrocodone bitartrate plus paracetamol'/exp/mj	89
	'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
	'oxycodone'/exp/mj	3,061
	'oxycodone plus paracetamol'/exp/mj	182
	'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
	'hydromorphone'/exp/mj	1,845
	'pethidine'/exp/mj	10,015
	'fentanyl'/exp/mj	17,302
	'tramadol'/exp/mj	4,303
	'paracetamol plus tramadol'/exp/mj	102
	'methadone'/exp/mj	14,042
	'codeine phosphate'/exp/mj	390
	'hydromorphone plus naloxone'/exp/mj	1
	'morphine'/exp/mj	46,837
	'ketobemidone'/exp/mj	207
	'tapentadol'/exp/mj	609
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	128,998
	4-25 (OR)	155,755

Study types: randomized controlled trials[7]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,222,531
	'animal'/exp NOT 'human'/exp	5,026,979
	27 NOT 28	*2,006,444*
Limits: language, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim)	
	([article]/lim OR [article in press]/lim OR [erratum]/lim) AND [1990-2020]/py	
Combined sets		
	3 AND 26 AND 29 AND 30 AND 31	**57**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 13 December 2019
Title: Diabetic neuropathies – drug therapy(opioides)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	21942
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	13055
	1-2 (OR)	*26733*
Intervention: Opioides		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/ OR exp Tapentadol/	78138
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or	94191

[7] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict).ab,kf,ti.	
	4- 5(OR)	*111519*
Study types: randomised controlled trials and other trials		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not exp humans/)	2659118
Limits: publication year, language		
	(yr="1990 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**90**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Embase via Elsevier 25 juni 2018
Title: Diabetic neuropathies – drug therapy (SNRI)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp	22082
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland":ab,ti	16576
	1 OR 2	*27369*
Intervention: drug therapy (SNRI)		
	'venlafaxine'/exp OR 'duloxetine'/exp	25197
	dobupal:ab,ti OR efexor:ab,ti OR effexor:ab,ti OR 'sila venlafaxine':ab,ti OR trevilor:ab,ti OR vandral:ab,ti OR venlafaxin:ab,ti OR venlafaxine:ab,ti OR 'wy 45030':ab,ti OR '1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl':ab,ti OR 'cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride':ab,ti OR cymbalta:ab,ti OR 'duloxetine':ab,ti OR duloxetine:ab,ti OR 'ly 227942':ab,ti OR 'ly 248686':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide':ab,ti	8653
	4 OR 5	*25624*
Study types: randomised controlled trials[8]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl*	2247142

[8] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
	'animal'/exp NOT 'human'/exp	5058314
	7 NOT 8	*2028237*
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2015]/py	18476420
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	23476420
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**145**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Embase via Elsevier 13 December 2019
Title: Diabetic neuropathies – drug therapy (SNRI)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp	24,304
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland".ab,ti	18,334
	1 OR 2	*29,905*
Intervention: SNRI		
	'venlafaxine'/exp OR 'duloxetine'/exp	27,105
	dobupal:ab,ti OR efexor:ab,ti OR effexor:ab,ti OR 'sila venlafaxine':ab,ti OR trevilor:ab,ti OR vandral:ab,ti OR venlafaxin:ab,ti OR venlafaxine:ab,ti OR 'wy 45030':ab,ti OR '1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl':ab,ti OR 'cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride':ab,ti OR cymbalta:ab,ti OR 'duloxetine':ab,ti OR duloxetine:ab,ti OR 'ly 227942':ab,ti OR 'ly 248686':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine':ab,ti OR 'n-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide':ab,ti	9,520
	4 OR 5	*27,586*
Study types: randomised controlled trials[9]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,222,531
	'animal'/exp NOT 'human'/exp	5,026,979

[9] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	7 NOT 8	2,006,444
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2016-2020]/py	
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**36**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 25 juni 2018
Title: Diabetic neuropathies – drug therapy (SNRI)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	20459
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11962
	1 OR 2	*24692*
Intervention: drug therapy (SNRI)		
	exp Venlafaxine Hydrochloride/ OR exp Duloxetine Hydrochloride/	3657
	(dobupal OR efexor OR effexor OR sila-venlafaxine OR trevilor OR vandral OR venlafaxin OR venlafaxine OR "wy 45030" OR "1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl" OR "cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride" OR cymbalta OR duloxetin OR duloxetine OR "LY 227942" OR "LY 248686" OR "N-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine" OR "N-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide").ab,ti	5418
	4 OR 5	*5925*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2420239
Limits: publication year, language		
	(yr="1990 - 2015" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**124**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Medline via OvidSP 13 December 2019
Title: Diabetic neuropathies – drug therapy (SNRI)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	21942
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	13055
	1-2 (OR)	*26733*
Intervention: Drug therapy (SNRI)		
	exp Venlafaxine Hydrochloride/ OR exp Duloxetine Hydrochloride/	3919
	(Dobupal or efexor or effexor or sila-venlafaxine or trevilor or vandral or venlafaxin or venlafaxine or "wy 45030" or "1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl" or "cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride" or cymbalta or duloxetin or duloxetine or "LY 227942" or "LY 248686" or "N-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine" or "N-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide").ab,kf,ti.	5941
	4 OR 5	*6474*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2659118
Limits: publication year, language		
	(yr="2016 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**21**

The search result, usually found at the end of the documentation, forms the list of abstracts.
.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Embase via Elsevier 25 juni 2018
Title: Diabetic neuropathies – drug therapy (Topical treatment)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp	22082
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland".ab,ti	16576
	1 OR 2	*27369*
Intervention: drug therapy (Topical treatment)		
	'lidocaine'/exp OR 'capsaicin'/exp	86915
	dalcaine:ti,ab OR lidocain:ti,ab OR lidocaine:ti,ab OR lignocaine:ti,ab OR octocaine:ti,ab OR xylesthesin:ti,ab OR xylocaine:ti,ab OR xylocitin:ti,ab OR xyloneural:ti,ab OR '2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide':ab,ti OR '2-2etn-2mephacn':ti,ab OR instillagel:ti,ab OR cophenylcaine:ti,ab OR aurobin:ti,ab OR 'neo lidocaton':ti,ab OR axsain:ti,ab OR capsaicin:ti,ab OR capsaicine:ti,ab OR capsicum:ti,ab OR capsidol:ti,ab OR capsin:ti,ab OR capzasin:ti,ab OR gelcen:ti,ab OR katrum:ti,ab OR zacin:ti,ab OR zostrix:ti,ab OR 'ngx4010':ti,ab OR '8-methyl-n-vanillyl-6-nonenamide':ti,ab	48637

	4 OR 5	*95167*
Study types: randomised controlled trials[10]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2247142
	'animal'/exp NOT 'human'/exp	5058314
	7 NOT 8	*2028237*
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2015]/py	18527160
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	23476420
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**102**

The search result, usually found at the end of the documentation, forms the list of abstracts.
/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Embase via Elsevier 13 December 2019
Title: Diabetic neuropathies – drug therapy (Topical treatment)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp OR 'diabetic neuropathic pain'/exp	24,304
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland":ab,ti	18,334
	1 OR 2	*29,905*
Intervention: Topical treatment		
	'lidocaine'/exp OR 'capsaicin'/exp	91,816
	dalcaine:ti,ab OR lidocain:ti,ab OR lidocaine:ti,ab OR lignocaine:ti,ab OR octocaine:ti,ab OR xylesthesin:ti,ab OR xylocaine:ti,ab OR xylocitin:ti,ab OR xyloneural:ti,ab OR '2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide':ab,ti OR '2-2etn-2mephacn':ti,ab OR instillagel:ti,ab OR cophenylcaine:ti,ab OR aurobin:ti,ab OR 'neo lidocaton':ti,ab OR axsain:ti,ab OR capsaicin:ti,ab OR capsaicine:ti,ab OR capsicum:ti,ab OR capsidol:ti,ab OR capsin:ti,ab OR capzasin:ti,ab OR gelcen:ti,ab OR katrum:ti,ab OR zacin:ti,ab OR zostrix:ti,ab OR 'ngx4010':ti,ab OR '8-methyl-n-vanillyl-6-nonenamide':ti,ab	52,049
	4 OR 5	*100,796*
Study types: randomised controlled trials[11]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl*	2,222,531

[10] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

[11] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
	'animal'/exp NOT 'human'/exp	5,026,979
	7 NOT 8	*2,006,444*
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2016-2020]/py	
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**23**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 25 juni 2018
Title: Diabetic neuropathies – drug therapy (Topical treatment)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	20459
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11962
	1 OR 2	*24692*
Intervention: drug therapy (Topical treatment)		
	exp Lidocaine/ OR exp Capsaicin/	32996
	(dalcaine OR lidocain OR lidocaine OR lignocaine OR octocaine OR xylesthesin OR xylocaine OR xylocitin OR xyloneural OR "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " OR "2-2etn-2mephacn" OR instillagel OR cophenylcaine OR aurobin OR "neo lidocaton" OR axsain OR capsaicin OR capsaicine OR capsicum OR capsidol OR capsin OR capzasin OR gelcen OR katrum OR zacin OR zostrix OR "NGX4010 " OR "8-Methyl-N-Vanillyl-6-Nonenamide").ab,ti.	37938
	4 OR 5	*47314*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2396759
Limits: publication year, language		
	(yr="1990 - 2015" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**92**

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.mp=text, heading word, subject area node, title

Medline via OvidSP 13 December 2019
Title: Diabetic neuropathies – drug therapy (Topical treatment)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	21942
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	13055
	1 OR 2	*26733*
Intervention: Drug therapy (Topical treatment)		
	exp Lidocaine/ OR exp Capsaicin/	34192
	(dalcaine or lidocain or lidocaine or lignocaine or octocaine or xylesthesin or xylocaine or xylocitin or xyloneural or "2-(diethylamino)-n-(2,6-dimethylphenyl)acetamide " or "2-2etn-2mephacn" or instillagel or cophenylcaine or aurobin or "neo lidocaton" or axsain or capsaicin or capsaicine or capsicum or capsidol or capsin or capzasin or gelcen or katrum or zacin or zostrix or "NGX4010 " or "8-Methyl-N-Vanillyl-6-Nonenamide").ab,kf,ti.	40817
	4 OR 5	*50048*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2659118
Limits: publication year, language		
	(yr="2016 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**21**

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.mp=text, heading word, subject area node, title

Embase via Elsevier 13 December 2019
Title: Diabetic neuropathies – drug therapy (Tricyclic antidepressants)

Search terms		Items found
Population: Diabetic neuropathies		
	'diabetic neuropathy'/exp OR 'diabetic neuropathic pain'/exp	24,304
	((diabetic) NEAR/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ab,ti OR (diabet* NEAR/15 neuropath* NEAR/15 pain*):ab,ti OR "Bruns-Garland":ab,ti	18,334
	1 OR 2	*29,905*
Intervention: Tricyclic antidepressants		
	'amitriptyline'/exp OR 'amitriptyline plus perphenazine'/exp OR 'amitriptyline plus chlordiazepoxide'/exp OR 'nortriptyline'/exp OR 'maprotiline'/exp OR 'clomipramine'/exp	57,423
	amineurin:ti,ab OR amitrip:ti,ab OR amitriptylin:ti,ab OR amitriptyline:ti,ab OR amitrol:ti,ab OR anapsique:ti,ab OR 'apo amitriptyline':ti,ab OR damilen:ti,ab OR domical:ti,ab OR	12,803

	elavil:ti,ab OR endep:ti,ab OR laroxyl:ti,ab OR lentizol:ti,ab OR novoprotect:ti,ab OR saroten:ti,ab OR sarotex:ti,ab OR syneudon:ti,ab OR triptafen:ti,ab OR tryptanol:ti,ab OR tryptine:ti,ab OR tryptizol:ti,ab OR allegron:ti,ab OR 'apo nortriptyline':ti,ab OR aventyl:ti,ab OR desitriptyline:ti,ab OR desmethylamitriptylin:ti,ab OR 'gen nortriptyline':ti,ab OR norfenazin:ti,ab OR nortrilen:ti,ab OR nortriptylin:ti,ab OR nortriptyline:ti,ab OR 'novo nortriptyline':ti,ab OR 'nu nortriptyline':ti,ab OR pamelor:ti,ab OR paxtibi:ti,ab OR 'pms nortriptyline':ti,ab OR 'ratio nortriptyline':ti,ab OR deprilept:ti,ab OR dibencycladine:ti,ab OR ludiomil:ti,ab OR maprolu:ti,ab OR maprotilin:ti,ab OR maprotiline:ti,ab OR mirpan:ti,ab OR 'novo maprotiline':ti,ab OR psymion:ti,ab OR 'ba34,276':ti,ab OR 'ba-34,276':ti,ab OR 'n-methyl-9,10-ethanoanthracene-9(10h)-propylamine':ti,ab OR anafranil:ti,ab OR chlomipramin:ti,ab OR chlomipramine:ti,ab OR clomipramin:ti,ab OR clomipramine:ti,ab OR chlorimipramine:ti,ab OR hydiphen:ti,ab	
	4 OR 5	*58,397*
Study types: randomised controlled trials[12]		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,504,191
	'animal'/exp NOT 'human'/exp	5,368,004
	7 NOT 8	2,259,901
Limits: language, publication year, publication type		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2016-2020]/py	
	([article]/lim OR [article in press]/lim OR [erratum]/lim)	
Combined sets		
	3 AND 6 AND 9 AND 10 AND 11	**21**

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Medline via OvidSP 13 December 2019
Title: Diabetic neuropathies – drug therapy (Tricyclic antidepressants)

Search terms		Items found
Population: Diabetic neuropathies		
	exp Diabetic Neuropathies/	21942
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	13055
	1 OR2	*26733*
Intervention: Drug therapy (Tricyclic antidepressants)		
	exp amitriptyline/ or exp nortriptyline/ OR exp Maprotiline/ OR exp Clomipramine/	11206
	(amineurin OR amitrip OR amitriptylin OR amitriptyline OR amitrol OR anapsique OR apo-amitriptyline OR damilen OR domical OR elavil OR endep OR laroxyl OR lentizol OR novoprotect OR saroten OR sarotex OR syneudon OR triptafen OR tryptanol OR tryptine OR tryptizol OR allegron OR apo-Nortriptyline OR aventyl OR desitriptyline OR desmethylamitriptylin OR gen-nortriptyline OR norfenazin OR nortrilen OR nortriptylin OR	9627

[12] Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

	nortriptyline OR novo-nortriptyline OR nu-nortriptyline OR pamelor OR paxtibi OR PMS-nortriptyline OR ratio-nortriptyline OR deprilept OR dibencycladine OR ludiomil OR maprolu OR maprotilin OR maprotiline OR mirpan OR novo-maprotiline OR psymion OR "Ba34,276" OR "Ba-34,276" OR "N-Methyl-9,10-ethanoanthracene-9(10H)-propylamine" OR anafranil OR chlomipramin OR chlomipramine OR chlorimipramine OR clomipramin OR clomipramine OR clorimipramine OR hydiphen):ti,ab,kf	
	4 OR 5	*14814*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not humans.sh.)	2659118
Limits: publication year, language		
	(yr="2016 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	3 AND 6 AND 7 AND 8	**7**

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.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
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.ti. = Title
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.mp=text, heading word, subject area node, title

Part III Pain associated with spinal compression fractures/Kotkompression

Systematic reviews/Systematiska översikter

CRD via NIHR Centre for Reviews and Dissemination 2 May 2018 (CRD, HTA)
Title: Title: Spinal compression fractures – drug therapy

Search terms		Items found
Population: Spinal compression fractures		
	MeSH DESCRIPTOR Spinal fractures EXPLODE ALL TREES IN DARE, HTA	144
	MeSH DESCRIPTOR spinal injuries EXPLODE ALL TREES IN DARE, HTA	161
	MeSH DESCRIPTOR Spine EXPLODE ALL TREES IN DARE, HTA	510
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*) TI	1021
	2-4 (OR)	*1255*
	MeSH DESCRIPTOR Bone fractures EXPLODE ALL TREES IN DARE, HTA	755
	(fractur* or compress*) TI	1106
	6-7 (OR)	*1281*
	5 AND 8	*218*
	1 OR 9	*218*
Limits: publication year		
	FROM 01/01/1990 TO 02/05/2018	
Combined sets		
	9 AND 10 AND 11	**218**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
TI = title
* = Truncation
" " = Citation Marks; searches for an exact phrase

DARE = Database Abstracts of Reviews of Effects, "other reviews"
HTA = Health Technology Assessments

Prospero via NIHR Centre for Reviews and Dissemination 2 May 2018
Title: Spinal compression fractures

Search terms		Items found
Population: Spinal compression fractures		
	MeSH DESCRIPTOR spinal fractures EXPLODE ALL TREES	**25**
	"vertebral fracture*" OR "spinal fracture*" OR "spine fracture*" OR "thoracolumbar spine fracture*"	**72**

The search result, usually found at the end of the documentation, forms the list of abstracts.

MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
* = Truncation
" " = Citation Marks; searches for an exact phrase

Cochrane Library via Wiley 29 January 2020 (CDSR)
Title: Spinal compression fractures – drug therapy (NSAID)

Search terms	Items found
Population: Spinal compression fractures	
[mh "Spinal fractures"]	677
(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
[mh Spine]	4613
[mh "Spinal Injuries"]	772
(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
3-5 (OR)	42460
[mh "Fractures, Bone"]	5600
(fractur* or compress*):ti,ab,kw	30640
7 OR 8	30662
6 AND 9	6171
1 OR 2 OR 10	*6245*
Intervention: NSAID	
MeSH descriptor: [Aspirin] explode all trees	5540
MeSH descriptor: [Diclofenac] explode all trees	1852
MeSH descriptor: [Piroxicam] explode all trees	649
MeSH descriptor: [Ibuprofen] explode all trees	1830
MeSH descriptor: [Naproxen] explode all trees	1094
MeSH descriptor: [Ketoprofen] explode all trees	542
MeSH descriptor: [Celecoxib] explode all trees	871
MeSH descriptor: [Ketorolac] explode all trees	805
MeSH descriptor: [Meloxicam] explode all trees	214
("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	30874
12 -21 (OR)	*31560*
Limits: Publication year	
from 1990 to 2020	
Combined sets	
11 AND 22 AND 23	**CDSR/1**

The search result, usually found at the end of the documentation, forms the list of abstracts.

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MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword

* = Truncation
“ “ = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (NSAID)

Search terms	Items found
Population: Spinal compression fractures	
'spine fracture'/exp	35,252
'vertebra compression'/exp	439
'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
3 OR 4	704,096
'fracture'/exp	315,753
fractur*:ti,ab OR compress*:ti,ab	480,409
6 OR 7	567,292
5 AND 8	89,438
1 OR 2 OR 9	*96,974*
Intervention: NSAID	
'acetylsalicylic acid'/exp/mj	59,969
'diclofenac'/exp/mj	10,587
'diclofenac potassium'/exp/mj	230
'diclofenac plus misoprostol'/exp/mj	44
'piroxicam'/exp/mj	3,941
'piroxicam beta cyclodextrin'/exp/mj	76
'cinnoxicam'/exp/mj	47
'ibuprofen'/exp/mj	13,225
'naproxen'/exp/mj	7,384
'ketoprofen'/exp/mj	4,350
'ketoprofen lysine'/exp/mj	68
'celecoxib'/exp/mj	4,777
'ketorolac'/exp/mj	1,893
'tenoxicam'/exp/mj	657
'meloxicam'/exp/mj OR 'florfenicol plus meloxicam'/exp/mj	1,547
'ketorolac trometamol plus phenylephrine'/exp/mj OR 'ketorolac trometamol'/exp/mj	805
'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR	138,698

	synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	
	11-27 (OR)	*170,334*
Study types: systematic reviews, meta analysis		
	'systematic review'/de	231,101
	'meta analysis'/de	177,573
	[cochrane review]/lim	21,017
	'review'/exp AND [1990-2007]/py	1,125,820
	(systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab	344,935
	29-33 (OR)	*1,417,885*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
Combined sets		
	10 AND 28 AND 34 AND 35	**26**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 29 January 2020
Title: Spinal compression fractures – drug therapy (NSAIDs)

Search terms	Items found
Population: Spinal compression fractures	
exp Spinal Fractures/	14574
(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	1390
exp Spine/	29885
exp Spinal Injuries/	22744
(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	525773
3-5 (OR)	535085
exp fractures, bone/	63310
(fractur* or compress*).ab,kf,ti.	350044
7 OR 8	363627
6 AND 9	54562
1 OR 2 OR 10	*57799*
Intervention: NSAID	

	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/ OR exp Ketorolac/ OR exp Meloxicam/	72942
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	92305
	12 OR 13	*111017*
Study types: systematic reviews, metaanalysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	11 AND 14 AND 15 AND 16	**4**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 29 January 2020 (CDSR)
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms	Items found
Population: Spinal compression fractures	
[mh "Spinal fractures"]	677
(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
[mh Spine]	4613
[mh "Spinal Injuries"]	772
(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
3-5 (OR)	42460
[mh "Fractures, Bone"]	5600
(fractur* or compress*):ti,ab,kw	30640
7 OR 8	30662
6 AND 9	6171
1 OR 2 OR 10	*6245*

Intervention: Opioides		
	MeSH descriptor: [Buprenorphine] explode all trees	1044
	MeSH descriptor: [Buprenorphine, Naloxone Drug Combination] explode all trees	111
	MeSH descriptor: [Codeine] explode all trees	1606
	MeSH descriptor: [Hydrocodone] explode all trees	202
	MeSH descriptor: [Oxycodone] explode all trees	845
	MeSH descriptor: [Hydromorphone] explode all trees	342
	MeSH descriptor: [Morphine] explode all trees	4749
	MeSH descriptor: [Meperidine] explode all trees	1138
	MeSH descriptor: [Fentanyl] explode all trees	5289
	MeSH descriptor: [Tramadol] explode all trees	1070
	MeSH descriptor: [Methadone] explode all trees	1189
	MeSH descriptor: [Tapentadol] explode all trees	60
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddic)t:ti,ab,kw (Word variations have been searched)	39300
	12 -24 (OR)	*40374*
Limits: Publication year		
	from 1990 to 2020	
Combined sets		
	11 AND 25 AND 26	**CDSR/0**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
“ “ = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms	Items found
Population: Spinal compression fractures	
'spine fracture'/exp	35,252
'vertebra compression'/exp	439
'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
3 OR 4	704,096
'fracture'/exp	315,753
fractur*:ti,ab OR compress*:ti,ab	480,409
6 OR 7	567,292
5 AND 8	89,438
1 OR 2 OR 9	*96,974*
Intervention: Opioides	
'buprenorphine'/exp/mj	6,476
'buprenorphine plus naloxone'/exp/mj	596
'codeine'/exp/mj	6,693
'cocodamol'/exp/mj	156
'hydrocodone'/exp/mj	724
'hydrocodone bitartrate plus paracetamol'/exp/mj	92
'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
'oxycodone'/exp/mj	3,088
'oxycodone plus paracetamol'/exp/mj	183
'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
'hydromorphone'/exp/mj	1,848
'pethidine'/exp/mj	10,018
'fentanyl'/exp/mj	17,349
'tramadol'/exp/mj	4,323
'paracetamol plus tramadol'/exp/mj	102
'methadone'/exp/mj	14,080
'codeine phosphate'/exp/mj	390
'hydromorphone plus naloxone'/exp/mj	1
'morphine'/exp/mj	46,916
'ketobemidone'/exp/mj	207
'tapentadol'/exp/mj	613
morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR	129,770

	tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	
	11-32 (OR)	*156,559*
Study types: systematic reviews, meta analysis		
	'systematic review'/de	231,101
	'meta analysis'/de	177,573
	[cochrane review]/lim	21,017
	'review'/exp AND [1990-2007]/py	1,125,820
	(systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab	344,935
	34-38 (OR)	*1,417,885*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
Combined sets		
	10 AND 33 AND 39 AND 40	**30**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 30 April 2018
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms	Items found
Population: Spinal compression fractures	
exp Spinal Fractures/	14560
(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	1390
exp Spine/	29877
exp Spinal Injuries/	22728
(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	525586
3-5 (OR)	534896
exp fractures, bone/	63303
(fractur* or compress*).ab,kf,ti.	349907
7 OR 8	363490
6 AND 9	54536
1 OR 2 OR 10	*57771*
Intervention: Opioides	

	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/ OR exp Tapentadol/	78432
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict).ab,kf,ti.	94733
	12 OR 13	*112100*
Study types: systematic reviews, metaanalysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	11 AND 14 AND 15 AND 16	**6**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 29 January 2020 (CDSR)
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	[mh "Spinal fractures"]	677
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
	[mh Spine]	4613
	[mh "Spinal Injuries"]	772
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
	3-5 (OR)	42460
	[mh "Fractures, Bone"]	5600
	(fractur* or compress*):ti,ab,kw	30640
	7 OR 8	30662

	6 AND 9	6171
	1 OR 2 OR 10	*6245*
Intervention: Paracetamol		
	[mh Acetaminophen]	2992
	acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl:ti,ab,kw (Word variations have been searched)	10109
	12 OR 13	*10109*
Limits: Publication year		
	from 1990 to 2020	
Combined sets		
	11 AND 14 AND 15	**CDSR/1**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	'spine fracture'/exp	35,252
	'vertebra compression'/exp	439
	'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
	vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
	3 OR 4	704,096
	'fracture'/exp	315,753
	fractur*:ti,ab OR compress*:ti,ab	480,409
	6 OR 7	567,292
	5 AND 8	89,438
	1 OR 2 OR 9	*96,974*
Intervention: Paracetamol		
	'paracetamol'/exp	88,957
	'cocodamol'/exp	1,609
	'oxycodone plus paracetamol'/exp	1,527
	'hydrocodone bitartrate plus paracetamol'/exp	1,380
	'dextropropoxyphene plus paracetamol'/exp	964
	(acetaminophen:ab,ti,kw,de OR paracetamol:ab,ti,kw,de OR acetominophen:ab,ti,kw,de OR hydroxyacetanilide:ab,ti,kw,de OR apap:ab,ti,kw,de OR 'p acetamidophenol':ab,ti,kw,de OR 'p hydroxyacetanilide':ab,ti,kw,de OR 'n-(4-hydroxyphenyl)acetanilide':ab,ti,kw,de OR acetamidophenol:ab,ti,kw,de OR 'n-acetyl-p-aminophenol':ab,ti,kw,de OR 'n-acetyl-para-aminophenol':ab,ti,kw,de OR acephen:ab,ti,kw,de OR acetaco:ab,ti,kw,de OR tylenol:ab,ti,kw,de OR 'anacin 3':ab,ti,kw,de OR anacin3:ab,ti,kw,de OR datril:ab,ti,kw,de OR panadol:ab,ti,kw,de OR acamol:ab,ti,kw,de OR algotropyl):ab,ti,kw,de	96,152
	11-16 (OR)	*96,749*

Study types: systematic reviews, meta analysis		
	'systematic review'/de	231,101
	'meta analysis'/de	177,573
	[cochrane review]/lim	21,017
	'review'/exp AND [1990-2007]/py	1,125,820
	(systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab	344,935
	18-22 (OR)	*1,417,885*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [1990-2020]/py	
Combined sets		
	10 AND 17 AND 23 AND 24	**72**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 28 January 2020
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	exp Spinal Fractures/	14560
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	1390
	exp Spine/	29877
	exp Spinal Injuries/	22728
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	525586
	3-5 (OR)	534896
	exp fractures, bone/	63303
	(fractur* or compress*).ab,kf,ti.	349907
	7 OR 8	363490
	6 AND 9	54536
	1 OR 2 OR 10	*57771*
Intervention: Paracetamol		
	exp Acetaminophen/	17819
	(acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl).ab,kf,kw,ti.	25056
	12 OR 13	*25848*
Study types: systematic reviews, metaanalysis		
	Publication type: meta analysis OR systematic reviews	
Limits: publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	11 AND 14 AND 15 AND 16	**4**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Primary studies/Primärstudier

Cochrane Library via Wiley 29 January 2020 (Central)
Title: Spinal compression fractures – drug therapy (NSAID)

Search terms		Items found
Population: Spinal compression fractures		
	[mh "Spinal fractures"]	677
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
	[mh Spine]	4613
	[mh "Spinal Injuries"]	772
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
	3-5 (OR)	42460
	[mh "Fractures, Bone"]	5600
	(fractur* or compress*):ti,ab,kw	30640
	7 OR 8	30662
	6 AND 9	6171
	1 OR 2 OR 10	*6245*
Intervention: NSAID		
	MeSH descriptor: [Aspirin] explode all trees	5540
	MeSH descriptor: [Diclofenac] explode all trees	1852
	MeSH descriptor: [Piroxicam] explode all trees	649
	MeSH descriptor: [Ibuprofen] explode all trees	1830
	MeSH descriptor: [Naproxen] explode all trees	1094
	MeSH descriptor: [Ketoprofen] explode all trees	542
	MeSH descriptor: [Celecoxib] explode all trees	871
	MeSH descriptor: [Ketorolac] explode all trees	805
	MeSH descriptor: [Meloxicam] explode all trees	214
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen	30874

	OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	
	12 -21 (OR)	*31560*
Limits: Publication year		
	from 2014 to 2020	
Combined sets		
	11 AND 22 AND 23	**Central/ 38**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (NSAID)

Search terms	Items found
Population: Spinal compression fractures	
'spine fracture'/exp	35,252
'vertebra compression'/exp	439
'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
3 OR 4	704,096
'fracture'/exp	315,753
fractur*:ti,ab OR compress*:ti,ab	480,409
6 OR 7	567,292
5 AND 8	89,438
1 OR 2 OR 9	*96,974*
Intervention: NSAID	
'acetylsalicylic acid'/exp/mj	59,969
'diclofenac'/exp/mj	10,587
'diclofenac potassium'/exp/mj	230
'diclofenac plus misoprostol'/exp/mj	44
'piroxicam'/exp/mj	3,941
'piroxicam beta cyclodextrin'/exp/mj	76
'cinnoxicam'/exp/mj	47
'ibuprofen'/exp/mj	13,225
'naproxen'/exp/mj	7,384
'ketoprofen'/exp/mj	4,350
'ketoprofen lysine'/exp/mj	68
'celecoxib'/exp/mj	4,777
'ketorolac'/exp/mj	1,893
'tenoxicam'/exp/mj	657
'meloxicam'/exp/mj OR 'florfenicol plus meloxicam'/exp/mj	1,547

	'ketorolac trometamol plus phenylephrine'/exp/mj OR 'ketorolac trometamol'/exp/mj	805
	'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	138,698
	11-27 (OR)	*170,334*
Study types: randomised controlled trials and other trials		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,528,669
	'animal'/exp NOT 'human'/exp	5,391,331
	14 NOT 15	*2,282,439*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND ([1-1-2014]/sd NOT [30-1-2020]/sd)	
Combined sets		
	10 AND 28 AND 31 AND 32	**27**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 29 January 2020
Title: Spinal compression fractures – drug therapy (NSAIDs)

Search terms	Items found
Population: Spinal compression fractures	
exp Spinal Fractures/	14574
(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	1390
exp Spine/	29885
exp Spinal Injuries/	22744
(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	525773
3-5 (OR)	535085
exp fractures, bone/	63310
(fractur* or compress*).ab,kf,ti.	350044
7 OR 8	363627
6 AND 9	54562
1 OR 2 OR 10	*57799*
Intervention: NSAIDs	
Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/ OR exp Ketorolac/ OR exp Meloxicam/	72942
("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	92305
12 OR 13	*111017*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)	
((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or equivalence trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not exp humans/)	2414303
Limits: Publication year, language	
(yr="2014 - Current" and (danish or english or norwegian or swedish))	
Combined sets	
11 AND 14 AND 15 AND 16	**9**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 29 January 2020 (Central)
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms		Items found
Population: Spinal compression fractures		
	[mh "Spinal fractures"]	677
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
	[mh Spine]	4613
	[mh "Spinal Injuries"]	772
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
	3-5 (OR)	42460
	[mh "Fractures, Bone"]	5600
	(fractur* or compress*):ti,ab,kw	30640
	7 OR 8	30662
	6 AND 9	6171
	1 OR 2 OR 10	*6245*
Intervention: Opioides		
	MeSH descriptor: [Buprenorphine] explode all trees	1044
	MeSH descriptor: [Buprenorphine, Naloxone Drug Combination] explode all trees	111
	MeSH descriptor: [Codeine] explode all trees	1606
	MeSH descriptor: [Hydrocodone] explode all trees	202
	MeSH descriptor: [Oxycodone] explode all trees	845
	MeSH descriptor: [Hydromorphone] explode all trees	342
	MeSH descriptor: [Morphine] explode all trees	4749
	MeSH descriptor: [Meperidine] explode all trees	1138
	MeSH descriptor: [Fentanyl] explode all trees	5289
	MeSH descriptor: [Tramadol] explode all trees	1070
	MeSH descriptor: [Methadone] explode all trees	1189
	MeSH descriptor: [Tapentadol] explode all trees	60
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddic)t:ti,ab,kw (Word variations have been searched)	39300
	12 -24 (OR)	*40374*
Limits: Publication year		
	from 2014 to 2020	
Combined sets		
	11 AND 25 AND 26	**Central/ 117**

The search result, usually found at the end of the documentation, forms the list of abstracts.
:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy

this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms	Items found
Population: Spinal compression fractures	
'spine fracture'/exp	35,252
'vertebra compression'/exp	439
'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
3 OR 4	704,096
'fracture'/exp	315,753
fractur*:ti,ab OR compress*:ti,ab	480,409
6 OR 7	567,292
5 AND 8	89,438
1 OR 2 OR 9	*96,974*
Intervention: Opioides	
'buprenorphine'/exp/mj	6,476
'buprenorphine plus naloxone'/exp/mj	596
'codeine'/exp/mj	6,693
'cocodamol'/exp/mj	156
'hydrocodone'/exp/mj	724
'hydrocodone bitartrate plus paracetamol'/exp/mj	92
'hydrocodone bitartrate plus ibuprofen'/exp/mj	3
'oxycodone'/exp/mj	3,088
'oxycodone plus paracetamol'/exp/mj	183
'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj	19
'hydromorphone'/exp/mj	1,848
'pethidine'/exp/mj	10,018
'fentanyl'/exp/mj	17,349
'tramadol'/exp/mj	4,323
'paracetamol plus tramadol'/exp/mj	102
'methadone'/exp/mj	14,080
'codeine phosphate'/exp/mj	390
'hydromorphone plus naloxone'/exp/mj	1
'morphine'/exp/mj	46,916
'ketobemidone'/exp/mj	207
'tapentadol'/exp/mj	613
morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR	129,770

	burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	
	11-32 (OR)	*156,559*
Study types: randomised controlled trials and other trials		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,528,669
	'animal'/exp NOT 'human'/exp	5,391,331
	34 NOT 35	*2,282,439*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND ([1-1-2014]/sd NOT [30-1-2020]/sd)	
Combined sets		
	10 AND 33 AND 36 AND 37	**69**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 25 May 2018
Title: Spinal compression fractures – drug therapy (Opioides)

Search terms		Items found
Population: Spinal compression fractures		
	exp Spinal Fractures/	13293
	(Osteoporosis/co [Complications] OR Osteoporosis, Postmenopausal/co [Complications]) AND (Fractures, Bone/et [Etiology])	1863
	exp Spine/	132013
	exp Spinal Injuries/	21197
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	485515
	3-5 (OR)	522242
	exp fractures, bone/	168820
	(fractur* or compress*).ab,kf,ti.	357902
	7 OR 8	395998
	6 AND 9	58910
	1 OR 2 OR 10	*60144*
Intervention: Opioides		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/	75052
	(morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict).ab,kf,ti.	88380
	12 OR 13	*105316*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not exp humans/)	2414303
Limits: Publication year, language		
	(yr="2014 - 2019" and (danish or english or norwegian or swedish))	
Combined sets		
	11 AND 14 AND 15 AND 16	**30**

The search result, usually found at the end of the documentation, forms the list of abstracts.
.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cochrane Library via Wiley 29 January 2020 (Central)
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	[mh "Spinal fractures"]	677
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	278
	[mh Spine]	4613
	[mh "Spinal Injuries"]	772
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*):ti,ab,kw (Word variations have been searched)	42294
	3-5 (OR)	42460
	[mh "Fractures, Bone"]	5600
	(fractur* or compress*):ti,ab,kw	30640
	7 OR 8	30662
	6 AND 9	6171
	1 OR 2 OR 10	*6245*
Intervention: Paracetamol		
	[mh Acetaminophen]	2992
	acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl:ti,ab,kw (Word variations have been searched)	10109
	12 OR 13	*10109*
Limits: Publication year		
	from 2014 to 2020	
Combined sets		
	11 AND 14 AND 15	**Central/ 38**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Embase via Elsevier 29 January 2020
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	'spine fracture'/exp	35,252
	'vertebra compression'/exp	439
	'spine'/exp OR 'spine injury'/de OR 'cervical spine injury'/de	205,355
	vertebra*:ab,ti OR spine:ab,ti OR spinal:ab,ti OR lumbal:ab,ti OR lumbar:ab,ti OR thoracolumb*:ab,ti	660,471
	3 OR 4	704,096
	'fracture'/exp	315,753
	fractur*:ti,ab OR compress*:ti,ab	480,409
	6 OR 7	567,292

	5 AND 8	89,438
	1 OR 2 OR 9	*96,974*
Intervention: Paracetamol		
	'paracetamol'/exp	88,957
	'cocodamol'/exp	1,609
	'oxycodone plus paracetamol'/exp	1,527
	'hydrocodone bitartrate plus paracetamol'/exp	1,380
	'dextropropoxyphene plus paracetamol'/exp	964
	(acetaminophen:ab,ti,kw,de OR paracetamol:ab,ti,kw,de OR acetominophen:ab,ti,kw,de OR hydroxyacetanilide:ab,ti,kw,de OR apap:ab,ti,kw,de OR 'p acetamidophenol':ab,ti,kw,de OR 'p hydroxyacetanilide':ab,ti,kw,de OR 'n-(4-hydroxyphenyl)acetanilide':ab,ti,kw,de OR acetamidophenol:ab,ti,kw,de OR 'n-acetyl-p-aminophenol':ab,ti,kw,de OR 'n-acetyl-para-aminophenol':ab,ti,kw,de OR acephen:ab,ti,kw,de OR acetaco:ab,ti,kw,de OR tylenol:ab,ti,kw,de OR 'anacin 3':ab,ti,kw,de OR anacin3:ab,ti,kw,de OR datril:ab,ti,kw,de OR panadol:ab,ti,kw,de OR acamol:ab,ti,kw,de OR algotropyl):ab,ti,kw,de	96,152
	11-16 (OR)	*96,749*
Study types: randomised controlled trials and other trials		
	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,528,669
	'animal'/exp NOT 'human'/exp	5,391,331
	18 NOT 19	*2,282,439*
Limits: publication year, language		
	([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND ([1-1-2014]/sd NOT [30-1-2020]/sd)	
Combined sets		
	10 AND 17 AND 20 AND 21	**46**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
“ “ = Citation Marks; searches for an exact phrase

Medline via OvidSP 28 January 2020
Title: Spinal compression fractures – drug therapy (Paracetamol)

Search terms		Items found
Population: Spinal compression fractures		
	exp Spinal Fractures/	14560
	(Osteoporosis/co [Complications] AND Fractures, Bone/et [Etiology])	1390
	exp Spine/	29877
	exp Spinal Injuries/	22728
	(vertebra* or spine or spinal or lumbal or lumbar or thoracolumb*).ab,kf,ti.	525586
	3-5 (OR)	534896
	exp fractures, bone/	63303
	(fractur* or compress*).ab,kf,ti.	349907
	7 OR 8	363490
	6 AND 9	54536
	1 OR 2 OR 10	*57771*
Intervention: Paracetamol		
	exp Acetaminophen/	17819
	(acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl).ab,kf,kw,ti.	25056
	12 OR 13	*25848*
Study types: randomised controlled trials and other trials (Cochrane "Highly Sensitive Search Strategy" in Medline: sensitivity-maximizing version (2008 revision) with modifications)		
	((randomized or randomised or placebo or randomly or trial or groups).ab. or exp controlled clinical trial/ or exp randomized controlled trial/ or equivalence trial/ or exp pragmatic clinical trial/ or exp Clinical Trials as Topic/ or drug therapy/) not (exp animals/ not exp humans/)	2680812
Limits: Publication year, language		
	(yr="2014 - Current" and (danish or english or norwegian or swedish))	
Combined sets		
	11 AND 14 AND 15 AND 16	**7**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Part IV Adverse effects/Biverkningar

Systematic reviews/Systematiska översikter

Cochrane Library via Wiley 12 December 2019
Title: NSAIDS – adverse effects in the elderly

Search terms		Items found
Intervention: NSAIDS		
	[mh Aspirin]	5531
	[mh Diclofenac]	1849
	[mh Piroxicam]	649
	[mh Ibuprofen]	1824
	[mh Naproxen]	1093
	[mh Ketoprofen]	542
	[mh Celecoxib]	869
	("acetylsalicylic acid" or "2-(Acetyloxy)benzoic Acid" or aspirin or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or diclophenac or dicrofenac or dichlofenal or "diclonate P" or feloran or voltarol or novapirina or orthofen or ortofen or orthophen or voltaren or diclofenac or piroxicam or feldene or reutenox or artriunic or "Novo-Tenoxicam" or mobiflex or tilcotil or "Apo-Tenoxicam" or tenoxicam or reumoxicam or miloxicam or movalis or uticox or mobic or mobicox or mobec or masflex or movicox or parocin or meloxicam or ibumetin or ibuprofen or motrin or nuprin or rufen or salprofen or "Trauma-Dolgit Gel" or "Trauma Dolgit Gel" or "TraumaDolgit Gel" or brufen or methoxypropiocin or anaprox or naproxen or aleve or proxen or synflex or naprosin or naprosyn or "naproxenate sodium" or "benzoylhydratropic acid" or "2-(3-Benzoylphenyl)propionic Acid" or profenid or alrheumum or orudis or alrheumat or dexibuprofen or s-ibuprofen or "S ibuprofen" or badyket or ketesse or sympal or quiralam or quirgel or adolquir or enangel or keral or enantyum or ketoprofen or dexketoprofen or celcoxib or celebrex or etoricoxib or arcoxia or nabumetone or arthraxan or "Gen-Nabumetone" or listran or relafen or relif or relifex or mebutan or "Rhoxal-nabumetone" or "Apo-Nabumetone" or celecoxib or nabucox):ti,ab,kw (Word variations have been searched)	30692
	[mh "Anti-Inflammatory Agents, Non-Steroidal"]	7456
	("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID OR NSAIDS):ti,ab,kw	6674
	1-10 (OR)	37212
Outcome: Adverse effects		
	(adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology"):ti,ab,kw	603558
	[mh "Abnormalities, Drug-Induced"]	47
	[mh "Adverse Drug Reaction Reporting Systems"]	88
	[mh Contraindications]	259
	[mh "Drug Recalls"]	1
	[mh "Drug Hypersensitivity"]	964
	[mh "Drug Monitoring"]	1723
	[mh "Drug-Related Side Effects and Adverse Reactions"]	3417
	[mh Poisoning]	2076
	[mh "Safety-Based Drug Withdrawals"]	11
	[mh "Substance-Related Disorders"]	14062
	[mh "Long Term Adverse Effects"]	26
	[mh Risk]	36965

	[mh ^Mortality]	502
	[mh "Medication Errors"]	404
	[mh Pharmacoepidemiology]	17
	"peptic ulcer*" or "gastroduodenal ulcer*" or "marginal ulcer*" or "gastrointestinal bleeding" or "gastrointestinal hemorrhage*" or "impaired renal function" or "edema" or "congestive heart failure" or "stroke" or "myocardial infarction*" or "cardiovascular stroke" or "heart attack" or "myocardial infarct*" or "hypertension" or "High Blood Pressure":ti,ab,kw (Word variations have been searched)	169011
	[mh "Peptic Ulcer"]	3704
	[mh "Gastrointestinal Hemorrhage"]	1889
	[mh Kidney/DE]	1864
	[mh "Renal Insufficiency"]	8202
	[mh Edema]	1661
	[mh "Heart Failure"]	8482
	[mh Stroke]	8696
	[mh "Myocardial Infarction"]	10473
	[mh Hypertension]	16969
	Any MeSH descriptor in all MeSH products and with qualifier(s): [administration & dosage - AD, complications - CO, poisoning - PO, adverse effects - AE, chemically induced - CI]	274637
	12-38 (OR)	810808
Population: Aged		
	[mh Aged]	1280
	("care homes" or "community-dwelling" or frail or frailty or geriatric* or "nursing homes" or "old age" or "old people" or "older adults" or "older people"):ti,ab,kw or (aged or older or old or elder or elders or elderly):ti	50604
	40 or 41	51063
Combined sets		
	11 AND 39 AND 42	CDSR/**17** DARE/0 HTA/0

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Cochrane Library via Wiley 12 December 2019
Title: Opioids – adverse effects in the elderly

Search terms		Items found
Intervention: Opioids		
	[mh Buprenorphine]	1043
	[mh "Buprenorphine, Naloxone Drug Combination"]	110
	[mh Codeine]	1605
	[mh Hydrocodone]	202
	[mh Oxycodone]	844
	[mh Hydromorphone]	342
	[mh Morphine]	4747
	[mh Meperidine]	1138
	[mh Fentanyl]	5282
	[mh Tramadol]	1067
	[mh Methadone]	1187
	morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict:ti,ab,kw (Word variations have been searched)	36839
	[mh "Chronic Pain"/DT]	315
	[mh "Analgesics, Opioid"]	7132
	((opioid or opioids)):ti	4578
	1-15 (OR)	40813
Outcome: Adverse effects		
	adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology":ti,ab,kw (Word variations have been searched)	613088
	[mh "Abnormalities, Drug-Induced"]	47
	[mh "Adverse Drug Reaction Reporting Systems"]	88
	[mh Contraindications]	259
	[mh "Drug Recalls"]	1
	[mh "Drug Hypersensitivity"]	964
	[mh "Drug Monitoring"]	1723
	[mh "Drug-Related Side Effects and Adverse Reactions"]	3417
	[mh Poisoning]	2076
	[mh "Safety-Based Drug Withdrawals"]	11
	[mh "Substance-Related Disorders"]	14062
	[mh "Long Term Adverse Effects"]	26
	[mh Risk]	36965

	[mh ^Mortality]	502
	[mh "Medication Errors"]	404
	[mh Pharmacoepidemiology]	17
	Any MeSH descriptor in all MeSH products and with qualifier(s): [administration & dosage - AD, complications - CO, poisoning - PO, adverse effects - AE, chemically induced - CI]	261546
	[mh Constipation]	1544
	[mh Confusion]	745
	[mh "Opioid-Related Disorders"]	1779
	[mh "Conscious Sedation"]	1382
	[mh Nausea]	5420
	[mh Vomiting]	5165
	[mh Dizziness]	689
	[mh "Respiratory Insufficiency"]	2451
	"constipation" or "confusion" or "addiction" or "opioid abuse" or "opioid depencence" or "opiate addiction" or "sedation" or "nausea" or "vomiting" or "dizziness" or "respiratory suppression":ti,ab,kw (Word variations have been searched)	89401
	17-42 (OR)	762131
Population: Aged		
	[mh Aged]	1280
	("care homes" or "community-dwelling" or frail or frailty or geriatric* or "nursing homes" or "old age" or "old people" or "older adults" or "older people"):ti,ab,kw or (aged or older or old or elder or elders or elderly):ti (Word variations have been searched)	50604
	44 or 45	51063
Combined sets		
	16 AND 43 AND 46 with Cochrane Library publication date from Jan 1990 to 2019	CDSR/**42** DARE/0 HTA/0

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Cochrane Library via Wiley 12 december 2019
Title: Paracetamol – adverse effects in the elderly

Search terms		Items found
Intervention: Paracetamol		
	[mh Acetaminophen]	2988
	acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl:ti,ab,kw (Word variations have been searched)	10409
	1 OR 2	10410
Outcome: Adverse effects		
	adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology":ti,ab,kw (Word variations have been searched)	603562
	[mh "Abnormalities, Drug-Induced"]	47
	[mh "Adverse Drug Reaction Reporting Systems"]	88
	[mh "Contraindications"]	259
	[mh "Drug Recalls"]	1
	[mh "Drug Hypersensitivity"]	964
	[mh "Drug Monitoring"]	1723
	[mh "Drug-Related Side Effects and Adverse Reactions"]	3417
	[mh "Poisoning"]	2076
	[mh "Safety-Based Drug Withdrawals"]	11
	[mh "Substance-Related Disorders"]	14062
	[mh "Long Term Adverse Effects"]	26
	[mh "Risk"]	36965
	[mh "Mortality] this term only	502
	[mh "Medication Errors"]	404
	[mh "Pharmacoepidemiology"]	17
	4-19 (OR)	616550
	"peptic ulcer*" or "gastroduodenal ulcer*" or "marginal ulcer*" or "gastrointestinal bleeding" or "gastrointestinal hemorrhage*" or "impaired renal function" or "edema" or "congestive heart failure" or "stroke" or "myocardial infarction*" or "cardiovascular stroke" or "heart attack" or "myocardial infarct*" or "hypertension" or "High Blood Pressure":ti,ab,kw (Word variations have been searched)	169011
	[mh "Peptic Ulcer"]	3752
	[mh "Gastrointestinal Hemorrhage"]	1889
	[mh "Kidney"/DE]	1864
	[mh "Renal Insufficiency"]	8202
	[mh Edema]	1661
	[mh "Heart Failure"]	8482
	[mh Stroke]	8696
	[mh "Myocardial Infarction"]	10473
	[mh Hypertension]	16969
	Any MeSH descriptor in all MeSH products and with qualifier(s): [administration & dosage - AD, complications - CO, poisoning - PO, adverse effects - AE, chemically induced - CI]	274637
	21-31 (OR)	810811
	20 AND 32	221009
Population: Aged		
	[mh Aged]	1280
	"care homes" or "community-dwelling" or frail or frailty or geriatric* or "nursing homes" or "old age" or "old people" or "older adults" or "older people":ti,ab,kw or aged or older or old or elder or elders or elderly:ti (Word variations have been searched)	50604

34 OR 35	51063
Combined sets	
3 AND 33 AND 36	CDSR/**30** DARE/0 HTA/0

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Embase via Elsevier 12 December 2019
Title: NSAIDs – adverse effects in the elderly

Search terms	Items found
Intervention: NSAIDs	
'acetylsalicylic acid'/exp/mj OR 'acetylsalicylic acid' OR 'diclofenac'/exp/mj OR 'diclofenac potassium'/exp/mj OR 'diclofenac plus misoprostol'/exp/mj OR 'piroxicam'/exp/mj OR 'piroxicam beta cyclodextrin'/exp/mj OR 'cinnoxicam'/exp/mj OR 'ibuprofen'/exp/mj OR 'naproxen'/exp/mj OR 'ketoprofen'/exp/mj OR 'ketoprofen lysine'/exp/mj OR 'celecoxib'/exp/mj OR 'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR	321773

	mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	
	'nonsteroid antiinflammatory agent'/exp OR 'nonsteroid antiinflammatory agent':ab,ti,kw OR 'nonsteroidal anti-inflammatory drugs':ab,ti,kw OR nsaid:ab,ti,kw OR nsaids:ab,ti,kw OR 'cox2 inhibitors':ab,ti,kw OR 'cox-2 inhibitors':ab,ti,kw OR 'cyclo-oxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase 2 inhibitor*':ab,ti,kw	745238
	1 OR 2	755527
Outcome: Adverse effects		
	adrs:ab,kw,ti or "adverse drug effect*":ab,kw,ti or "adverse drug reaction*":ab,kw,ti or "adverse effect*":ab,kw,ti or "adverse event*":ab,kw,ti or "adverse outcome*":ab,kw,ti or "adverse reaction*":ab,kw,ti or complication*:ab,kw,ti or harm:ab,kw,ti or harmful:ab,kw,ti or harms:ab,kw,ti or risk:ab,kw,ti or safe:ab,kw,ti or "adverse outcome*":ab,kw,ti or safely:ab,kw,ti or safety:ab,kw,ti or "side effect*":ab,kw,ti or tolerability:ab,kw,ti or toxicity:ab,kw,ti or "treatment emergent":ab,kw,ti or "undesirable effect*":ab,kw,ti or "undesirable event*":ab,kw,ti or "unexpected effect*":ab,kw,ti or "unexpected event*" or pharmacoepidemiology:ab,kw,ti	5610715
	'adverse drug reaction'/exp OR 'drug safety'/exp OR 'drug monitoring'/exp OR 'drug hypersensitivity'/exp OR 'drug surveillance program'/exp OR 'medication error'/exp OR 'intoxication'/exp OR 'side effect'/exp OR 'postmarketing surveillance'/exp OR 'drug recall'/exp OR 'product recall'/exp OR 'risk'/exp OR 'mortality'/exp OR 'medication error'/exp OR 'pharmacoepidemiology'/exp	4254246
	ae.fs. OR am.fs. OR co.fs. OR si.fs. OR to.fs.	714
	"peptic ulcer*":ab,kw,ti or "gastroduodenal ulcer*":ab,kw,ti or "marginal ulcer*":ab,kw,ti or "gastrointestinal bleeding":ab,kw,ti OR "gastrointestinal hemorrhage*":ab,kw,ti or "impaired renal function":ab,kw,ti or "edema":ab,kw,ti or "congestive heart failure":ab,kw,ti or "stroke":ab,kw,ti or "myocardial infarction*":ab,kw,ti or "cardiovascular stroke":ab,kw,ti or "heart attack":ab,kw,ti or "myocardial infarct*":ab,kw,ti or "hypertension":ab,kw,ti or "High Blood Pressure":ab,kw,ti	1398043
	'peptic ulcer'/exp or 'gastrointestinal hemorrhage'/exp or 'kidney function'/exp or 'kidney failure'/exp or 'edema'/exp or 'congestive heart failure'/exp or 'cerebrovascular accident'/exp or 'heart infarction'/exp or 'hypertension'/exp	2214057
	4-8 (OR)	8701992
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3785259
Study types: 'systematic review'		
	'systematic review'/de or 'meta analysis'/de or [cochrane review]/lim or ((systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab)	426402
Combined sets/Limits: publication date, language		
	3 AND 9 AND 10 AND 11 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**1305**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Embase via Elsevier 12 December 2019
Title: Opioids – adverse effects in the elderly

Search terms		Items found
Intervention: Opioids		
	'buprenorphine'/exp/mj or 'buprenorphine plus naloxone'/exp/mj or 'codeine'/exp/mj or 'cocodamol'/exp/mj or 'hydrocodone'/exp/mj or 'hydrocodone bitartrate plus or aracetamol'/exp/mj or 'hydrocodone bitartrate plus ibuprofen'/exp/mj or 'oxycodone'/exp/mj or 'oxycodone plus paracetamol'/exp/mj or 'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj or 'hydromorphone'/exp/mj or 'pethidine'/exp/mj or 'fentanyl'/exp/mj or 'tramadol'/exp/mj or 'paracetamol plus tramadol'/exp/mj or 'methadone'/exp/mj or 'codeine phosphate'/exp/mj or 'hydromorphone plus naloxone'/exp/mj or 'morphine'/exp/mj	95134
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	128968
	'narcotic analgesic agent'/exp OR opioid:ti OR opioids:ti OR 'chronic pain'/exp/mj/dm_dt OR 'chronic inflammatory pain'/exp/mj/dm_dt	348722
	1-3 (OR)	359204
Outcome: Adverse effects		
	adrs:ab,kw,ti or "adverse drug effect*":ab,kw,ti or "adverse drug reaction*":ab,kw,ti or "adverse effect*":ab,kw,ti or "adverse event*":ab,kw,ti or "adverse outcome*":ab,kw,ti or "adverse reaction*":ab,kw,ti or complication*:ab,kw,ti or harm:ab,kw,ti or harmful:ab,kw,ti or harms:ab,kw,ti or risk:ab,kw,ti or safe:ab,kw,ti or "adverse outcome*":ab,kw,ti or safely:ab,kw,ti or safety:ab,kw,ti or "side effect*":ab,kw,ti or tolerability:ab,kw,ti or toxicity:ab,kw,ti or "treatment emergent”:ab,kw,ti or "undesirable effect*":ab,kw,ti or "undesirable event*":ab,kw,ti or "unexpected effect*":ab,kw,ti or "unexpected event*" or pharmacoepidemiology:ab,kw,ti	5610715
	'adverse drug reaction'/exp OR ‘drug safety’/exp OR ‘drug monitoring’/exp OR ‘drug hypersensitivity’/exp OR ‘drug surveillance program’/exp OR 'medication error'/exp OR ‘intoxication’/exp OR ‘side effect’/exp OR ‘postmarketing surveillance’/exp OR ‘drug recall’/exp OR ‘product recall’/exp OR 'risk'/exp OR 'mortality'/exp OR 'medication error'/exp OR 'pharmacoepidemiology'/exp	4254246
	ae.fs. OR am.fs. OR co.fs. OR si.fs. OR to.fs.	714

	'constipation'/exp or 'confusion'/exp or 'opiate addiction'/exp or 'sedation'/exp or 'nausea and vomiting'/exp or 'dizziness'/exp or 'respiratory distress'/exp or constipation:ab,kw,ti or confusion:ab,kw,ti or addiction:ab,kw,ti or "opioid abuse":ab,kw,ti or "opioid depencence":ab,kw,ti or "opiate addiction":ab,kw,ti or sedation:ab,kw,ti or nausea:ab,kw,ti or vomiting:ab,kw,ti or dizziness:ab,kw,ti or "respiratory suppression":ab,kw,ti or "respiratory insufficiency":ab,kw,ti	785861
	5-8 (OR)	7655729
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3785259
Study types: 'systematic review'		
	'systematic review'/de or 'meta analysis'/de or [cochrane review]/lim or ((systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab)	426402
Combined sets/Limits: publication date, language		
	4 AND 9 AND 10 AND 11 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**415**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Embase via Elsevier 12 December 2019
Title: Paracetamol – adverse effects in the elderly

Search terms		Items found
Intervention: Paracetamol		
	'paracetamol'/exp OR 'cocodamol'/exp OR 'oxycodone plus paracetamol'/exp OR 'hydrocodone bitartrate plus paracetamol'/exp OR 'dextropropoxyphene plus paracetamol'/exp	90973
	acetaminophen:ab,kw,ti OR paracetamol:ab,kw,ti OR acetominophen:ab,kw,ti OR hydroxyacetanilide:ab,kw,ti OR apap:ab,kw,ti OR 'p acetamidophenol':ab,kw,ti OR 'p hydroxyacetanilide':ab,kw,ti OR 'n-(4-hydroxyphenyl)acetanilide':ab,kw,ti OR acetamidophenol:ab,kw,ti OR 'n-acetyl-p-aminophenol':ab,kw,ti OR 'n-acetyl-para-aminophenol':ab,kw,ti OR acephen:ab,kw,ti OR acetaco:ab,kw,ti OR tylenol:ab,kw,ti OR 'anacin 3':ab,kw,ti OR anacin3:ab,kw,ti OR datril:ab,kw,ti OR panadol:ab,kw,ti OR acamol:ab,kw,ti OR algotropyl:ab,kw,ti	39536
	1 OR 2	95339
Outcome: Adverse effects		
	adrs:ab,kw,ti or "adverse drug effect*":ab,kw,ti or "adverse drug reaction*":ab,kw,ti or "adverse effect*":ab,kw,ti or "adverse event*":ab,kw,ti or "adverse outcome*":ab,kw,ti or "adverse reaction*":ab,kw,ti or complication*:ab,kw,ti or harm:ab,kw,ti or harmful:ab,kw,ti or harms:ab,kw,ti or risk:ab,kw,ti or safe:ab,kw,ti or "adverse outcome*":ab,kw,ti or safely:ab,kw,ti or safety:ab,kw,ti or "side effect*":ab,kw,ti or tolerability:ab,kw,ti or toxicity:ab,kw,ti or "treatment emergent":ab,kw,ti or "undesirable effect*":ab,kw,ti or "undesirable event*":ab,kw,ti or "unexpected effect*":ab,kw,ti or "unexpected event*" or pharmacoepidemiology:ab,kw,ti	5610715

	'adverse drug reaction'/exp OR 'drug safety'/exp OR 'drug monitoring'/exp OR 'drug hypersensitivity'/exp OR 'drug surveillance program'/exp OR 'medication error'/exp OR 'intoxication'/exp OR 'side effect'/exp OR 'postmarketing surveillance'/exp OR 'drug recall'/exp OR 'product recall'/exp OR 'risk'/exp OR 'mortality'/exp OR 'medication error'/exp OR 'pharmacoepidemiology'/exp	4254246
	ae.fs. OR am.fs. OR co.fs. OR si.fs. OR to.fs.	714
	"peptic ulcer*":ab,kw,ti or "gastroduodenal ulcer*":ab,kw,ti or "marginal ulcer*":ab,kw,ti or "gastrointestinal bleeding":ab,kw,ti OR "gastrointestinal hemorrhage*":ab,kw,ti or "impaired renal function":ab,kw,ti or "edema":ab,kw,ti or "congestive heart failure":ab,kw,ti or "stroke":ab,kw,ti or "myocardial infarction*":ab,kw,ti or "cardiovascular stroke":ab,kw,ti or "heart attack":ab,kw,ti or "myocardial infarct*":ab,kw,ti or "hypertension":ab,kw,ti or "High Blood Pressure":ab,kw,ti	1398043
	'peptic ulcer'/exp or 'gastrointestinal hemorrhage'/exp or 'kidney function'/exp or 'kidney failure'/exp or 'edema'/exp or 'congestive heart failure'/exp or 'cerebrovascular accident'/exp or 'heart infarction'/exp or 'hypertension'/exp	2214057
	4-8 (OR)	8701992
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3785259
Study types: 'systematic review'		
	'systematic review'/de or 'meta analysis'/de or [cochrane review]/lim or ((systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab)	426402
Combined sets/Limits: publication date, language		
	3 AND 9 AND 10 AND 11 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**189**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 12 December 2019
Title: NSAID – adverse effects in the elderly

Search terms		Items found
Intervention: NSAID		
	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/	70247
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	91748
	exp Anti-Inflammatory Agents, Non-Steroidal/ OR ("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID or NSAIDS).ab,kf,kw,ti.	215433
	1-3 (OR)	244791
Outcome: adverse effects		
	(adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology").ab,kf,kw,ti.	3953714
	(ae or co or de).fs or (safe of safety or side effect* or undesireable effect* or treatment emergement or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or event or events or outcome or outcomes))).ab,kf,kw,ti.	6507949
	exp ABNORMALITIES, DRUG-INDUCED/ OR exp Adverse Drug Reaction Reporting Systems/ OR exp CONTRAINDICATIONS/ OR exp Drug Recalls/ OR exp Drug Hypersensitivity/ OR exp Drug Monitoring/ OR exp "Drug-Related Side Effects and Adverse Reactions"/ OR exp POISONING/ OR exp SAFETY-BASED DRUG WITHDRAWALS/ OR exp Substance-Related Disorders/ OR exp Long Term Adverse Effects/ OR exp Risk/ OR Mortality/ OR exp Medication Errors/ OR exp Pharmacoepidemiology/ OR exp Proportional hazards models/	1735997
	exp Peptic Ulcer/ or exp Gastrointestinal hemorrhage/ or Kidney/de, me or Renal Insufficiency/ or exp Edema/ or exp Heart failure/ or exp Stroke/ or exp Myocardial infarction/ or exp hypertension/ or ("peptic ulcer*" OR "gastroduodenal ulcer*" or "marginal ulcer*" or "gastrointestinal bleeding" OR "gastrointestinal hemorrhage*" or "impaired renal function" or edema or "congestive heart failure" or stroke or "myocardial infarction*" or "cardiovascular stroke" or "heart attack" or "myocardial infarct*" or hypertension or "High Blood Pressure").ab,kf,kw,ti.	1354340
	ae.xs OR ci.fs OR co.fs OR de.fs OR po.fs OR to.fs	6272100
	5-9 (OR)	9799819
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3224256
Study types: systematic review		

	(Publication type: meta analysis or systematic reviews).af. or ("systematic review" or "systematic review and meta analyses" or "systematic review and meta analysis" or "systematic review meta analysis" or systematic reviews).kw. or (systematic adj2 review*).ti,ab.	145284
Combined sets /Limits: publication year, language		
	4 AND 10 AND 11 AND 12 limit to (yr="1990 - July 23 2018" and (danish or english or norwegian or swedish)) [search date: July 23 2018]	**152**
	4 AND 10 AND 11 limit to (yr="2018 - 2019" and (danish or english or norwegian or swedish) and systematic reviews pre 2019)	**68**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Medline via OvidSP 12 December 2019
Title: Opioids – adverse effects in the elderly

Search terms		Items found
Intervention: Opioids		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/	78015
	(morphia OR morphine OR pentahydrate OR "MS Contin" OR "Oramorph SR" OR duramorph OR dihydromorphinone OR hydromorphon OR palladone OR laudacon OR dilaudid OR hydromorphone OR dihydrone OR oxycone OR dihydrohydroxycodeinone OR oxycodeinon OR eucodal OR theocodin OR oxycodone OR oxycontin OR pancodine OR dinarkon OR oxiconum OR cetobemidon OR ketobemidone OR pethidine OR fentanyl OR isonipecain OR dolsin OR dolosal OR dolin OR "operidine EPJ-I" OR "operidine EPJ I" OR dolantin OR dolargan OR meperidine OR lidol OR lydol OR demerol OR dolcontral OR burenorphine OR codeine OR tramadol OR tapentadol OR methadone OR tramundin OR biodalgic OR jutadol OR nobligan OR prontofort OR zytram OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR biokanol OR tramabeta OR tramadin OR tramadolratiopharm OR tramadoc OR ranitidin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR adolonta OR contramal OR amadol OR phentanyl OR fentanest OR dentanyl OR sublimaze OR duragesic OR durogesic OR fentora OR buprenex OR prefin OR subutex OR buprex OR temgesic OR buprenorphine OR N-Methylmorphine OR Isocodeine OR Codeine OR Ardinex OR Biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict).ab,kf,kw,ti.	94171
	exp Chronic Pain/dt or exp Analgesics, Opioid/ or opioid.ti. or opioids.ti.	132432
	1-3 (OR)	158526
Outcome: adverse effects		
	(adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology").ab,kf,kw,ti.	3953714

	(ae or co or de).fs or (safe of safety or side effect* or undesireable effect* or treatment emergement or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or event or events or outcome or outcomes))).ab,kf,kw,ti.	6507949
	exp ABNORMALITIES, DRUG-INDUCED/ OR exp Adverse Drug Reaction Reporting Systems/ OR exp CONTRAINDICATIONS/ OR exp Drug Recalls/ OR exp Drug Hypersensitivity/ OR exp Drug Monitoring/ OR exp "Drug-Related Side Effects and Adverse Reactions"/ OR exp POISONING/ OR exp SAFETY-BASED DRUG WITHDRAWALS/ OR exp Substance-Related Disorders/ OR exp Long Term Adverse Effects/ OR exp Risk/ OR Mortality/ OR exp Medication Errors/ OR exp Pharmacoepidemiology/ OR exp Proportional hazards models/	1735997
	Constipation/ or Confusion/ or exp Opioid-Related Disorders/ or exp DEEP SEDATION/ or exp CONSCIOUS SEDATION/ or exp NAUSEA/ or exp VOMITING/ or exp DIZZINESS/ or exp Respiratory Insufficiency/ or (constipation or confusion or addiction or "opioid abuse" or "opioid depencence " or "opiate addiction " or sedation or nausea or vomiting or dizziness or "respiratory suppression ").ab,kf,kw,ti.	337096
	ae.xs OR ci.fs OR co.fs OR de.fs OR po.fs OR to.fs	6272100
	5-9 (OR)	9377776
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3224256
Study types: systematic review [no filter]		
	(Publication type: meta analysis or systematic reviews).af. or ("systematic review" or "systematic review and meta analyses" or "systematic review and meta analysis" or "systematic review meta analysis" or systematic reviews).kw. or (systematic adj2 review*).ti,ab.	145284
Combined sets /Limits: publication year, language		
	4 AND 10 AND 11 AND 12 limit to (yr="1990 -Current" and (danish or english or norwegian or swedish))	**65**
	4 AND 10 AND 11 limit to (yr="2018 - 2019" and (danish or english or norwegian or swedish) and systematic reviews pre 2019)	**43**

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Medline via OvidSP 12 December 2019
Title: Paracetamol – adverse effects in the elderly

Search terms		Items found
Intervention: Paracetamol		
	exp Acetaminophen/	17719
	(acetaminophen or paracetamol or tylenol or acetominophen or hydroxyacetanilide or APAP or p-acetamidophenol or p-hydroxyacetanilide or "N-(4-Hydroxyphenyl)acetanilide" or acetamidophenol or "N-Acetyl-p-aminophenol" or "N-acetyl-para-aminophenol" or Acephen or Acetaco or Tylenol or Anacin-3 or "Anacin 3" or Anacin3 or Datril or Panadol or Acamol or Algotropyl).ab,kf,kw,ti.	24877
	1 OR 2	28220
Outcome: adverse effects		

	(adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology").ab,kf,kw,ti.	3953714
	(ae or co or de).fs or (safe of safety or side effect* or undesireable effect* or treatment emergement or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or event or events or outcome or outcomes))).ab,kf,kw,ti.	6507949
	exp ABNORMALITIES, DRUG-INDUCED/ OR exp Adverse Drug Reaction Reporting Systems/ OR exp CONTRAINDICATIONS/ OR exp Drug Recalls/ OR exp Drug Hypersensitivity/ OR exp Drug Monitoring/ OR exp "Drug-Related Side Effects and Adverse Reactions"/ OR exp POISONING/ OR exp SAFETY-BASED DRUG WITHDRAWALS/ OR exp Substance-Related Disorders/ OR exp Long Term Adverse Effects/ OR exp Risk/ OR Mortality/ OR exp Medication Errors/ OR exp Pharmacoepidemiology/ OR exp Proportional hazards models/	1735997
	exp Peptic Ulcer/ or exp Gastrointestinal hemorrhage/ or Kidney/de, me or Renal Insufficiency/ or exp Edema/ or exp Heart failure/ or exp Stroke/ or exp Myocardial infarction/ or exp hypertension/ or ("peptic ulcer*" OR "gastroduodenal ulcer*" or "marginal ulcer*" or "gastrointestinal bleeding" OR "gastrointestinal hemorrhage*" or "impaired renal function" or edema or "congestive heart failure" or stroke or "myocardial infarction*" or "cardiovascular stroke" or "heart attack" or "myocardial infarct*" or hypertension or "High Blood Pressure").ab,kf,kw,ti.	1354340
	ae.xs OR ci.fs OR co.fs OR de.fs OR po.fs OR to.fs	6272100
	4-8 (OR)	9799819
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3224256
Study types: systematic review		
	(Publication type: meta analysis or systematic reviews).af. or ("systematic review" or "systematic review and meta analyses" or "systematic review and meta analysis" or "systematic review meta analysis" or systematic reviews).kw. or (systematic adj2 review*).ti,ab.	145284
Combined sets /Limits: publication year, language		
	4 AND 9 AND 10 AND 11 limit to (yr="1990 -Current" and (danish or english or norwegian or swedish))	**152**
	4 AND 9 AND 10 limit to (yr="1990 - 2019" and (danish or english or norwegian or swedish) and systematic reviews pre 2019)	**64**

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.mp=text, heading word, subject area node, title

Embase via Elsevier 13 December 2019
Title: SNRI - adverse effects in the elderly

Search terms		Items found
Interventions: SNRI		
	'venlafaxine'/exp OR 'duloxetine'/exp	27615
	dobupal:ab,kw,ti OR efexor:ab,kw,ti OR effexor:ab,kw,ti OR 'sila venlafaxine':ab,kw,ti OR trevilor:ab,kw,ti OR vandral:ab,kw,ti OR venlafaxin:ab,kw,ti OR venlafaxine:ab,kw,ti OR 'wy 45030':ab,kw,ti OR '1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl':ab,kw,ti OR 'cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride':ab,kw,ti OR cymbalta:ab,kw,ti OR duloxetin:ab,kw,ti OR duloxetine:ab,kw,ti OR 'ly 227942':ab,kw,ti OR 'ly 248686':ab,kw,ti OR 'n-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine':ab,kw,ti OR 'n-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide':ab,kw,ti	9662
	'serotonin noradrenalin reuptake inhibitor'/exp or NRIs:ab,kw,ti or "Serotonin and Noradrenaline Uptake Inhibitors":ab,kw,ti or SNRIs:ab,kw,ti or "Serotonin and Norepinephrine Reuptake Inhibitors":ab,kw,ti or "Serotonin and Norepinephrine Uptake Inhibitors":ab,kw,ti	169052
	1-3 (OR)	169495
Population:		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3786696
	'neuralgia'/exp or 'diabetic neuropathy'/exp or "nerve pain":ab,kw,ti or neuralgias:ab,kw,ti or "neuropathic pain":ab,kw,ti or "paroxysmal nerve pain*":ab,kw,ti or "perineal neuralgi*":ab,kw,ti or "diabetic neuropathy":ab,kw,ti or "diabetic neuralgias":ab,kw,ti or "diabetic peripheral neuropathy":ab,kw,ti or "postherpetic neuralgia":ab,kw,ti	137014
	5 AND 6	23791
Study types: 'systematic review'		
	'systematic review'/de or 'meta analysis'/de or [cochrane review]/lim or ((systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab)	426768
Combined sets/Limits: publication date, language		
	4 AND 7 AND 8 AND ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**34**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 13 December 2019
Title: SNRI - adverse effects in the elderly

Search terms		Items found
Intervention: SNRI		
	exp "Serotonin and Noradrenaline Reuptake Inhibitors"/ or (NRIs or "Serotonin and Noradrenaline Uptake Inhibitors" or SNRIs or "Serotonin and Norepinephrine Reuptake Inhibitors" or "Serotonin and Norepinephrine Uptake Inhibitors").ti,ab,kw,kf.	5663
	exp Venlafaxine Hydrochloride/ OR exp Duloxetine Hydrochloride/	3919
	(Dobupal OR efexor OR effexor OR sila-venlafaxine OR trevilor OR vandral OR venlafaxin OR venlafaxine OR "wy 45030" OR "1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)cyclohexanol hcl" OR "cyclohexanol, 1-(2-(dimethylamino)-1-(4-methoxyphenyl)ethyl)-, hydrochloride" OR cymbalta OR duloxetin OR duloxetine OR "LY 227942" OR "LY 248686" OR "N-methyl-3-(1-naphthalenyloxy)-2-thiophenepropanamine" OR "N-methyl-3-(1-naphthalenyloxy)-3-(2-thiophene)propanamide").ti,ab,kw,kf.	5941
	1-3 (OR)	7968
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3224492
Study types: systematic review		
	(Publication type: meta analysis or systematic reviews).af. or ("systematic review" or "systematic review and meta analyses" or "systematic review and meta analysis" or "systematic review meta analysis" or systematic reviews).kw. or (systematic adj2 review*).ti,ab.	141670
Combined sets /Limits: publication year, language		
	4 AND 5 AND 6 limit to (yr="1990 -Current" and (danish or english or norwegian or swedish))	**26**

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.ti. = Title
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.mp=text, heading word, subject area node, title

Embase via Elsevier 13 December 2019
Title: TCA – adverse effects in the elderly

Search terms		Items found
Intervention: Tricyclic antidepressants		
	'tricyclic antidepressant agent'/exp or "tricyclic antidepressive agents":ab,kw,ti or "tricyclic antidepressant*":ab,kw,ti	114262
	'amitriptyline'/exp OR 'amitriptyline plus perphenazine'/exp OR 'amitriptyline plus chlordiazepoxide'/exp OR 'nortriptyline'/exp OR 'maprotiline'/exp OR 'clomipramine'/exp	57431
	amineurin:ti,ab OR amitrip:ti,ab OR amitriptylin:ti,ab OR amitriptyline:ti,ab OR amitrol:ti,ab OR anapsique:ti,ab OR 'apo amitriptyline':ti,ab OR damilen:ti,ab OR domical:ti,ab OR elavil:ti,ab OR endep:ti,ab OR laroxyl:ti,ab OR lentizol:ti,ab OR novoprotect:ti,ab OR saroten:ti,ab OR sarotex:ti,ab OR syneudon:ti,ab OR triptafen:ti,ab OR tryptanol:ti,ab OR tryptine:ti,ab OR tryptizol:ti,ab OR allegron:ti,ab OR 'apo nortriptyline':ti,ab OR aventyl:ti,ab OR desitriptyline:ti,ab OR desmethylamitriptylin:ti,ab OR 'gen nortriptyline':ti,ab OR norfenazin:ti,ab OR nortrilen:ti,ab OR nortriptylin:ti,ab OR nortriptyline:ti,ab OR 'novo	15900

	nortriptyline':ti,ab OR 'nu nortriptyline':ti,ab OR pamelor:ti,ab OR paxtibi:ti,ab OR 'pms nortriptyline':ti,ab OR 'ratio nortriptyline':ti,ab OR deprilept:ti,ab OR dibencycladine:ti,ab OR ludiomil:ti,ab OR maprolu:ti,ab OR maprotilin:ti,ab OR maprotiline:ti,ab OR mirpan:ti,ab OR 'novo maprotiline':ti,ab OR psymion:ti,ab OR 'ba34,276':ti,ab OR 'ba-34,276':ti,ab OR 'n-methyl-9,10-ethanoanthracene-9(10h)-propylamine':ti,ab OR anafranil:ti,ab OR chlomipramin:ti,ab OR chlomipramine:ti,ab OR clomipramin:ti,ab OR clomipramine:ti,ab OR chlorimipramine:ti,ab OR hydiphen:ti,ab	
	1-3 (OR)	116160
Population:		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3786696
	'neuralgia'/exp or 'diabetic neuropathy'/exp or "nerve pain":ab,kw,ti or neuralgias:ab,kw,ti or "neuropathic pain":ab,kw,ti or "paroxysmal nerve pain*":ab,kw,ti or "perineal neuralgi*":ab,kw,ti or "diabetic neuropathy":ab,kw,ti or "diabetic neuralgias":ab,kw,ti or "diabetic peripheral neuropathy":ab,kw,ti or "postherpetic neuralgia":ab,kw,ti	137014
	5 AND 6	25899
Study types: 'systematic review'		
	'systematic review'/de or 'meta analysis'/de or [cochrane review]/lim or ((systematic* NEXT/3 (review* OR overview)):ti,ab OR (systematic* NEXT/3 bibliographic*):ti,ab OR (systematic* NEXT/3 literature):ti,ab OR (meta-analy* or metaanaly*):ti,ab)	352897
Combined sets		
	4 AND 7 AND 8 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**266**

The search result, usually found at the end of the documentation, forms the list of abstracts.

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:ab = Abstract
:au = Author
:ti = Article Title
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* = Truncation
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Medline via OvidSP 13 December 2019
Title: TCA - adverse effects in the elderly

Search terms		Items found
Intervention: TCA		
	"Antidepressive Agents, Tricyclic"/ or ("tricyclic antidepressive agents" or "tricyclic antidepressant*").ti,ab,kw,kf.	16034
	exp amitriptyline/ or exp nortriptyline/ OR exp Maprotiline/ OR exp Clomipramine/	11206
	(amineurin OR amitrip OR amitriptylin OR amitriptyline OR amitrol OR anapsique OR apo-amitriptyline OR damilen OR domical OR elavil OR endep OR laroxyl OR lentizol OR novoprotect OR saroten OR sarotex OR syneudon OR triptafen OR tryptanol OR tryptine OR tryptizol OR allegron OR apo-Nortriptyline OR aventyl OR desitriptyline OR desmethylamitriptylin OR gen-nortriptyline OR norfenazin OR nortrilen OR nortriptylin OR nortriptyline OR novo-nortriptyline OR nu-nortriptyline OR pamelor OR paxtibi OR PMS-nortriptyline OR ratio-nortriptyline OR deprilept OR dibencycladine OR ludiomil OR maprolu OR maprotilin OR maprotiline OR mirpan OR novo-maprotiline OR psymion OR "Ba34,276" OR "Ba-34,276" OR "N-Methyl-9,10-ethanoanthracene-9(10H)-propylamine" OR anafranil OR chlomipramin OR chlomipramine OR chlorimipramine OR clomipramin OR clomipramine OR clorimipramine OR hydiphen).ti,ab,kw,kf.	11984

	1-3 (OR)	27442
Population: Elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3224492
Study types: systematic review		
	(Publication type: meta analysis or systematic reviews).af. or ("systematic review" or "systematic review and meta analyses" or "systematic review and meta analysis" or "systematic review meta analysis" or systematic reviews).kw. or (systematic adj2 review*).ti,ab.	178758
Combined sets /Limits: publication year, language		
	4 AND 5 AND 6 limit to (yr="1990 -Current" and (danish or english or norwegian or swedish))	**45**

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* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Primary studys/Primärstudier

Risk of acute renal failure/Risk för akut njurpåverkan

Cochrane Library via Wiley 11 December 2019
Title: NSAID – adverse effects - kidney

Search terms	Items found
Intervention: NSAID	
[mh Aspirin]	5531
[mh Diclofenac]	1849
[mh Piroxicam]	649
[mh Ibuprofen]	1824
[mh Naproxen]	1093
[mh Ketoprofen]	542
[mh Celecoxib]	869
("acetylsalicylic acid" or "2-(Acetyloxy)benzoic Acid" or aspirin or acylpyrin or aloxiprimum or colfarit or dispril or easprin sor ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or diclophenac or dicrofenac or dichlofenal or "diclonate P" or feloran or voltarol or novapirina or orthofen or ortofen or orthophen or voltaren or diclofenac or piroxicam or feldene or reutenox or artriunic or "Novo-Tenoxicam" or mobiflex or tilcotil or "Apo-Tenoxicam" or tenoxicam or reumoxicam or miloxicam or movalis or uticox or mobic or mobicox or mobec or masflex or movicox or parocin or meloxicam or ibumetin or ibuprofen or motrin or nuprin or rufen or salprofen or "Trauma-Dolgit Gel" or "Trauma Dolgit Gel" or "TraumaDolgit Gel" or brufen or methoxypropiocin or anaprox or naproxen or aleve or proxen or synflex or naprosin or naprosyn or "naproxenate sodium" or "benzoylhydratropic acid" or "2-(3-Benzoylphenyl)propionic Acid" or profenid or alrheumum or orudis or alrheumat or dexibuprofen or s-ibuprofen or "S ibuprofen" or badyket or ketesse or sympal or quiralam	30692

	or quirgel or adolquir or enangel or keral or enantyum or ketoprofen or dexketoprofen or celcoxib or celebrex or etoricoxib or arcoxia or nabumetone or arthraxan or "Gen-Nabumetone" or listran or relafen or relif or relifex or mebutan or "Rhoxal-nabumetone" or "Apo-Nabumetone" or celecoxib or nabucox):ti,ab,kw (Word variations have been searched)	
	MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees	7456
	("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID OR NSAIDS):ti,ab,kw	6674
	1-10 (OR)	37212
Outcome: Adverse effects		
	(kidney or renal):ti,ab,kw	74520
	MeSH descriptor: [Kidney] explode all trees	3861
	MeSH descriptor: [Renal Insufficiency] explode all trees	8202
	12-14 (OR)	74530
Population: Aged		
	((aged or older or old or elder or elders or elderly or "care home" or "care homes" or "community-dwelling" or frail or frailty or geriatric or "nursing home" or "nursing homes")):ti,ab,kw	557237
Combined sets		
	11 AND 15 AND 16 with Cochrane Library publication date from Jan 2016 to Dec 2019	**Central 533**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Embase via Elsevier 11 December 2019
Title: NSAID – adverse effects - kidney

Search terms		Items found
Intervention: NSAID		
	'acetylsalicylic acid'/exp/mj OR 'acetylsalicylic acid' OR 'diclofenac'/exp/mj OR 'diclofenac potassium'/exp/mj OR 'diclofenac plus misoprostol'/exp/mj OR 'piroxicam'/exp/mj OR 'piroxicam beta cyclodextrin'/exp/mj OR 'cinnoxicam'/exp/mj OR 'ibuprofen'/exp/mj OR 'naproxen'/exp/mj OR 'ketoprofen'/exp/mj OR 'ketoprofen lysine'/exp/mj OR 'celecoxib'/exp/mj OR 'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR	321737

	'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	
	'nonsteroid antiinflammatory agent'/exp OR 'nonsteroid antiinflammatory agent':ab,ti,kw OR 'nonsteroidal anti-inflammatory drugs':ab,ti,kw OR nsaid:ab,ti,kw OR nsaids:ab,ti,kw OR 'cox2 inhibitors':ab,ti,kw OR 'cox-2 inhibitors':ab,ti,kw OR 'cyclo-oxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase 2 inhibitor*':ab,ti,kw	745160
	1 OR 2	755450
Outcome: Adverse effects		
	'kidney function'/exp or 'kidney failure'/exp or kidney:ti or "kidney failure":ab,kw,ti or "kidney function":ab,kw,ti or "kidney injur*":ab,kw,ti or renal:ti or "renal graft function":ab,kw,ti or "renal function":ab,kw,ti or "renal failure":ab,kw,ti or "renal impairment":ab,kw,ti	909709
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3784656
Combined sets/Limits: publication date, language		
	3 AND 4 AND 5 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [2016-2020]/py	**2452**

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
“ ” = Citation Marks; searches for an exact phrase

Medline via OvidSP 11 December 2019
Title: NSAID – adverse effect - kidney

Search terms		Items found
Intervention: NSAID		
	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/	70205
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	91679
	exp Anti-Inflammatory Agents, Non-Steroidal/ OR ("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID or NSAIDS).ab,kf,kw,ti.	2015292
	1-3 (OR)	244618
Outcome: adverse effects liver		
	Kidney/de, me or Renal Insufficiency/ or kidney.ti or "kidney failure".ab,kf,kw,ti. or "kidney function".ab,kf,kw,ti. or "kidney injur*".ab,kf,kw,ti. or renal.ti or "renal graft function".ab,kf,kw,ti. or "renal function".ab,kf,kw,ti. or "renal failure".ab,kf,kw,ti. or "renal impairment".ab,kf,kw,ti.	552697
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3221778
Combined sets /Limits: publication year, language		
	4 AND 5 AND 6 limit to yr="2016 -Current" and ((danish or english or norwegian or swedish))	**198**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

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

Cochrane Library via Wiley 11 December 2019
Title: NSAID – adverse effects - peptic ulcer hemorrhages

Search terms		Items found
Intervention: NSAID		
	[mh Aspirin]	5531
	[mh Diclofenac]	1984
	[mh Piroxicam]	649
	[mh Ibuprofen]	1824
	[mh Naproxen]	1093
	[mh Ketoprofen]	542
	[mh Celecoxib]	869
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox):ti,ab,kw (Word variations have been searched)	30692
	[mh “Anti-Inflammatory Agents, Non-Steroidal”]	7456
	("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID OR NSAIDS):ti,ab,kw	6674
	1-10 (OR)	37212
Outcome: Adverse effects		
	[mh "Peptic Ulcer"]	3752
	[mh "Gastrointestinal Hemorrhage"]	1889
	((bleeding OR hemorrhage* OR perforat*)):ti AND ((ulcer OR gastro*)):ti	1380
	("bleeding gastric ulcer" OR "bleeding gastroduodenal ulcer*" OR "bleeding peptic ulcer*" OR "gastroduodenal ulcer" OR "gastrointestinal bleeding" OR "gastrointestinal hemorrhage*" OR "hemorrhagic gastroduodenal ulcer" OR "marginal ulcer*" OR "peptic ulcer" OR "small bowel bleeding" OR "small bowel ulcer bleeding" OR "small bowel bleeding" OR "small bowel ulcer bleeding" OR "ulcer perforation*"):ti,ab,kw	7718
	12-15 (OR)	10392
	adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology":ti,ab,kw (Word variations have been searched)	613088
	[mh "Abnormalities, Drug-Induced"]	47
	[mh "Adverse Drug Reaction Reporting Systems"]	88
	[mh "Contraindications"]	259
	[mh "Drug Recalls"]	1
	[mh "Drug Hypersensitivity"]	964
	[mh "Drug Monitoring"]	1723
	[mh "Drug-Related Side Effects and Adverse Reactions"]	3417

	[mh Poisoning]	2076
	[mh "Safety-Based Drug Withdrawals"]	11
	[mh "Long Term Adverse Effects"]	26
	[mh Risk]	36965
	[mh ^Mortality]	502
	[mh "Medication Errors"]	404
	[mh Pharmacoepidemiology]	17
	17-31 (OR)	617911
	16 AND 32	5899
Population: Aged		
	((aged OR older OR old OR elder OR elders OR elderly OR "care home" OR "care homes" OR "community-dwelling" OR frail OR frailty OR geriatric OR "nursing home" OR "nursing homes")):ti,ab,kw	557238
Combined sets		
	11 AND 33 AND 34 with Cochrane Library publication date from Jan 1990 to 2019	**Central 603**

The search result, usually found at the end of the documentation, forms the list of abstracts.
:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase
CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Embase via Elsevier 11 December 2019
Title: NSAID – adverse effects - peptic ulcer hemorrhages

Search terms		Items found
Intervention: NSAID		
	'acetylsalicylic acid'/exp/mj OR 'acetylsalicylic acid' OR 'diclofenac'/exp/mj OR 'diclofenac potassium'/exp/mj OR 'diclofenac plus misoprostol'/exp/mj OR 'piroxicam'/exp/mj OR 'piroxicam beta cyclodextrin'/exp/mj OR 'cinnoxicam'/exp/mj OR 'ibuprofen'/exp/mj OR 'naproxen'/exp/mj OR 'ketoprofen'/exp/mj OR 'ketoprofen lysine'/exp/mj OR 'celecoxib'/exp/mj OR 'acetylsalicylic acid':ab,ti,kw OR '2-(acetyloxy)benzoic acid':ab,ti,kw OR aspirin:ab,ti,kw OR acylpyrin:ab,ti,kw OR aloxiprimum:ab,ti,kw OR colfarit:ab,ti,kw OR dispril:ab,ti,kw OR easprin:ab,ti,kw OR ecotrin:ab,ti,kw OR endosprin:ab,ti,kw OR magnecyl:ab,ti,kw OR micristin:ab,ti,kw OR polopirin:ab,ti,kw OR polopiryna:ab,ti,kw OR solprin:ab,ti,kw OR solupsan:ab,ti,kw OR zorprin:ab,ti,kw OR acetysal:ab,ti,kw OR diclophenac:ab,ti,kw OR dicrofenac:ab,ti,kw OR dichlofenal:ab,ti,kw OR 'diclonate p':ab,ti,kw OR feloran:ab,ti,kw OR voltarol:ab,ti,kw OR novapirina:ab,ti,kw OR orthofen:ab,ti,kw OR ortofen:ab,ti,kw OR orthophen:ab,ti,kw OR voltaren:ab,ti,kw OR diclofenac:ab,ti,kw OR piroxicam:ab,ti,kw OR feldene:ab,ti,kw OR reutenox:ab,ti,kw OR artriunic:ab,ti,kw OR 'novo-tenoxicam':ab,ti,kw OR mobiflex:ab,ti,kw OR tilcotil:ab,ti,kw OR 'apo-tenoxicam':ab,ti,kw OR tenoxicam:ab,ti,kw OR reumoxicam:ab,ti,kw OR miloxicam:ab,ti,kw OR movalis:ab,ti,kw OR uticox:ab,ti,kw OR mobic:ab,ti,kw OR mobicox:ab,ti,kw OR mobec:ab,ti,kw OR masflex:ab,ti,kw OR movicox:ab,ti,kw OR parocin:ab,ti,kw OR meloxicam:ab,ti,kw OR ibumetin:ab,ti,kw OR ibuprofen:ab,ti,kw OR motrin:ab,ti,kw OR nuprin:ab,ti,kw OR rufen:ab,ti,kw OR salprofen:ab,ti,kw OR 'trauma-dolgit gel':ab,ti,kw OR 'trauma dolgit gel':ab,ti,kw OR 'traumadolgit gel':ab,ti,kw OR brufen:ab,ti,kw OR methoxypropiocin:ab,ti,kw OR anaprox:ab,ti,kw OR naproxen:ab,ti,kw OR aleve:ab,ti,kw OR proxen:ab,ti,kw OR synflex:ab,ti,kw OR naprosin:ab,ti,kw OR naprosyn:ab,ti,kw OR 'naproxenate sodium':ab,ti,kw OR 'benzoylhydratropic acid':ab,ti,kw OR '2-(3-benzoylphenyl)propionic acid':ab,ti,kw OR profenid:ab,ti,kw OR	321737

	alrheumum:ab,ti,kw OR orudis:ab,ti,kw OR alrheumat:ab,ti,kw OR dexibuprofen:ab,ti,kw OR 's ibuprofen':ab,ti,kw OR badyket:ab,ti,kw OR ketesse:ab,ti,kw OR sympal:ab,ti,kw OR quiralam:ab,ti,kw OR quirgel:ab,ti,kw OR adolquir:ab,ti,kw OR enangel:ab,ti,kw OR keral:ab,ti,kw OR enantyum:ab,ti,kw OR ketoprofen:ab,ti,kw OR dexketoprofen:ab,ti,kw OR celcoxib:ab,ti,kw OR celebrex:ab,ti,kw OR etoricoxib:ab,ti,kw OR arcoxia:ab,ti,kw OR nabumetone:ab,ti,kw OR arthraxan:ab,ti,kw OR 'gen-nabumetone':ab,ti,kw OR listran:ab,ti,kw OR relafen:ab,ti,kw OR relif:ab,ti,kw OR relifex:ab,ti,kw OR mebutan:ab,ti,kw OR 'rhoxal-nabumetone':ab,ti,kw OR 'apo-nabumetone':ab,ti,kw OR celecoxib:ab,ti,kw OR nabucox:ab,ti,kw	
	'nonsteroid antiinflammatory agent'/exp OR 'nonsteroid antiinflammatory agent':ab,ti,kw OR 'nonsteroidal anti-inflammatory drugs':ab,ti,kw OR nsaid:ab,ti,kw OR nsaids:ab,ti,kw OR 'cox2 inhibitors':ab,ti,kw OR 'cox-2 inhibitors':ab,ti,kw OR 'cyclo-oxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase inhibitor*':ab,ti,kw OR 'cyclooxygenase 2 inhibitor*':ab,ti,kw	745160
	1 OR 2	755450
Outcome: Adverse effects		
	'ulcer perforation'/exp OR 'peptic ulcer'/exp OR 'peptic ulcer bleeding'/exp OR ((bleeding:ti OR hemorrhage*:ti OR perforat*:ti) AND (ulcer:ti OR gastro*:ti)) OR 'bleeding gastric ulcer':ab,ti,kw OR 'bleeding gastroduodenal ulcer*':ab,ti,kw OR 'bleeding peptic ulcer*':ab,ti,kw OR 'gastroduodenal bleed*':ab,ti,kw OR 'gastroduodenal ulcer*':ab,ti,kw OR 'gastrointestinal bleeding':ab,ti,kw OR 'gastrointestinal hemorrhage*':ab,ti,kw OR 'hemorrhagic gastroduodenal ulcer':ab,ti,kw OR 'marginal ulcer':ab,ti,kw OR 'peptic ulcer*':ab,ti,kw OR 'small bowel bleeding':ab,ti,kw OR 'small bowel ulcer bleeding':ab,ti,kw OR 'ulcer perforation*':ab,ti,kw	169132
	adrs:ab,kw,ti OR 'adverse drug effect*':ab,kw,ti OR 'adverse drug reaction*':ab,kw,ti OR "adverse effect*":ab,kw,ti OR "adverse event*":ab,kw,ti OR "adverse outcome*":ab,kw,ti OR "adverse reaction*":ab,kw,ti OR complication*:ab,kw,ti OR harm:ab,kw,ti OR harmful:ab,kw,ti OR harms:ab,kw,ti OR risk:ab,kw,ti OR safe:ab,kw,ti OR "adverse outcome*":ab,kw,ti OR safely:ab,kw,ti OR safety:ab,kw,ti OR "side effect*":ab,kw,ti OR tolerability:ab,kw,ti OR toxicity:ab,kw,ti OR "treatment emergent":ab,kw,ti OR "undesirable effect*":ab,kw,ti OR "undesirable event*":ab,kw,ti OR "unexpected effect*":ab,kw,ti OR "unexpected event*" OR pharmacoepidemiology:ab,kw,ti	5609772
	'adverse drug reaction'/exp OR 'drug safety'/exp OR 'drug monitoring'/exp OR 'drug hypersensitivity'/exp OR 'drug surveillance program'/exp OR 'medication error'/exp OR 'intoxication'/exp OR 'side effect'/exp OR 'postmarketing surveillance'/exp OR 'drug recall'/exp OR 'product recall'/exp OR 'risk'/exp OR 'mortality'/exp OR 'medication error'/exp OR 'pharmacoepidemiology'/exp	4253692
	ae.fs. OR am.fs. OR co.fs. OR si.fs. OR to.fs.	714
	5-7 (OR)	7304426
	4 AND 8	59714
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3784656
Combined sets/Limits: publication date, language		
	3 AND 9 AND 10 AND ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [embase]/lim AND [1990-2019]/py	**2877**

The search result, usually found at the end of the documentation, forms the list of abstracts.
/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 11 December 2019
Title: NSAID – adverse effect - peptic ulcer hemorrhages

Search terms		Items found
Intervention: NSAID		
	Aspirin/ OR exp Diclofenac/ OR exp Piroxicam/ OR exp Ibuprofen/ OR exp Naproxen/ OR exp Ketoprofen/ OR exp Celecoxib/	70205
	("acetylsalicylic acid" OR "2-(Acetyloxy)benzoic Acid" OR aspirin OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR diclophenac OR dicrofenac OR dichlofenal OR "diclonate P" OR feloran OR voltarol OR novapirina OR orthofen OR ortofen OR orthophen OR voltaren OR diclofenac OR piroxicam OR feldene OR reutenox OR artriunic OR "Novo-Tenoxicam" OR mobiflex OR tilcotil OR "Apo-Tenoxicam" OR tenoxicam OR reumoxicam OR miloxicam OR movalis OR uticox OR mobic OR mobicox OR mobec OR masflex OR movicox OR parocin OR meloxicam OR ibumetin OR ibuprofen OR motrin OR nuprin OR rufen OR salprofen OR "Trauma-Dolgit Gel" OR "Trauma Dolgit Gel" OR "TraumaDolgit Gel" OR brufen OR methoxypropiocin OR anaprox OR naproxen OR aleve OR proxen OR synflex OR naprosin OR naprosyn OR "naproxenate sodium" OR "benzoylhydratropic acid" OR "2-(3-Benzoylphenyl)propionic Acid" OR profenid OR alrheumum OR orudis OR alrheumat OR dexibuprofen OR s-ibuprofen OR "S ibuprofen" OR badyket OR ketesse OR sympal OR quiralam OR quirgel OR adolquir OR enangel OR keral OR enantyum OR ketoprofen OR dexketoprofen OR celcoxib OR celebrex OR etoricoxib OR arcoxia OR nabumetone OR arthraxan OR "Gen-Nabumetone" OR listran OR relafen OR relif OR relifex OR mebutan OR "Rhoxal-nabumetone" OR "Apo-Nabumetone" OR celecoxib OR nabucox).ab,kf,kw,ti.	91679
	exp Anti-Inflammatory Agents, Non-Steroidal/ OR ("COX2 Inhibitors" OR "COX-2 Inhibitors" OR "Cyclo-Oxygenase Inhibitor*" OR "Cyclooxygenase Inhibitor*" OR "Cyclooxygenase 2 Inhibitor*" OR "Nonsteroidal anti-inflammatory drugs" OR NSAID or NSAIDS).ab,kf,kw,ti.	215292
	1-3 (OR)	244618
Outcome: adverse effects		
	exp peptic ulcer/ OR exp Gastrointestinal hemorrhage/ or (("bleeding".ti. or "hemorrhage*".ti. or "perforat*".ti.) AND (ulcer.ti. or gastro*.ti.)) or ("bleeding gastric ulcer" or "bleeding gastroduodenal ulcer*" or "bleeding peptic ulcer*" or "gastroduodenal ulcer" or "gastrointestinal bleeding" or "gastrointestinal hemorrhage*" or "hemorrhagic gastroduodenal ulcer" or "marginal ulcer*"or "peptic ulcer*" OR "peptic ulcer bleed" or "peptic ulcer bleeding" or "peptic ulcer perforation*" or "perforated peptic ulcer*" or "small bowel bleeding" or "small bowel ulcer bleeding" or "ulcer perforation*").ab,kf,kw,ti.	130993
	(adrs or "adverse drug effect*" or "adverse drug reaction*" or "adverse effect*" or "adverse event*" or "adverse outcome*" or "adverse reaction*" or complication* or harm or harmful or harms or risk or safe or "adverse outcome*" or safely or safety or "side effect*" or tolerability or toxicity or "treatment emergent" or "undesirable effect*" or "undesirable event*" or "unexpected effect*" or "unexpected event*" or "pharmacoepidemiology").ab,kf,kw,ti.	3667151
	exp ABNORMALITIES, DRUG-INDUCED/ OR exp Adverse Drug Reaction Reporting Systems/ OR exp CONTRAINDICATIONS/ OR exp Drug Recalls/ OR exp Drug Hypersensitivity/ OR exp Drug Monitoring/ OR exp "Drug-Related Side Effects and Adverse Reactions"/ OR exp POISONING/ OR exp SAFETY-BASED DRUG WITHDRAWALS/ OR exp Substance-Related Disorders/ OR exp Long Term Adverse Effects/ OR exp Risk/ OR Mortality/ OR exp Medication Errors/ OR exp Pharmacoepidemiology/ OR exp Proportional hazards models/	1734591
	ae.xs OR ci.fs OR co.fs OR de.fs OR po.fs OR to.fs	6268304
	6-8 (OR)	9251323
	5 AND 9	74472
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3221778
Combined sets /Limits: publication year, language		
	4 AND 10 AND 11 limit to yr="1990 -Current" and ((danish or english or norwegian or swedish))	**1695**

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* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Opioids and the risk of falls/Risk för fall vid opioid-behandling

Cochrane Library via Wiley 11 Dec 2019
Title: Opioids – accidental falls

Search terms		Items found
Intervention: Opioids		
	[mh Buprenorphine]	1043
	[mh "Buprenorphine, Naloxone Drug Combination"]	110
	[mh Codeine]	1605
	[mh Hydrocodone]	202
	[mh Oxycodone]	844
	[mh Hydromorphone]	342
	[mh Morphine]	4747
	[mh Meperidine]	1138
	[mh Fentanyl]	5282
	[mh Tramadol]	1067
	[mh Methadone]	1187
	morphia or morphine or pentahydrate or "MS Contin" or "Oramorph SR" or duramorph or dihydromorphinone or hydromorphon or palladone or laudacon or dilaudid or hydromorphone or dihydrone or oxycone or dihydrohydroxycodeinone or oxycodeinon or eucodal or theocodin or oxycodone or oxycontin or pancodine or dinarkon or oxiconum or cetobemidon or ketobemidone or pethidine or fentanyl or isonipecain or dolsin or dolosal or dolin or "operidine EPJ-I" or "operidine EPJ I" or dolantin or dolargan or meperidine or lidol or lydol or demerol or dolcontral or burenorphine or codeine or tramadol or tapentadol or methadone or tramundin or biodalgic or jutadol or nobligan or prontofort or zytram or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or biokanol or tramabeta or tramadin or tramadolratiopharm or tramadoc or ranitidin or trasedal or ultram or "xymel 50" or zamudol or zumalgic or zydol or tramadoldolgit or tramadolhameln or tramadolor or tramadura or tramagetic or tramagit or tramake or tramal or tramex or adolonta or contramal or amadol or phentanyl or fentanest or dentanyl or sublimaze or duragesic or durogesic or fentora or buprenex or prefin or subutex or buprex or temgesic or buprenorphine or N-Methylmorphine or Isocodeine or Codeine or Ardinex or Biodone or Dolophine or Metadol or Metasedin or Symoron or Methadone or Methadose or Methex or Phenadone or Physeptone or Phymet or Pinadone or Amidone or Methaddict:ti,ab,kw (Word variations have been searched)	36839
	[mh "Chronic Pain" /DT]	315
	[mh "Analgesics, Opioid"]	7132
	((opioid or opioids)):ti	4578
	1-15 (OR)	40813
Outcome: Accidental falls		
	[mh "Accidental Falls"]	1393

	(fall* or fell or stumbl* or slip* or trip*):ti	8582
	17 or 18	9160
Population: Aged		
	[mh Aged]	1280
	("care homes" or "community-dwelling" or frail or frailty or geriatric* or "nursing homes" or "old age" or "old people" or "older adults" or "older people"):ti,ab,kw OR (aged or older or old or elder or elders or elderly):ti	50604
	20 or 21	51063
Combined sets		
	16 and 19 and 22 with Cochrane Library publication date from Jan 2016 to Dec 2019	CDSR/0 DARE/0 HTA/0

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:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Embase via Elsevier 11 December 2019
Title: Opioids – accidental falls

Search terms		Items found
Intervention: Opioids		
	'buprenorphine'/exp/mj or 'buprenorphine plus naloxone'/exp/mj or 'codeine'/exp/mj or 'cocodamol'/exp/mj or 'hydrocodone'/exp/mj or 'hydrocodone bitartrate plus or aracetamol'/exp/mj or 'hydrocodone bitartrate plus ibuprofen'/exp/mj or 'oxycodone'/exp/mj or 'oxycodone plus paracetamol'/exp/mj or 'acetylsalicylic acid plus oxycodone plus oxycodone terephthalate'/exp/mj or 'hydromorphone'/exp/mj or 'pethidine'/exp/mj or 'fentanyl'/exp/mj or 'tramadol'/exp/mj or 'paracetamol plus tramadol'/exp/mj or 'methadone'/exp/mj or 'codeine phosphate'/exp/mj or 'hydromorphone plus naloxone'/exp/mj or 'morphine'/exp/mj	95132
	morphia:ab,kw,ti OR morphine:ab,kw,ti OR pentahydrate:ab,kw,ti OR 'ms contin':ab,kw,ti OR 'oramorph sr':ab,kw,ti OR duramorph:ab,kw,ti OR dihydromorphinone:ab,kw,ti OR hydromorphon:ab,kw,ti OR palladone:ab,kw,ti OR laudacon:ab,kw,ti OR dilaudid:ab,kw,ti OR hydromorphone:ab,kw,ti OR dihydrone:ab,kw,ti OR oxycone:ab,kw,ti OR dihydrohydroxycodeinone:ab,kw,ti OR oxycodeinon:ab,kw,ti OR eucodal:ab,kw,ti OR theocodin:ab,kw,ti OR oxycodone:ab,kw,ti OR oxycontin:ab,kw,ti OR pancodine:ab,kw,ti OR dinarkon:ab,kw,ti OR oxiconum:ab,kw,ti OR cetobemidon:ab,kw,ti OR ketobemidone:ab,kw,ti OR pethidine:ab,kw,ti OR fentanyl:ab,kw,ti OR isonipecain:ab,kw,ti OR dolsin:ab,kw,ti OR dolosal:ab,kw,ti OR dolin:ab,kw,ti OR 'operidine epj-i':ab,kw,ti OR 'operidine epj i':ab,kw,ti OR dolantin:ab,kw,ti OR dolargan:ab,kw,ti OR meperidine:ab,kw,ti OR lidol:ab,kw,ti OR lydol:ab,kw,ti OR demerol:ab,kw,ti OR dolcontral:ab,kw,ti OR burenorphine:ab,kw,ti OR tramadol:ab,kw,ti OR tapentadol:ab,kw,ti OR tramundin:ab,kw,ti OR biodalgic:ab,kw,ti OR jutadol:ab,kw,ti OR nobligan:ab,kw,ti OR prontofort:ab,kw,ti OR zytram:ab,kw,ti OR takadol:ab,kw,ti OR theradol:ab,kw,ti OR tiral:ab,kw,ti OR topalgic:ab,kw,ti OR tradol:ab,kw,ti OR tradolpuren:ab,kw,ti OR tradonal:ab,kw,ti OR tralgiol:ab,kw,ti OR trama:ab,kw,ti OR tramadorsch:ab,kw,ti OR biokanol:ab,kw,ti OR	128959

	tramabeta:ab,kw,ti OR tramadin:ab,kw,ti OR tramadolratiopharm:ab,kw,ti OR tramadoc:ab,kw,ti OR ranitidin:ab,kw,ti OR trasedal:ab,kw,ti OR ultram:ab,kw,ti OR 'xymel 50':ab,kw,ti OR zamudol:ab,kw,ti OR zumalgic:ab,kw,ti OR zydol:ab,kw,ti OR tramadoldolgit:ab,kw,ti OR tramadolhameln:ab,kw,ti OR tramadolor:ab,kw,ti OR tramadura:ab,kw,ti OR tramagetic:ab,kw,ti OR tramagit:ab,kw,ti OR tramake:ab,kw,ti OR tramal:ab,kw,ti OR tramex:ab,kw,ti OR adolonta:ab,kw,ti OR contramal:ab,kw,ti OR amadol:ab,kw,ti OR phentanyl:ab,kw,ti OR fentanest:ab,kw,ti OR dentanyl:ab,kw,ti OR sublimaze:ab,kw,ti OR duragesic:ab,kw,ti OR durogesic:ab,kw,ti OR fentora:ab,kw,ti OR buprenex:ab,kw,ti OR prefin:ab,kw,ti OR subutex:ab,kw,ti OR buprex:ab,kw,ti OR temgesic:ab,kw,ti OR buprenorphine:ab,kw,ti OR 'n methylmorphine':ab,kw,ti OR isocodeine:ab,kw,ti OR codeine:ab,kw,ti OR ardinex:ab,kw,ti OR biodone:ab,kw,ti OR dolophine:ab,kw,ti OR metadol:ab,kw,ti OR metasedin:ab,kw,ti OR symoron:ab,kw,ti OR methadone:ab,kw,ti OR methadose:ab,kw,ti OR methex:ab,kw,ti OR phenadone:ab,kw,ti OR physeptone:ab,kw,ti OR phymet:ab,kw,ti OR pinadone:ab,kw,ti OR amidone:ab,kw,ti OR methaddict:ab,kw,ti	
	'narcotic analgesic agent'/exp OR opioid:ti OR opioids:ti OR 'chronic pain'/exp/mj/dm_dt OR 'chronic inflammatory pain'/exp/mj/dm_dt	348674
	1-3 (OR)	359153
Outcome: accidental falls		
	'falling'/exp	36306
	fall?:ab,kw,ti OR fell:ab,kw,ti OR falling:ab,kw,ti OR fallen:ab,kw,ti OR faller:ab,kw,ti OR stumble?:ab,kw,ti OR stumbling:ab,kw,ti OR stumbles:ab,kw,ti OR slip:ab,kw,ti OR slips:ab,kw,ti OR slipping:ab,kw,ti OR slipped:ab,kw,ti OR trip:ab,kw,ti OR tripped:ab,kw,ti	203304
	5 or 6	221809
Population: Elderly		
	'aged'/exp or aged:ab,kw,ti OR 'care home*':ab,kw,ti OR 'community-dwelling':ab,kw,ti OR elderly:ab,kw,ti OR elders:ab,kw,ti OR elder:ab,kw,ti OR frail:ab,kw,ti OR frailty:ab,kw,ti OR geriatric:ab,kw,ti OR 'nursing home*':ab,kw,ti OR old:ti OR 'old age':ab,kw,ti OR 'old people':ab,kw,ti OR older:ti OR 'older adults':ab,kw,ti OR 'older people':ab,kw,ti OR 'senior citizen':ab,kw,ti	3784656
Combined sets/Limits: publication date, language		
	4 AND 7 AND 8 ([danish]/lim OR [english]/lim OR [norwegian]/lim OR [swedish]/lim) AND [2016-2019]/py	**297**

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* = Truncation
“ “ = Citation Marks; searches for an exact phrase

Medline via OvidSP 11 December 2019
Title: Opioids – accidental falls

Search terms		Items found
Intervention: Opioids		
	buprenorphine/ or buprenorphine, naloxone drug combination/ or codeine/ or hydrocodone/ or oxycodone/ or exp hydromorphone/ or exp morphine/ or exp Meperidine/ or exp Fentanyl/ or exp Tramadol/ or exp Methadone/	77992
	(morphia OR morphine OR pentahydrate OR "MS Contin" OR "Oramorph SR" OR duramorph OR dihydromorphinone OR hydromorphon OR palladone OR laudacon OR dilaudid OR hydromorphone OR dihydrone OR oxycone OR dihydrohydroxycodeinone OR oxycodeinon OR eucodal OR theocodin OR oxycodone OR oxycontin OR pancodine OR dinarkon OR oxiconum OR cetobemidon OR ketobemidone OR pethidine OR fentanyl OR isonipecain OR dolsin OR dolosal OR dolin OR "operidine EPJ-I" OR "operidine EPJ I" OR dolantin OR dolargan OR meperidine OR lidol OR lydol OR demerol OR dolcontral OR burenorphine OR codeine OR tramadol OR tapentadol OR methadone OR tramundin OR biodalgic OR jutadol OR nobligan OR prontofort OR zytram OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR biokanol OR tramabeta OR tramadin OR tramadolratiopharm OR tramadoc OR ranitidin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR adolonta OR contramal OR amadol OR phentanyl OR fentanest OR dentanyl OR sublimaze OR duragesic OR durogesic OR fentora OR buprenex OR prefin OR subutex OR buprex OR temgesic OR buprenorphine OR N-Methylmorphine OR Isocodeine OR Codeine OR Ardinex OR Biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict).ab,kf,kw,ti.	94130
	exp Chronic Pain/dt or exp Analgesics, Opioid/ or opioid.ti. or opioids.ti.	132356
	1-3 (OR)	158437
Outcome: accidental falls		
	Accidental Falls/	23135
	(fall? or fell or falling or fallen or faller or stumble? or stumbling or stumbles or slip or slips or slipping or slipped or trip or tripped).ab,kf,ti.	248290
	5 or 6	254305
Population: elderly		
	exp AGED/ or aged.ti. OR care homes.ti,ab,kw,kf. OR community-dwelling.ti,ab,kw,kf. OR elderly.ti. OR elders.ti. OR elder.ti. OR frail.ti. OR frailty.ti. OR geriatric*.ti. OR nursing homes.ti,ab,kw,kf. OR old.ti OR old age.ti,ab,kw,kf. OR old people.ti,ab,kw,kf. OR older.ti. OR older adults.ti,ab,kw,kf. OR older people.ti,ab,kw,kf.	3221778
Combined sets /Limits: publication year, language		
	4 and 7 and 8 limit to (yr="2016 -Current" and (danish or english or norwegian or swedish))	**64**

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* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Part V 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

Systematic reviews/Systematiska översikter

Cochrane Library via Wiley 27 January 2020 (CDSR)
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (systematiska översikter, metasynteser)

Search terms		Items found
Population: Pain		
	[mh ^Pain/DT,PX]	4462
	[mh "Chronic Pain"/DT,PX]	577
	[mh "Pain Management"/PX]	75
	(chronic or persistent) NEAR/3 (pain)	16176
	1-4 (OR)	*20093*
Population: Osteoarthritis		
	[mh Osteoarthritis/DT,PX]	1874
	(osteoarthr* or degenerative next arthrit* or "degenerative joint disease"):ti,ab,kw	10029
	6 OR 7	*10029*
Population: Diabetic neuropathies		
	[mh "Diabetic Neuropathies"/DT,PX]	569
	((diabetic) next/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ti,ab,kw	2182
	((diabet* and neuropath*) near/15 (pain*)):ti,ab,kw	688
	"Bruns-Garland":ti,ab,kw	1
	9-12 (OR)	*2348*
Population: Osteoporotic vertebral fractures		
	[mh "Spinal Fractures"/DT,PX]	59
	[mh Spine] or [mh Osteoporosis/CO]	4978
	(vertebral or spine or spinal):ti,ab,kw	36443
	[mh "Fractures, Bone"/ET]	546
	(fracture* or compression*):ti,ab,kw	29068
	14 OR ((15 OR 16) AND (17 OR 18))	*5901*
Patients experiences		
	[mh Attitude] or [mh "Attitude to Health"] or [mh "Patient Acceptance "] or [mh "Patient Satisfaction"] or [mh "Patient Preference"] or [mh Optimism] or [mh Pessimism] or [mh Stereotyping] or [mh Emotions] or [mh "Expressed Emotion"] or [mh Patients/PX] or [mh Inpatients/PX] or [mh Outpatients/PX] or [mh "Personal Satisfaction"] or [mh Prejudice] or [mh Ageism]	52355
	((patient* or women* or men or people* or individual* or adult* or resident*) near/15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)):ti,ab,kw	160232
	20 OR 21	*190723*
Health care, home care, community care		
	[mh "Housing for the Elderly"] or [mh "Homes for the Aged"] or [mh "Nursing Homes"] or [mh "Pain Clinics"] or [mh "Home Care Services"] or [mh "Home Health Nursing"] or [mh "Community Health Nursing"] or [mh "Long Term Care"] or [mh "Attitude of Helth Personnel"] or [mh "Delivery of Helath Care"] or [mh "Pain Management"] or [mh "Professional-Patient Relations"] or [mh "Nurse-Patient Relations"] or [mh "Physician-Patient Relations"] or [mh "Researcher-Subject Relations"]	10691

	((psycholog* or emotion or emotions or experience or experiences or meaning or perception or perspective* or view or views or value or trust or stigma or satisf* or dissatif* or unsatisfied or interpretation or relation or belie* or disbelie* or encounter* or "self-report" or embodied or consultation or attitude*or opinion* or barrier* or enabler*) near/25 (professional* or doctor* or "general practitioner*" or gp or physician* or "health car*" or nurs* or provider* or "long term care" or "primary care" or "residential care" or clinic or clinics or clinician* or "health personnel" or "nursing home*" or care)):ti,ab,kw	52878
	23 OR 24	*61020*
Limits: Publication year		
	From 1990 to 2020	
Combined sets		
	(5 OR 8 OR 13 OR 19) AND 22 AND 25 AND 26	**CDSR/ 34**

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:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CDSR = Cochrane Database of Systematic Review

Medline via OvidSP 21 January 2020
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (systematiska översikter, metasynteser)

Search terms		Items found
Population: Pain		
	Pain/dt, px [Drug Therapy, Psychology]	42296
	Chronic Pain/dt, px [Drug Therapy, Psychology]	6002
	Pain Management/px [Psychology]	629
	((chronic or persistent) adj3 pain).ab,kf,ti.	69449
	1-4 (OR)	*105371*
Population: Osteoarthritis		
	exp Osteoarthritis/dt, px [Drug Therapy, Psychology]	9277
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,ti.	75570
	6 OR 7	*77451*
Population: Diabetic neuropathies		
	Diabetic Neuropathies/dt, px [Drug Therapy, Psychology]	3361
	(diabetic adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 pain*).ab,kf,ti. or "Bruns-Garland".ab,kf,ti.	13144
	9 OR 10	*14668*
Population: Osteoporotic vertebral fractures		
	Spinal Fractures	14536
	Spine/	29847
	Osteoporosis/co [Complications]	7446
	(vertebral or spine or spinal).ab,kf,ti.	350466
	12-15 (OR)	*398517*
	Osteoporotic Fractures/	5233
	Fractures, Compression/	2173
	Fractures, Bone/etiology	8358

	(fracture* or compression*).ab,kf,ti.	349526
	17-20(OR)	*352047*
	12 OR (16 AND 21)	*55137*
Patients experiences		
	attitude/ or attitude to health/ or "patient acceptance of health care"/ or patient satisfaction/ or patient preference/ or optimism/ or pessimism/ or stereotyping/	260374
	emotions/ or expressed emotion/	66324
	Patients/px [Psychology]	8131
	Inpatients/px [Psychology]	4463
	Outpatients/px [Psychology]	1785
	personal satisfaction/	18027
	PREJUDICE/	24490
	((patient* or women* or men or people* or individual* or adult* or resident*) adj15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)).ab,kf,ti.	1120277
	"life world".ab,kf,ti.	331
	23-31 (OR)	*1364540*
Health care, home care, community care		
	Housing for the Elderly/	1600
	Nursing Homes/	34169
	Pain Clinics/	1457
	Home Care Services/	32931
	Community Health Nursing/	19495
	Long-Term Care/	25545
	"Attitude of Health Personnel"/	119101
	"Delivery of Health Care"/	88018
	Pain Management/	32448
	interpersonal relations/ or professional-patient relations/ or nurse-patient relations/ or physician-patient relations/ or researcher-subject relations/	199577
	((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics)).ab,kf,ti.	248226
	"pain management".ab,kf,ti.	23830
	33-44 (OR)	*725780*
Study types: systematiska översikter, metasynteser		
	Publication type: (meta analysis or systematic reviews)	
	((review or systematic or meta or synthes*) adj3 (qualitative or narrative or interpret* or integrative or evidence)).af. OR ((meta) adj3 (study or studies or synthes* or ethnograph* or "data analys*" or summary)).af. OR ((realist or framework or thematic or "mixed method*") adj3 (synthes* or review)).af. OR ((meta* or review or synthes* or systematic) adj3 ("grounded theory")).af. OR ((information or data) adj2 (synthes*)).af. OR ((data) adj2 (extract*)).af. OR (metasynthes* or metaethnograph* or "qualitative cross-case analysis" or "aggregated analys*").af.	149260
Limits: Publication year, language		
	(yr="1990 - Current") and (danish or english or norwegian or swedish)	
Combined sets		
	Smärta: (5 AND 32 AND 45) AND (46 OR 47) AND 48	**249**
	Artros: (8 AND 32 AND 45) AND (46 OR 47) AND 48	**52**
	Diabetesneuropati: (11 AND 32 AND 45) AND (46 OR 47) AND 48	**4**
	Kotkompressioner: (22 AND 32 AND 45) AND (46 OR 47) AND 48	**9**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

Cinahl via EBSCO 27 January 2020

Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (systematiska översikter, metasynteser)

Search terms	Items found
Population: Pain	
(MH "Pain+/DT/PF") OR (MH "Pain Management")	49,947
TI ((chronic or persistent) N3 (pain)) OR AB ((chronic or persistent) N3 (pain)) OR SU ((chronic or persistent) N3 (pain))	39,486
1 OR 2	*77,429*
Population: Osteoarthritis	
(MH "Osteoarthritis+/PF/DT")	3,670
TI (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR AB (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR SU (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease")	34,652
4 OR 5	*34,655*
Population: Diabetic neuropathies	
(MH "Diabetic Neuropathies/DT/PF")	925
TI ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)) OR AB ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)) OR SU ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))	6,284
TI ((diabet* and neuropath*) N15 (pain*)) OR AB ((diabet* and neuropath*) N15 (pain*)) OR SU ((diabet* and neuropath*) N15 (pain*))	1,410
TI "Bruns-Garland" OR AB "Bruns-Garland" OR SU "Bruns-Garland"	3
7-10 (OR)	*6,470*
Population: Osteoporotic vertebral fractures	
(MH "Spinal Fractures+")	5,042
(MH "Spine+")	39,770
(MH "Osteoporosis")	20,199
TI (vertebral or spine or spinal) OR AB (vertebral or spine or spinal) OR SU vertebral or spine or spinal)	102,115
13-15(OR)	126,692
(MH "Osteoporotic Fractures")	397
(MH "Fractures, Compression+")	1,182
TI (fracture* or compression*) OR AB (fracture* or compression*) OR SU (fracture* or compression*)	96,098
17-19 (OR)	96,098
12 OR (16 AND 20)	*135,562*
3 OR 6 OR 11 OR 21	
Patients experiences	
(MH "Attitude") OR (MH "Attitude to Medical Treatment") OR (MH "Attitude to Health") OR (MH "Consumer Attitudes") OR (MH "Patient Attitudes") OR (MH "Personal Satisfaction")	111,482
(MH "Patient Satisfaction")	50,542
(MH "Optimism") OR (MH "Pessimism")	2,616
(MH "Stereotyping") OR (MH "Stigma") OR (MH "Psychosocial Aspects of Illness")	22,995

	(MH "Patients/PF") OR (MH "Aged, Hospitalized/PF") OR (MH "Diabetic Patients/PF") OR (MH "Homebound Patients/PF") OR (MH "Inpatients/PF") OR (MH "Nursing Home Patients/PF") OR (MH "Outpatients/PF")	7,804
	(MH "Prejudice")	5,170
	TI (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR AB (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR SU (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)))	493,986
	TI "life world" OR AB "life world" OR SU "life world"	291
	23-30 (OR)	*566,772*
Health care, home care, community care		
	(MH "Health Care Delivery") OR (MH "Health Services Accessibility") OR (MH "Primary Health Care") OR (MH "Secondary Health Care")	168,936
	(MH "Housing for the Elderly") OR (MH "Pain Clinics") OR (MH "Nurse-Managed Centers") OR (MH "Ambulatory Care Facilities") OR (MH "Health Facilities") OR (MH "Senior Centers") OR (MH "Community Health Centers") OR (MH "Outpatient Service") OR (MH "Home Health Agencies") OR (MH "Residential Facilities") OR (MH "Nursing Homes+")	67,524
	(MH "Home Health Care") OR (MH "Home Nursing, Professional") OR (MH "Community Health Nursing") OR (MH "Community Health Services")	68,749
	(MH "Long Term Care") OR (MH "Home Nursing") OR (MH "Attitude of Health Personnel") OR (MH "Nurse Attitudes") OR (MH "Occupational Therapist Attitudes") OR (MH "Pain Management") OR (MH "Professional-Patient Relations") OR (MH "Nurse-Patient Relations") OR (MH "Physician-Patient Relations") OR (MH "Researcher-Subject Relations")	176,109
	TI (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics))) OR AB (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics))) OR SU (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics)))	205,777
	TI "pain management" OR AB "pain management" OR SU "pain management"	19,271
	32-37 (OR)	*558,755*
Study types: systematic reviews, meta synthesis		
	(MH "Systematic Review" OR ZT "systematic review" OR MH "Meta Analysis" OR ZT "meta analysis") OR ((TI (systematic* n3 review*)) or (AB (systematic* n3 review*)) or (TI (systematic* n3 bibliographic*)) or (AB (systematic* n3 bibliographic*)) or (TI (systematic* n3 literature)) or (AB (systematic* n3 literature)) or (TI (comprehensive* n3 literature)) or (AB (comprehensive* n3 literature)) or (TI (comprehensive* n3 bibliographic*)) or (AB (comprehensive* n3 bibliographic*)) or (TI (integrative n3 review)) or (AB (integrative n3 review)) or (JN "Cochrane Database of Systematic Reviews") or (TI (information n2 synthesis)) or (TI (data n2 synthesis)) or (AB (information n2 synthesis)) or (AB (data n2 synthesis)) or (TI (data n2 extract*)) or (AB (data n2 extract*)) or (TI (medline or pubmed or psyclit or cinahl or (psycinfo not "psycinfo database") or "web of science" or scopus or embase)) or (AB (medline or pubmed or psyclit or cinahl or (psycinfo not "psycinfo database") or "web of science" or scopus or embase)) or (TI (meta-analy* or metaanaly*)) or (AB (meta-analy* or metaanaly*)))	191,018
	(MH "Meta Synthesis") OR ((((review or systematic or meta or synthes*) N3 (qualitative or narrative or interpret* or integrative OR evidence)) OR (meta W3 (study or studies or synthes* or ethnograph* or "data analys*" or summary)) OR ((realist or framework or thematic or "mixed method*") N3 (synthes* or review)) OR ((meta* or review or synthes* or systematic) N3 ("grounded theory")) OR ((information OR data) N2 synthes*) OR data	62,864

	W2 extract* OR (metasynthes* OR metaethnograph* OR "qualitative cross-case analysis" OR "aggregated analys*"))	
Limits: publication year, language		
	Limiters - Published Date: 19900101-20200131; Language: Danish, English, Norwegian, Swedish	
Combined sets		
	22 AND 31 AND 38 AND (39 OR 40) AND 41	**381**

The search result, usually found at the end of the documentation, forms the list of abstracts.

AB = Abstract
AU = Author
DE = Term from the thesaurus
MM = Major Concept
TI = Title
TX = All Text. Performs a keyword search of all the database's searchable fields
ZC = Methodology Index
* = Truncation
" " = Citation Marks; searches for an exact phrase

PsycInfo via EBSCO 1 February 2018
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (systematiska översikter, metasynteser)

Search terms		Items found
Population: Pain		
	DE "Back Pain" OR DE "Chronic Pain" OR DE "Neuropathic Pain" OR DE "Neuralgia" OR DE "Pain" OR DE "Peripheral Neuropathy"	51,955
	TI (((chronic or persistent) N3 (pain))) OR AB (((chronic or persistent) N3 (pain))) OR KW (((chronic or persistent) N3 (pain)))	21,191
	1 OR 2	*55,805*
Population: Osteoarthritis		
	DE "Joint Disorders" OR DE "Arthritis"	2,805
	TI (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR AB (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR SU (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease")	2,065
	4 OR 5	*3,725*
Population: Diabetic neuropathies		
	DE "Neuropathic Pain" OR DE "Peripheral Neuropathy"	4,168
	TI (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))) OR AB (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))) OR KW (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)))	1,027
	TI (((diabet* and neuropath*) N15 (pain*))) OR AB (((diabet* and neuropath*) N15 (pain*))) OR KW (((diabet* and neuropath*) N15 (pain*)))	683
	TI "Bruns-Garland" OR AB "Bruns-Garland" OR KW "Bruns-Garland"	0
	7-10 (OR)	*4,911*
Population: Osteoporotic vertebral fractures		
	DE "Spinal Cord Injuries"	6,011
	DE "Spinal Column" OR DE "Spinal Cord"	11,948
	DE "Osteoporosis"	1,288
	TI ((vertebral or spine or spinal)) OR AB ((vertebral or spine or spinal)) OR KW ((vertebral or spine or spinal))	33,764
	12-15(OR)	36,699
	TI ((fracture* or compression*)) OR AB ((fracture* or compression*)) OR KW ((fracture* or compression*))	7,993
	16 AND 17	1,335
	3 OR 6 OR 11 OR 18	*55,192*

Patient experiences		
	(DE "Attitude Formation" OR DE "Pessimism" OR DE "Optimism") OR (DE "Client Attitudes" OR DE "Client Satisfaction" OR DE "Physical Illness (Attitudes Toward)" OR DE "Attitudes" OR DE "Health Attitudes")	65,683
	(DE "Satisfaction" OR DE "Client Satisfaction" OR DE "Life Satisfaction") OR (DE "Need Satisfaction")	27,148
	(DE "Stigma" OR DE "Stereotyped Attitudes") OR (DE "Labeling")	26,647
	DE "Patients" OR DE "Geriatric Patients" OR DE "Hospitalized Patients" OR DE "Medical Patients" OR DE "Outpatients"	66,448
	DE "Prejudice"	13,530
	TI (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR AB (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR KW (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)))	661,327
	TI "life world" OR AB "life world" OR SU "life world"	590
	20-26 (OR)	775,572
Health care, home care, community care		
	DE "Health Care Delivery" OR DE "Home Care" OR DE "Hospice" OR DE "Long Term Care" OR DE "Primary Health Care" OR DE "Residential Care Institutions" OR DE "Hospitals" OR DE "Nursing Homes" OR DE "Group Homes" OR DE "Retirement Communities"	86,921
	DE "Home Visiting Programs" OR DE "Elder Care" OR DE "Home Care" OR DE "Home Care Personnel"	12,116
	DE "Health Personnel Attitudes" OR DE "Pain Management"	30,307
	TI (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics))) OR AB (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics))) OR KW (((attitud* or belie* or disbelie* or consult* or encounter*) AND (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics)))	157,318
	TI "pain management" OR AB "pain management" OR KW "pain management"	7,279
	28-32 (OR)	258,647
Study types: systematic reviews, meta analysis, meta synthesis		
	DE "Meta Analysis" OR ZC "systematic review" OR ZC "meta analysis"	42,857
	TX (systematic* N3 review*) OR TX (metaanaly* OR meta-analy* OR "meta analy*") OR TX ((systematic* n3 bibliographic*) OR (systematic* n3 literature) OR (comprehensive* n3 literature) OR (comprehensive* n3 bibliographic*) OR (integrative n3 review) OR (information n2 synthesis) OR (data n2 synthesis) OR (data n2 extract*)) OR JN ("Cochrane Database of Systematic Reviews")	73,329
	34-35 (OR)	73,329
	(ZC "metasynthesis")	392
	(((review or systematic or meta or synthes*) N3 (qualitative or narrative or interpret* or integrative OR evidence)) OR (meta W3 (study or studies or synthes* or ethnograph* or "data analys*" or summary)) OR ((realist or framework or thematic or "mixed method*") N3 (synthes* or review)) OR ((meta* or review or synthes* or systematic) N3 ("grounded theory")) OR ((information OR data) N2 synthes*) OR data W2 extract* OR (metasynthes* OR metaethnograph* OR "qualitative cross-case analysis" OR "aggregated analys*")	55,272
	37-38 (OR)	55,306
	36 OR 39	106,062

Limits: publication year, language	
Limiters - Published Date: 1990-2020; Language: Danish, English, Norwegian, Swedish	
Combined sets	
19 AND 27 AND 33 AND 40 AND 41	**395**

The search result, usually found at the end of the documentation, forms the list of abstracts.

AB = Abstract
AU = Author
DE = Term from the thesaurus
MM = Major Concept
TI = Title
TX = All Text. Performs a keyword search of all the database's searchable fields
ZC = Methodology Index
* = Truncation
" " = Citation Marks; searches for an exact phrase

Primary studies/Primärstudier

Cochrane Library via Wiley 23 January 2020 (CENTRAL)
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer

Search terms	Items found
Population: Pain	
[mh ^Pain/DT,PX]	4462
[mh "Chronic Pain"/DT,PX]	577
[mh "Pain Management"/PX]	75
(chronic or persistent) NEAR/3 (pain)	16176
1-4 (OR)	*20093*
Population: Osteoarthritis	
[mh Osteoarthritis/DT,PX]	1874
(osteoarthr* or degenerative next arthrit* or "degenerative joint disease"):ti,ab,kw	10029
6 OR 7	*10029*
Population: Diabetic neuropathies	
[mh "Diabetic Neuropathies"/DT,PX]	569
((diabetic) next/3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)):ti,ab,kw	2182
((diabet* and neuropath*) near/15 (pain*)):ti,ab,kw	688
"Bruns-Garland":ti,ab,kw	1
9-12 (OR)	*2348*
Population: Osteoporotic vertebral fractures	
[mh "Spinal Fractures"/DT,PX]	59
[mh Spine] or [mh Osteoporosis/CO]	4978
(vertebral or spine or spinal):ti,ab,kw	36443
[mh "Fractures, Bone"/ET]	546
(fracture* or compression*):ti,ab,kw	29068
14 OR ((15 OR 16) AND (17 OR 18))	*5901*
Patients experiences	
[mh Attitude] or [mh "Attitude to Health"] or [mh "Patient Acceptance "] or [mh "Patient Satisfaction"] or [mh "Patient Preference"] or [mh Optimism] or [mh Pessimism] or [mh Stereotyping] or [mh Emotions] or [mh "Expressed Emotion"] or [mh Patients/PX] or [mh Inpatients/PX] or [mh Outpatients/PX] or [mh "Personal Satisfaction"] or [mh Prejudice] or [mh Ageism]	52355

	((patient* or women* or men or people* or individual* or adult* or resident*) near/15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)):ti,ab,kw	160232
	21 OR 22	*190723*
Health care, home care, community care		
	[mh "Housing for the Elderly"] or [mh "Homes for the Aged"] or [mh "Nursing Homes"] or [mh "Pain Clinics"] or [mh "Home Care Services"] or [mh "Home Health Nursing"] or [mh "Community Health Nursing"] or [mh "Long Term Care"] or [mh "Attitude of Helth Personnel"] or [mh "Delivery of Helath Care"] or [mh "Pain Management"] or [mh "Professional-Patient Relations"] or [mh "Nurse-Patient Relations"] or [mh "Physician-Patient Relations"] or [mh "Researcher-Subject Relations"]	10691
	((psycholog* or emotion or emotions or experience or experiences or meaning or perception or perspective* or view or views or value or trust or stigma or satisf* or dissatif* or unsatisfied or interpretation or relation or belie* or disbelie* or encounter* or "self-report" or embodied or consultation or attitude*or opinion* or barrier* or enabler*) near/25 (professional* or doctor* or "general practitioner*" or gp or physician* or "health car*" or nurs* or provider* or "long term care" or "primary care" or "residential care" or clinic or clinics or clinician* or "health personnel" or "nursing home*" or care)):ti,ab,kw	52878
	23 OR 24	*61020*
Limits: Publication year		
	From 1990 to 2020	
Combined sets		
	(5 OR 8 OR 13 OR 19) AND 22 AND 25 AND 26	**Central/ 1810**

The search result, usually found at the end of the documentation, forms the list of abstracts.

:au = Author
MeSH = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
this term only = Does not include terms found below this term in the MeSH hierarchy
:ti = title
:ab = abstract
:kw = keyword
* = Truncation
" " = Citation Marks; searches for an exact phrase

CENTRAL = Cochrane Central Register of Controlled Trials, "trials"

Cinahl via EBSCO 27 January 2020

Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (primärstudier)

Search terms		Items found
Population: Pain		
	(MH "Pain+/DT/PF")	49,947
	TI ((chronic or persistent) N3 (pain)) OR AB ((chronic or persistent) N3 (pain))	39,486
	1 OR 2	*77,429*
Population: Osteoarthritis		
	(MH "Osteoarthritis+/PF/DT")	3,670
	TI (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR AB (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR SU (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease")	34,652
	4 OR 5	*34,655*
Population: Diabetic neuropathies		
	(MH "Diabetic Neuropathies/DT/PF")	925
	TI ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)) OR AB ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or	6,284

	mononeuropath* or amyotroph*)) OR SU ((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))	
	TI ((diabet* and neuropath*) N15 (pain*)) OR AB ((diabet* and neuropath*) N15 (pain*)) OR SU ((diabet* and neuropath*) N15 (pain*))	1,410
	TI "Bruns-Garland" OR AB "Bruns-Garland" OR SU "Bruns-Garland"	3
	7-10 (OR)	*6,470*
Population: Osteoporotic vertebral fractures		
	(MH "Spinal Fractures+")	5,042
	(MH "Spine+") OR (MH "Osteoporosis")	39,770
	TI (vertebral or spine or spinal) OR AB (vertebral or spine or spinal) OR SU (vertebral or spine or spinal)	20,199
	13-14 (OR)	*102,115*
	(MH "Osteoporotic Fractures") OR (MH "Fractures, Compression+")	126,692
	TI (fracture* or compression*) OR AB (fracture* or compression*) OR SU (fracture* or compression*)	397
	16-17 (OR)	*1,182*
	12 OR (15 AND 18)	*96,098*
Patients experiences and attitudes		
	(MH "Attitude") OR (MH "Attitude to Medical Treatment") OR (MH "Attitude to Health") OR (MH "Consumer Attitudes") OR (MH "Patient Attitudes") OR (MH "Personal Satisfaction") OR (MH "Patient Satisfaction") OR (MH "Optimism") OR (MH "Pessimism") OR (MH "Stereotyping") OR (MH "Stigma") OR (MH "Psychosocial Aspects of Illness") OR (MH "Patients/PF") OR (MH "Aged, Hospitalized/PF") OR (MH "Diabetic Patients/PF") OR (MH "Homebound Patients/PF") OR (MH "Inpatients/PF") OR (MH "Nursing Home Patients/PF") OR (MH "Outpatients/PF") OR (MH "Prejudice")	189,625
	TI (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR AB (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR SU (((patient* or women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)))	493,986
	TI "life world" OR AB "life world" OR SU "life world"	291
	20-22 (OR)	*566,772*
Health care, home care, community care		
	(MH "Health Care Delivery") OR (MH "Health Services Accessibility") OR (MH "Primary Health Care") OR (MH "Secondary Health Care") OR (MH "Housing for the Elderly") OR (MH "Pain Clinics") OR (MH "Nurse-Managed Centers") OR (MH "Ambulatory Care Facilities") OR (MH "Health Facilities") OR (MH "Senior Centers") OR (MH "Community Health Centers") OR (MH "Outpatient Service") OR (MH "Home Health Agencies") OR (MH "Residential Facilities") OR (MH "Nursing Homes+") OR (MH "Home Health Care") OR (MH "Home Nursing, Professional") OR (MH "Community Health Nursing") OR (MH "Community Health Services") OR (MH "Long Term Care") OR (MH "Home Nursing") OR (MH "Attitude of Health Personnel") OR (MH "Nurse Attitudes") OR (MH "Occupational Therapist Attitudes") OR (MH "Pain Management") OR (MH "Professional-Patient Relations") OR (MH "Nurse-Patient Relations") OR (MH "Physician-Patient Relations") OR (MH "Researcher-Subject Relations")	433,106)
	(psycholog* or emotion or emotions or experience or experiences or meaning or perception or perspective* or view or views or value or trust or stigma or satisf* or dissatif* or unsatisfied or interpretation or relation or belie* or disbelie* or encounter* or "self-report" or embodied or consultation or attitude*or opinion* or barrier* or enabler*) N25 (professional* or doctor* or "general practitioner*" or gp or physician* or "health car*" or nurs* or provider* or "long term care" or "primary care" or "residential care" or clinic or clinics or clinician* or "health personnel" or "nursing home*" or care)	205,777
	TI "pain management" OR AB "pain management" OR SU "pain management"	19,271

	24-26 (OR)	*558,755*
Study types: qualitative research		
	(MH "Research, Nursing") OR (MH "Action Research") OR (MH "Descriptive Research") OR (MH "Ethnographic Research") OR (MH "Ethnological Research") OR (MH "Ethnonursing Research") OR (MH "Field Studies") OR (MH "Grounded Theory") OR (MH "Phenomenological Research") OR (MH "Thematic Analysis") OR (MH "Audiorecording") OR (MH "Focus Groups") OR (MH "Interviews") OR (MH "Semi-Structured Interview") OR (MH "Structured Interview") OR (MH "Unstructured Interview") OR (MH "Self Report") OR (MH "Patient-Reported Outcomes") OR (MH "Surveys") OR (MH "Videorecording") OR (MH "Cluster Sample") OR (MH "Empirical Research") OR (MH "Purposive Sample") OR (MH "Discourse Analysis") OR (MH "Theoretical Sample") OR (MH "Content Analysis") OR (MH "Constant Comparative Method") OR (MH "Narratives")	519,038
	(MH "Qualitative Studies+") OR (MH "Questionnaires+") OR (MH "Storytelling") OR (MH "Life Experiences")	501,068
	TI ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*")) OR AB ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*")) OR MH ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*"))	488,380
	TI (((field) N2 (research or study or studies or work)) OR ((grounded) N2 (theor* or study or studies or research or analys*)) OR ((lived or life) N2 (experience* or story or stories)) OR ((video or tape) N2 (record*)) OR (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) N3 (interview* or discussion* or questionnaire*))) OR AB (((field) N2 (research or study or studies or work)) OR ((grounded) N2 (theor* or study or studies or research or analys*)) OR ((lived or life) N2 (experience* or story or stories)) OR ((video or tape) N2 (record*)) OR (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) N3 (interview* or discussion* or questionnaire*))) OR MH (((field) N2 (research or study or studies or work)) OR ((grounded) N2 (theor* or study or studies or research or analys*)) OR ((lived or life) N2 (experience* or story or stories)) OR ((video or tape) N2 (record*)) OR (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) N3 (interview* or discussion* or questionnaire*)))	108,317
	TI (("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*")) OR AB (("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*")) OR MH (("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*"))	28,191
	28-32 (OR)	*954,410*
Limits: publication year, language		
	Limiters - Published Date: 19900101-20200131; Language: Danish, English, Norwegian, Swedish	
Combined sets		
	(3 OR 6 OR 11 OR 19) AND 23 AND 27 AND 33 AND 34	**2,763**

The search result, usually found at the end of the documentation, forms the list of abstracts.

AB = Abstract
AU = Author

DE = Term from the thesaurus
MM = Major Concept
TI = Title
TX = All Text. Performs a keyword search of all the database's searchable fields
ZC = Methodology Index
* = Truncation
" " = Citation Marks; searches for an exact phrase

Medline via OvidSP 23 January 2020
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer (primärstudier)

Search terms		Items found
Population: Pain		
	Pain/dt, px [Drug Therapy, Psychology]	39827
	Chronic Pain/dt, px [Drug Therapy, Psychology]	4243
	Pain Management/px [Psychology]	460
	((chronic or persistent) adj3 pain).ab,kf,ti.	59239
	1-4 (OR)	*92654*
Population: Osteoarthritis		
	exp Osteoarthritis/dt, px [Drug Therapy, Psychology]	8259
	(osteoarthr* or "degenerative arthrit*" or "degenerative joint disease" or coxarthr* or gonarthr* or ((heberdens or bochards) adj1 noduli)).ab,kf,ti.	64985
	6-7 (OR)	*66792*
Population: Diabetic neuropathies		
	Diabetic Neuropathies/dt, px [Drug Therapy, Psychology]	2208
	((diabetic) adj3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)).ab,kf,ti. OR ((diabet* and neuropath*) adj15 (pain*)).ab,kf,ti. OR "Bruns-Garland".ab,kf,ti.	11713
	9-10 (OR)	*12296*
Population: Osteoporotic vertebral fractures		
	Spinal Fractures	13037
	Spine/	27813
	Osteoporosis/co [Complications]	6994
	(vertebral or spine or spinal).ab,kf,ti.	352178
	13-15 (OR)	362953
	fractures, compression/ or osteoporotic fractures/	5136
	Fractures, Bone/et [Etiology]	7973
	(fracture* or compression*).ab,kf,ti.	313815
	17-19 (OR)	316215
	12 OR (16 AND 20)	*49908*
Patients experiences		
	attitude/ or attitude to health/ or "patient acceptance of health care"/ or patient satisfaction/ or patient preference/ or optimism/ or pessimism/ or stereotyping/	238589
	emotions/ or expressed emotion/	57923
	Patients/px [Psychology]	7284
	Inpatients/px [Psychology]	3865
	Outpatients/px [Psychology]	1512
	personal satisfaction/	15404
	prejudice/ or ageism/	24121
	((patient* or women* or men or people* or individual* or adult* or resident*) adj15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)).ab,kf,ti.	979233
	"life world".ab,kf,ti.	285
	22-30 (OR)	*1204731*
Health care, home care, community care		

	housing for the elderly/ or homes for the aged/	14120
	Nursing Homes/	31970
	Pain Clinics/	1337
	home care services/ or home health nursing/	31078
	Community Health Nursing/	19132
	Long-Term Care/	24133
	"Attitude of Health Personnel"/	109009
	"Delivery of Health Care"/	78084
	Pain Management/	27178
	professional-patient relations/ or nurse-patient relations/ or physician-patient relations/ or researcher-subject relations/	125009
	((psycholog* or emotion or emotions or experience or experiences or meaning or perception or perspective* or view or views or value or trust or stigma or satisf* or dissatif* or unsatisfied or interpretation or relation or belie* or disbelie* or encounter* or "self-report" or embodied or consultation or attitude*or opinion* or barrier* or enabler*) adj25 (professional* or doctor* or "general practitioner*" or gp or physician* or "health car*" or nurs* or provider* or "long term care" or "primary care" or "residential care" or clinic or clinics or clinician* or "health personnel" or "nursing home*" or care)).ab,kf,ti.	379098
	32-42 (OR)	605631
Study types: qualitative research		
	empirical research/ or grounded theory/ or qualitative research/	55330
	focus groups/ or interviews as topic/ or narration/ or "surveys and questionnaires"/	523913
	Interview, Psychological/	14930
	nursing research/ or nursing methodology research/	30891
	personal narratives as topic/	282
	Anecdotes as Topic/	4712
	exp tape recording/ or exp video recording/	44312
	patient reported outcome measures/	4784
	(qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*").ab,kf,ti.	1094831
	((field adj2 (research or study or studies or work)) or (grounded adj2 (theor* or study or studies or research or analys?s)) or ((lived or life) adj2 (experience* or story or stories)) or ((video or tape) adj2 record*) or (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*))).ab,kf,ti.	184542
	(("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*")	16147
	44-54 (OR)	1606589
Limits: publication year, language		
	limit to (yr="1990 - 2020" and (danish or english or norwegian or swedish))	
Combined sets		
	5 OR 8 OR 11 OR 21	246560
	31 AND 43 AND 55 AND 56 AND 57	**2617**

The search result, usually found at the end of the documentation, forms the list of abstracts.

.ab. =Abstract
.ab,ti. = Abstract or title
.af.= All fields
Exp= Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
.sh.= Term from the Medline controlled vocabulary
.ti. = Title
/ = Term from the Medline controlled vocabulary, but does not include terms found below this term in the MeSH hierarchy
* = Focus (if found in front of a MeSH-term)
* or $= Truncation (if found at the end of a free text term)
.mp=text, heading word, subject area node, title

PsycINFO via EBSCO 23 January 2020
Title: Upplevelse av möte med vården och upplevelse av läkemedelsbehandling av smärta hos äldre individer

Search terms		Items found
Population: Pain		
	DE "Back Pain" OR DE "Chronic Pain" OR DE "Neuropathic Pain" OR DE "Neuralgia" OR DE "Pain" OR DE "Peripheral Neuropathy"	51,955
	TI (((chronic or persistent) N3 (pain))) OR AB (((chronic or persistent) N3 (pain))) OR KW (((chronic or persistent) N3 (pain)))	21,191
	1 OR 2	*55,805*
Population: Osteoarthritis		
	DE "Joint Disorders" OR DE "Arthritis"	2,805
	TI (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR AB (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease") OR SU (osteoarthr* or "degenerative arthrit*" or "degenerative joint disease")	2,065
	4 OR 5	*3,725*
Population: Diabetic neuropathies		
	DE "Neuropathic Pain" OR DE "Peripheral Neuropathy"	4,168
	TI (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))) OR AB (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*))) OR KW (((diabetic) N3 (neuropath* or neuralg* or polyneuropath* or mononeuropath* or amyotroph*)))	1,027
	TI (((diabet* and neuropath*) N15 (pain*))) OR AB (((diabet* and neuropath*) N15 (pain*))) OR KW (((diabet* and neuropath*) N15 (pain*)))	683
	TI "Bruns-Garland" OR AB "Bruns-Garland" OR KW "Bruns-Garland"	0
	7-10 (OR)	*4,911*
Population: Osteoporotic vertebral fractures		
	DE "Spinal Cord Injuries"	6,011
	DE "Spinal Column" OR DE "Spinal Cord"	11,948
	DE "Osteoporosis"	1,288
	TI ((vertebral or spine or spinal)) OR AB ((vertebral or spine or spinal)) OR KW ((vertebral or spine or spinal))	33,764
	12-15(OR)	36,699
	TI ((fracture* or compression*)) OR AB ((fracture* or compression*)) OR KW ((fracture* or compression*))	7,993
	16 AND 17	1,335
	3 OR 6 OR 11 OR 18	*55,192*
Patient experiences		
	((DE "Attitude Formation" OR DE "Pessimism" OR DE "Optimism") OR (DE "Client Attitudes" OR DE "Client Satisfaction" OR DE "Physical Illness (Attitudes Toward)" OR DE "Attitudes" OR DE "Health Attitudes")) OR ((DE "Satisfaction" OR DE "Client Satisfaction" OR DE "Life Satisfaction") OR (DE "Need Satisfaction")) OR ((DE "Stigma" OR DE "Stereotyped Attitudes") OR (DE "Labeling")) OR DE "Prejudice"	122,67
	DE "Patients" OR DE "Geriatric Patients" OR DE "Hospitalized Patients" OR DE "Medical Patients" OR DE "Outpatients"	66,448
	20 AND 21	3,994

	TI (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR AB (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied))) OR KW (((client* or patient* OR women* or men or people* or individual* or adult* or resident*) N15 (psycholog* or emotion* or experience* or meaning or percept* or perspective* or view* or value or trust* or attitude* or stigma* or satisf* or dissatif* or unsatisf* or interpret* or relation or believ* or belief* or disbeliev* or disbelief* or encounter* or "self-report" or embodied)))	661,327
	TI "life world" OR AB "life world" OR SU "life world"	551
	20-24 (OR)	*662,542*
Health care, home care, community care		
	(DE "Health Care Delivery" OR DE "Home Care" OR DE "Hospice" OR DE "Long Term Care" OR DE "Primary Health Care" OR DE "Residential Care Institutions" OR DE "Hospitals" OR DE "Nursing Homes" OR DE "Group Homes" OR DE "Retirement Communities") OR (DE "Home Visiting Programs" OR DE "Elder Care" OR DE "Home Care" OR DE "Home Care Personnel") OR (DE "Health Personnel Attitudes" OR DE "Pain Management")	117,526
	TI (((attitud* or belie* or disbelie* or consult* or encounter*) N25 (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics))) OR AB (((attitud* or belie* or disbelie* or consult* or encounter*) N25 (professional* or doctor* or "general practitioner*" or gp or "health car*" or nurs* or provid* or "primary care" or "residential care" OR clinic OR clinics)))	81,987
	TI "pain management" OR AB "pain management" OR KW "pain management"	7,279
	26-28 (OR)	*188,827*
Study types: qualitative studies		
	DE "Content Analysis" OR DE "Discourse Analysis" OR DE "Qualitative Research" OR DE "Grounded Theory" OR DE "Surveys" OR DE "Questionnaires" OR DE "Narratives" OR DE "Storytelling" OR DE "Phenomenology" OR DE "Hermeneutics" OR DE "Videotape Recorders" OR DE "Life Experiences" OR DE "Action Research"	120,181
	TI ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*")) OR AB ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*")) OR KW ((qualitative* or interview* or "focus group*" or phenomeno* or ethnolog* or ethnograph* or ethnonurs* or ethnomethodolog* or "meta-ethnograph*" or hermeneutic* or "grounded theory" or observation or "lived experience*" or narrat* or "mixed method*" or "content analys*" or "discourse analys*" or poststructur* or "purposive sample*" or "social systems theor*" or "thematic analys*" or "theoretical sample*"))	690,298
	TI (((field W2 (research or study or studies or work))) OR AB (((field W2 (research or study or studies or work))) OR KW (((field W2 (research or study or studies or work)))	24,838
	TI ((grounded) W2 (theor* or study or studies or research or analys?s)) OR AB ((grounded) W2 (theor* or study or studies or research or analys?s)) OR KW ((grounded) W2 (theor* or study or studies or research or analys?s))	18,054
	TI ((lived or life) W2 (experience* or story or stories)) OR AB ((lived or life) W2 (experience* or story or stories)) OR KW ((lived or life) W2 (experience* or story or stories))	33,687
	TI ((video or tape) W2 (record*)) OR AB ((video or tape) W2 (record*)) OR KW ((video or tape) W2 (record*))	9,996

	TI (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) W3 (interview* or discussion* or questionnaire*)) OR AB (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) W3 (interview* or discussion* or questionnaire*)) OR KW (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) W3 (interview* or discussion* or questionnaire*))	98,689
	TI ("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*") OR AB ("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*") OR KW ("action research" or "cluster sample*" or "constant comparative method*" or "discourse analysis" or "discourse analyses" or "key informant*" or "maximum variation sampling*")	20,482
	30-37 (OR)	778,776
Limits: publication year, language		
	Limiters - Publication Year: 1990-2020; Language: Danish, English, Norwegian, Swedish	
Combined sets		
	19 AND 29 AND 38 AND 39	**817**

The search result, usually found at the end of the documentation, forms the list of abstracts.

AB = Abstract
AU = Author
DE = Term from the thesaurus
MM = Major Concept
TI = Title
TX = All Text. Performs a keyword search of all the database's searchable fields
ZC = Methodology Index
* = Truncation
“ “ = Citation Marks; searches for an exact phrase

Bilaga 2

Läkemedelsbehandling av vanliga smärttillstånd hos äldre personer/ Pharmacological treatment of common pain conditions in the elderly, rapport 315 (2020)

Appendix 2/Bilaga 2 Table of excluded studies/Tabeller över exkluderade studier

Table of contents/Innehållsförteckning

SBU Statens beredning för medicinsk och social utvärdering • www.sbu.se
Telefon 08-412 32 00 • **Fax** 08-411 32 60 • **Organisationsnummer** 202100-4417
Besöksadress S:t Eriksgatan 117, Stockholm • **Postadress** Box 6183, 102 33 Stockholm

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. Formulary, 2006; 41 (8): 372.	Wrong publication type - Conference abstract
Argoff CE. Recent developments in the treatment of osteoarthritis with NSAIDs. Curr Med Res Opin 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. Osteoarthritis Cartilage 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. Osteoarthritis Cartilage 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. Arthritis Rheum 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. Ann Intern Med 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. Eur J Pain 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. Osteoporos Int 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. Cochrane Database Syst Rev 2006:Cd005522.	More recent SR available
Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis: A systematic review and metaanalysis. J Rheumatol 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. Pharmacoepidemiol Drug Saf 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). Health Technology Assessment Database, 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. Lancet, 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. Cochrane Database of Systematic Reviews, 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. PLoS ONE [Electronic Resource], 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. Drugs Aging 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? J Fam Pract 2019;68:417-8.	Wrong study design
González-Pérez A, García Rodríguez LA. Upper gastrointestinal complications among users of paracetamol. Basic Clin Pharmacol Toxicol 2006;98:297-303.	Research question too narrow - paracetamol and upper GI-events
Gotzsche PC. NSAIDs. Clin Evid 2007;1:01.	Wrong study design - Review article
Gotzsche PC. NSAIDs. Clin Evid 2010;28:28.	Wrong population – Mixed population
Gregori D, Giacovelli 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. Arthritis Rheumatol 2016;68:369-70.	Wrong publication type - Conference abstract
Gregori D, Giacovelli 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. JAMA 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, Beaudart 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; 350h1225.	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-analysiss. 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, Giacovelli G, Minto C, Barbetta B, Gualtieri F, Azzolina D, et al. A new systematic reviewand 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.

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. Curr Med Res Opin 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 osteorthritis of knee. Indian J Rheumatol 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. Drugs Aging 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. Am J Geriatr Pharmacother 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. Osteoarthritis Cartilage 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. Pharmacotherapy 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. J Opioid Manag 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. Lancet 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. Am J Gastroenterol 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. Pharmacoepidemiol Drug Saf 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. J Am Geriatr Soc 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. Int J Clin Rheumtol 2014;9:13-20.	Wrong study design - subgroup analysis on intermittent/continous 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. Yonsei Med J 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. Curr Med Res Opin 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. Expert Opin Pharmacother 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. Circ J 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. Curr Med Res Opin 2014;30:575-87.	Wrong comparison - no control group
Kellner H, Essex M, Li C. Safety and efficacy of nsaids in elderly arthritis patients: A subgroup analysis. Osteoarthritis Cartilage 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. Curr Med Res Opin 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. Open Rheumatol J 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. Journal of rheumatic diseases 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. JAMA 2018;319:872-82.	Wrong population - mean age 58
Kushner P, Patel B, Garas SY. Minimal clinically important improvement (MCII) in knee osteoarthritis: a post hoc analysis of a prospective, randomized clinical trial of diclofenac sodium gel (DSG) 1%. J Gen Intern Med 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
Rauck R, Rapoport R, Thipphawong 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. Pharmacotherapy 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. Clin Interv Aging 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. Arthritis Rheum 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. Eur Heart J 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.). Open Rheumatol J 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. Curr Med Res Opin 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. Arthritis Rheum 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. Am J Med 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. Arthritis Rheumatol 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. Arthritis Rheumatol 2017;20:20.	Double publication
Sostres C, Carrera-Lasfuentes P, Lanas A. Non-steroidal anti-inflammatory drug related upper gastrointestinal bleeding: types of drug use and patient profiles in real clinical practice. Curr Med Res Opin 2017;33:1815-20.	Wrong outcome - Specific AE
Strand V, Bergman M, Parenti D, Nezzer J, Young C. A phase 3 randomized controlled trial of lower-dose diclofenac capsules in patients with osteoarthritis pain: Impact on patient-reported outcomes. Osteoarthritis Cartilage 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. Clinical Rheumatology 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. Pain Res Manag 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. Arthritis Rheum 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. Pak J Pharm Sci 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. Wien Klin Wochenschr 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. Ter Arkh 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. Osteoarthritis Cartilage 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. Diabetes Metab Res Rev 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. Pharmacoepidemiol Drug Saf 2019;28:131.	Wrong publication typ - conference abstract
Blair HA. Capsaicin 8% Dermal Patch: A Review in Peripheral Neuropathic Pain. Drugs 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. Curr Med Res Opin 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. Pharmacotherapy 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. J Gen Intern Med 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. Cochrane Database Syst Rev 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. J Pain Manag 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. J Pain Symptom Manage 2007;34:201-8.	Research question too narrow - anticonvulsants only
Hossain SM, Hussain SM, Ekram AR. Duloxetine in Painful Diabetic Neuropathy: A Systematic Review. Clin J Pain 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. Reg Anesth Pain Med 2008;33:389-94.	Research question too narrow - pregabalin only
Joss JD. Tricyclic antidepressant use in diabetic neuropathy. Ann Pharmacother 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. BMC Neurol 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. Pain Physician 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. Eur J Pain 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. Clin Ther 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. Swiss Med Wkly 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. BMJ (Int Ed) 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.	

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
Waldfogel 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 gropup
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. Diabet Med 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. Clin Drug Investig 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. Curr Med Res Opin 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. Diabetologia 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. Eur J Pain 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. Clin J Pain 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. Acta Neurol Scand 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. J Clin Outcomes Manag 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. PM R 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? Pain 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. Diabetes Care 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. Indian J Pharmacol 2013;45:S148.	Wrong study design - Conference abstract
Dellemijn PL, van Duijn H, Vanneste JA. Prolonged treatment with transdermal fentanyl in neuropathic pain. J Pain Symptom Manage 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. Indian J Pharmacol 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. Clin Ther 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. Neurology 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. Curr Med Res Opin 2007;23:147-61.	Wrong population - mean age <60
Freynhagen R, Busche P, Konrad C, Balkenohl M. Effectiveness and time to onset of pregabalin in patients with neuropathic pain. Schmerz 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. N Engl J Med 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. Clin J Pain 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. Br J Diabetes Vasc Dis 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. Int J Clin Pract 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. Clin J Pain 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. Chinese journal of evidence-based medicine 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 (Journal of Diabetes & Metabolic Disorders, (2019), 10.1007/s40200-019-00427-w). J Diabetes Metab Disord 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. J Diabetes Metab Disord 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. Diabet Med 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. Journal of isfahan medical school 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. Diabetes Care 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). Iran J Pharm Res 2015;14:1263-8.	Wrong intervention – amitryptiline 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. Diabet Med 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. J Peripher Nerv Syst 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. Acta Neurol Scand 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. QJM 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. Pharmaceuticals (Basel) 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. J Clin Neurosci 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. Prog Pain Res Manag 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. Pak J Pharm Sci 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. Drug Des Devel Ther 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. Pain 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. Pain 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. Clin Ther 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. Diabetes 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. Diabetologia 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. J Palliat Med 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. Neurology 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. Clin J Pain 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. Pain Pract 2013;13:485-96.	Wrong intervetion - 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. Clin J Pain 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. Neurosciences (Riyadh) 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. J Pain 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. Int J Gen Med 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. Diabetes Res Clin Pract 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. Diabetes Care 2009;32:e20.	
Satoh J, Yagihashi S, Baba M, Suzuki M, Arakawa A, Yoshiyama T. Efficacy and safety evaluation of pregabalin treatment over 52weeks in patients with diabetic neuropathic pain extended after a double-blind placebo-controlled trial. J Diabetes Investig 2011;2:457-63.	Wrong comparison - no control group
Sekar P, Punnagai 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. Biomedical and Pharmacology Journal 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. BMC Fam Pract 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. Pakistan Journal of Medical and Health Sciences 2011;5:745-7.	Wrong population - age not specified
Silver M, Blum D, Grainger J, Hammer AE, Quessy S. Double-Blind, Placebo-Controlled Trial of Lamotrigine in Combination with Other Medications for Neuropathic Pain. J Pain Symptom Manage 2007;34:446-54.	Wrong population - DPN only 65 %
Simpson DA. Gabapentin and venlafaxine for the treatment of painful diabetic neuropathy. J Clin Neuromuscul Dis 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. Diabetologia 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. Diabetologia 2015;58:S32.	Conference abstract
Sun DH, Ji CM, Ma L, Jiang CL. Efficacy and safety of pregabalin in patients with diabetic painful neuropathy. Chinese journal of new drugs 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. Pain Med 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. Pain 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. Pain 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. J Pain Res 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. Curr Ther Res Clin Exp 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. Pain Med 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. Diabetologia 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. Clin J Pain 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. J Diabetes Investig 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. Eur J Pain 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. Iran Red Crescent Med J 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. Diabetes Care 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. J Pain 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. J Neurol Neurosurg Psychiatry 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 (NANSAIDs) and serious upper gastrointestinal bleeding: A	Wrong population - not elderly

meta-analysis based on individual patient data. Br J Clin Pharmacol 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. Clin Interv Aging 2017;12:1761-78.	Wrong outcome
MacLean CH, Pencharz JN, Saag KG. Quality indicators for the care of osteoarthritis in vulnerable elders. J Am Geriatr Soc 2007;55:S383-S391.	Wrong study design - Guideline
Maree RD, Marcum ZA, Saghafi E, Weiner DK, Karp JF. A Systematic Review of Opioid and Benzodiazepine Misuse in Older Adults. Am J Geriatr Psychiatry 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. Fundam Clin Pharmacol 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. J Pain 2018;19:475.e1-475.e24.	Wrong popoulation - 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. Eur J Clin Pharmacol 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. Family Practice 2013;30:247-55.	Wrong outcome - effect on chronic kidney disease
Pellicano R. Gastrointestinal damage by non-steroidal anti-inflammatory drugs: Updated clinical considerations. Minerva Gastroenterol Dietol 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. Br J Clin Pharmacol 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. Eur J Epidemiol 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. Arch Intern Med 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. J Gastroenterol 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. Ther Clin Risk Manag 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. Drug Saf 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. Arch Intern Med 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. Aliment Pharmacol Ther 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?]. Reumatol Clin 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. J Rheumatol 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. Am J Geriatr Pharmacother 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. Biol Pharm Bull 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. J Am Geriatr Soc 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. Eur J Clin Pharmacol 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. Curr Drug Saf 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. Eur J Prev Cardiol 2019.	Wrong publication type - Conference abstract
Cabré M, Elias L, Garcia M, Palomera E, Serra-Prat M. Avoidable hospitalizations due to adverse drug reactions in an acute geriatric unit. Analysis of 3,292 patients. Med Clin (Barc) 2018;150:209-14.	Wrong comparison – examining prevalence, no control group
Caravaca-Fontan F, Villacorta J, Cordon A, Praga M, Fernàndez-Juàrez G. Clinical determinants of renal outcomes in druginduced acute interstitial nephritis. Nephrol Dial Transplant 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. Medicine (Baltimore) 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. J Manag Care Spec Pharm 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. Clin Nephrol 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. Ann Intensive Care 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. J Am Med Dir Assoc 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. Am J Manag Care 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. Eur J Intern Med 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. Int J Nephrol Renovasc Dis 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. BMC Med Inform Decis Mak 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. Clin Epidemiol 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. BMC Nephrol 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. Adv Ther 2017;34:2534-41.	Wrong comaprison
Nishtala P, Chyou TY. Association rule analysis to evaluate frequent drug combinations associated with acute kidney injury in older adults. Pharmacoepidemiol Drug Saf 2019;28:425.	Wrong publication type - Conference abstract
Novick TK, Grams ME. Safely treating pain in older adults. Nephrol Dial Transplant 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. Eur Geriatr Med 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 eldery from western India. Nephrol Dial Transplant 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. Eur J Clin Pharmacol 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. Arch Intern Med 1996;156:2433-9.	Wrong drug - most NSAIDs not available on Swedish market
Radulescu D, Peride I, David C, Bogeanu C, Niculae A, Checherita IA. Factors affecting prognosis of acute kidney injury in elderly. Nephrol Dial Transplant 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. J Am Coll Cardiol 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. Clin Interv Aging 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. Giornale italiano di farmacia clinica 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. BMJ 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. Am J Med 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. Arthritis Rheumatol 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, Helvaci I, Demir S, Kiykim AA. Clinical outcomes of acute kidney injury developing outside the hospital in elderly. Int Urol Nephrol 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. Medicine (Baltimore) 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). Rheumatology 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. Am J Gastroenterol 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. Br J Clin Pharmacol 2010;70:429-38.	Wrong population - mean age ca 55
García Rodríguez LA, Lanas 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. Ann Med 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. Curr Med Res Opin 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. Open Rheumatol J 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. BMJ Open Diabetes Res Care 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, Bjornsson 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. Pharmacien 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. Aging Clin Exp Res 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. Drugs Aging 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. Eur J Pain 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. Postgraduate Medicine 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. Geriatr Gerontol Int 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. Nurs Open 2019;6:1047-54.	Wrong population - median age 66
Baird CL, Yehle KS, Schmeiser D. Experiences of women with osteoarthritis in assisted living facilities. Clin Nurse Spec 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. Arthritis Rheum 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. Scand J Caring Sci 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. BMC Rheumatol 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. Australas J Ageing 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. Pain Med 2018;19:S19-S29.	
Franklin ZC, Smith NC, Fowler NE. A qualitative investigation of factors that matter to individuals in the pain management process. Disabil Rehabil 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. Int J Older People Nurs 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. Br J Gen Pract 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. Arthritis Rheum 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. J Clin Nurs 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. J Am Med Dir Assoc 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. Open Nurs J 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. J Clin Nurs 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. Int J Older People Nurs 2015;10:190-200.	Wrong study question
Kemper JA. Pain management of older adults after discharge from outpatient surgery. Pain Manag Nurs 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. Int J Clin Pharm 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. Age Ageing 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. Int J Nurs Stud 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. Pain Med 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. Aust J Prim Health 2013;19:138-43.	Wrong population

Paier GS. Specter of the crone: the experience of vertebral fracture. ANS Adv Nurs Sci 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. Disabil Rehabil 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. Br J Nurs 2013;22:808-12.	Wrong publication type
Schofield P. Pain management. Pain management of older people in care homes: a pilot study. Br J Nurs 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. BMC Health Serv Res 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. J Caring Sci 2017;6:81-93.	Wrong population

Bilaga 3

Läkemedelsbehandling av vanliga smärttillstånd hos äldre/
Pharmacological treatment of common pain conditions in the elderly,
rapport 315 (2020)

Appendix 3/Bilaga 3 Table of included studies/Tabeller över inkluderade studier

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Table of contents/Innehållsförteckning

Part I. Osteoarthritis (OA)/Artros

Systematic reviews/Systematiska översikter

Five systematic reviews [1-5] were included that presented data on efficacy and safety for pharmacological treatment of osteoarthritis (OA), see Table 1.

Table 1 Overview of included systematic reviews with specific interventions on pharmacological treatment of osteoarthritis.

	OA	Date search was made
Paracetamol	Leopoldini et al 2019	October 2017
Oral NSAIDs	Osani et al 2019	May 2018
Topical NSAIDs	Derry et al 2016	February 2016
Opioids except tramadol	da Costa et al 2014	August 2012
Tramadol	Toupin April et al 2019	February 2018

Table 2 Included systematic reviews on pharmacological treatment of osteoarthritis.

Author Year Reference	Study design Follow up	Population	Interventions Controls	Outcome - efficacy	Outcome - safety	Risk of bias SBU rating of risk of bias in the review
Paracetamol versus placebo						
Leopoldini et al 2019 [3]	Systematic review including 10 placebo controlled RCTs	3541 participants with clinical and imaging-based diagnosis of	**Intervention** Paracetamol, dose range 1.95 to 4 grams/day **Controls**	**Pain** Pain 0–100 VAS scale, mean difference: –3.23 (95% CI, –5.43 to –1.02) 7 RCTs 2355 participants GRADE: ⨁⨁⨁⨁	**Any adverse event:** Paracetamol: 328/1000 Placebo: 325/1000 Risk ratio: 1.01 (95% CI, 0.92 to 1.11)	Study eligibility criteria: *Low* Identification and selection of studies: *Low*

	Follow-up range 2–12 weeks	osteoarthritis in knee or hip	Placebo	**Function** Standardized WOMAC scale 0–100, mean difference: –2.92 (95% CI, –4.89 to –0.95) 7 RCTs 2354 participants GRADE: ⊕⊕⊕⊕ **Quality of life** No data	8 RCTs, 3252 participants GRADE: ⊕⊕⊕⊕ **Study withdrawal due to AE:** Paracetamol: 77/1000 Placebo: 65/1000 Risk ratio: 1.19 (95% CI 0.91 to 1.55) 7 RCTs, 3023 patients GRADE: ⊕⊕⊕ (–1 for imprecision) **Serious adverse events:** Paracetamol: 16/1000 Placebo: 11/1000 Risk ratio: 1.36 (95% CI, 0.73 to 2.53) 6 RCTs, 3209 participants GRADE: ⊕⊕⊕ (–1 for imprecision)	Data collection and study appraisal: *Low* Synthesis and findings: *Unclear* (no sensitivity analysis made) Overall risk of bias: *Low*
Oral NSAIDs versus placebo						
Osani et al 2019 [4]	Systematic review review and metanalysis including 72 randomized controlled trials Follow-up range 1–104 weeks,	Persons with knee osteoarthritis. Studies with combined knee and hip population were included if	**Intervention** NSAIDs which were categorized as: Traditional (non-selective) NSAIDs (including diclofenac, ibuprofen, indomethacin,	**Pain at 8 weeks** (7–10 weeks) This follow up period was closest to mean and median follow up periods in the included studies and therefore chosen to be extracted All NSAIDs:	**Treatment related adverse events, all NSAIDs:** Risk ratio: 1.21 (95% CI, 1.04 to 1.40), I^2=54% 24 RCTs, 9548 participants	Study eligibility criteria: *Low* Identification and selection of studies: *Unclear* (incomplete search strategy)

	mean 9 weeks, median 6 weeks	>70 had knee osteoarthritis Total group included 26424 persons	naproxen and piroxcam) Selective COX-2 inhibitors (celecoxib) Intermediate COX inhibitors (etodolac, meloxicam, nabumetone) **Controls** Placebo	SMD –0.36 (95% CI, –0.43 to –0.30), I^2=41% 13 studies, 6341 participants Traditional NSAID: SMD –0.37 (95% CI, –0.49 to –0.25), I^2=0 4 studies, 1218 participants Intermediate COX inhibitors: SMD –0.26 (95% CI, –0.49 to –0.04), I^2=0 1 study, 308 participants Celexocib: SMD –0.37 (95% CI, –0.46 to –0.28), I^2=56% 9 studies, 4970 participants **Function at 8 weeks** (7–10 weeks). This follow up period was closest to mean and median follow up periods in the included studies and therefore chosen to be extracted All NSAIDs: SMD –0.37 (95% CI, –0.45 to –0.29), I^2=0 7 studies, 2492 participants Traditional NSAID: SMD –0.40 (95% CI, –0.61 to –0.20), I^2=48% 3 studies, 911 participants	Median follow up 6 weeks. **Study withdrawal due to AE, all NSAIDs:** Risk ratio: 1.16 (95% CI, 1.02 to 1.32), I^2=22% 60 RCTs, 22993 participants Median follow up 6 weeks. **Serious adverse events, all NSAIDs:** Risk ratio: 0.90 (95% CI, 0.68 to 1.19), I^2=0 40 RCTs, 17278 participants Median follow up 12 weeks.	Data collection and study appraisal: *Low* Synthesis and findings: *Unclear* (no forest plots from meta-analysis presented) Overall risk of bias: *Low*

				Intermediate COX inhibitors (extracted at 4 weeks [3–6 weeks] due to missing data for 8 weeks): SMD –0.31 (95% CI, –0.56 to –0.07), I^2=NA 1 study, 263 participants Celexocib: SMD –0.35 (95% CI, –0.45 to –0.25), I^2=19% 4 studies, 1581 participants		
Topical NSAIDs versus carrier						
Derry et al 2016 [2]	Systematic review and meta-analysis including a total of 39 randomized controlled studies of which 23 were included in one or more meta-analysis Follow up range 2–12 weeks, mean 5 weeks, median 4 weeks	10631 adults with musculoskeletal pain of at least three months duration and at least moderate intensity Most included studies were populations with osteoarthritis with independent radiological verification at 3–6 months prior trial	**Intervention** Topical NSAIDs applied as solutions, gels, or plasters (patches) **Controls** Topical placebo was the carrier without the active NSAID Authors presents pooled results for diclofenac and ketoprofen only	**Pain** Clinical success, defined as at least 50% reduction in pain intensity. *Diclofenac:* Clinical success 60% (95% CI, 44 to 66) Control: Clinical success 50% (95% CI, 25 to 57) Clinical success RR: 1.20 (95% CI, 1.12 to 1.29) NNT 9.8 (95% CI, 7.1 to 16) 6 studies, 2343 participants. GRADE: ⊕⊕⊕ (–1 for imprecision) *Ketoprofen:* Clinical success 63% (95% CI, 41 to 89) Control: Clinical success 48% (95% CI, 28 to 78)	**Local adverse events** Diclofenac: 14% (range 0 to 51%) Control: 8% (range 0 to 43%) RR 1.8 (95% CI, 1.5 to 2.2) NNH 16 (95% CI, 12 to 23) 15 studies, 3658 participants GRADE: ⊕⊕⊕ (–1 for inconsistency) Ketoprofen: 15% (range 6 to 28%) Control: 13% (6 to 20%) RR 1.0 (95% CI, 0.85 to 1.3) NNH not calculated	Study eligibility criteria: *Low* Identification and selection of studies: *Low* Data collection and study appraisal: *Unclear (*incomplete search strategy) Synthesis and findings: *Unclear* (no sensitivity analysis made) Overall risk of bias: *Low*

				Clinical success RR: 1.10 (95% CI, 1.01 to 1.20) NNT 6.9 (95% CI, 5.4 to 9.3) 4 studies, 2573 participants. GRADE: ⊕⊕⊕ (–1 for inconsistency) **Function, Quality of life** No data	4 studies, 2621 participants GRADE: ⊕⊕⊕ (–1 for imprecision)	
da Costa et al 2014 [1]	Systematic review and meta-analyses including 22 RCT Follow up time 2–30 weeks, median follow-up time 10 weeks	Total of 8275 participants with clinically or radiologically confirmed osteoarthritis in the knee or hip	**Intervention** Any type of oral or transdermal opioid except tramadol. Dose ranges in primary studies: Buprenorphine 5–20 µg/hour, codeine 180–200 mg, fentanyl 25 µg/hour, hydromorphone 4–32 mg, morphine 30–160 mg, oxycodone dose range 10–100 mg, oxymorfon 20–100 mg, tapendatol 100–500 mg **Controls** Placebo/no intervention	**Pain** All opioids: SMD –0.28 (95% CI, –0.35 to –0.20) 22 RCTs, 8275 participants GRADE: ⊕⊕⊕⊕ *SMD –0.28 corresponds to a difference in pain scores of 7 mm (95% CI, 5 to 9 mm) on a VAS 0–100 mm between opioids and placebo.* Buprenorphine: SMD –0.19 (95% CI, –0.30 to –0.09) Codeine: SMD –0.51 (95% CI, –1.01 to –0.01) Fentanyl: SMD –0.22 (95% CI, –0.42 to –0.03) Hydromorphone: SMD 0.04 (95% CI, –0.19 to 0.28) Morphine: SMD –0.25 (95% CI, –0.42 to –0.09) Oxycodone: SMD –0.31 (95% CI, –0.47 to –0.15) Oxymorphone: SMD –0,39 (95 % CI –0.58 to –0.21)	**Any adverse event:** Opioids: 22% Placebo: 15% Risk ratio: 1.49 (95% CI, 1.35 to 1.63) 9 RCTs, 4898 participants GRADE: ⊕⊕⊕ (–1 for risk of bias) **Study withdrawal due to AE:** Opiods: 6.4% Placebo: 1.7% Risk ratio: 3.76 (95% CI, 2.93 to 4.82) 19 RCT:s, 7712 participants GRADE: ⊕⊕⊕⊕ **Serious adverse events:** Opioids: 1.3% Placebo: 0.4% Risk ratio: 3.35 (95% CI, 0.83 to 13.56)	SBU rating of risk of bias in the review: Study eligibility criteria: *Low* Identification and selection of studies: *Unclear (*incomplete search strategy) Data collection and study appraisal: *Low* Synthesis and findings: *Low* Overall risk of bias: *Low*

				Tapendatol: SMD – 0.31 (95% CI, –0.46 to –0.16) **Function** All opioids: SMD –0.26 (95% CI, –0.35 to –0.17) 12 RCTs, 3553participants GRADE: ⨁⨁⨁⨁ *SMD –0.26 corresponds to a difference in function scores of –0.6 units (95% CI, –0.8 to –0.4)* *between opioids and placebo on a standardised WOMAC disability scale ranging from 0 to 10.* Buprenorphine: SMD –0.23 (95% CI, –0.40 to –0.05) Codeine: SMD –0.42 (95% CI, –0.74 to –0.10) Fentanyl: SMD –0.28 (95% CI, –0.48 to –0.09) Morphine: SMD –0.20 (95% CI, –0.38 to –0.02) Oxycodone: SMD –0.30 (95% CI, –0.58 to –0.01) Tapendatol: SMD –0.15 (95% CI, –0.45 to 0.16) **Quality of life** No data	3 RCTs, 681 participants GRADE: ⨁⨁ (–1 for risk of bias, –1 for imprecision)	
Toupin April et al 2019 [5]	Systematic review and	Total of 6496 participants with clinically or	**Intervention** 3871 participants randomized to	**Pain** Assessed with VAS 0–100 mm	**Any adverse event** 2 039 participants, 4 RCTs	SBU rating of risk of bias in the review:

	meta-analyses including 22 RCT Follow up range 1–12 weeks. Mean follow-up time 8 weeks	radiologically confirmed osteoarthritis in any joint	tramadol alone or tramadol in combination with another analgesic. Seventeen studies evaluated tramadol alone and five evaluated tramadol plus acetaminophen. The dose of tramadol ranged from 37.5 mg to 400 mg and were pooled since the results were similar **Controls** 2625 participants randomized to placebo or active control. Thirteen studies used placebo controls and eleven studies used active controls. Two trials had both placebo and active arms	*Tramadol vs placebo* 3972 participants, 8 RCTs, mean difference: –4% absolute improvement (95% CI, –3% to –5%)* Corresponds to 4 mm better improvement with tramadol (95% CI, 3 to 5) GRADE: ⊕⊕⊕ (–1 risk of bias) **Function** Assessed with WOMAC physical funtion scale (0–1700) *Tramadol vs placebo* 2550 participants, 5 RCTs, mean difference: –4% absolute improvement (95% CI, –2% to –6%)* Corresponds to 4 units better improvement with tramadol (95% CI, 2 to 6) on a standardized WOMAC scale 0–100 GRADE: ⊕⊕⊕ (–1 for risk of bias) **Quality of life** No data *) Absolute effect on a common scale (e.g. 100 mm, 1700-point scale) calculated by multiplying the SMD by the	Tramadol: 659/1000 Placebo: 492/1000 Risk ratio: 1.34 (95% CI, 1.24 to 1.46) GRADE: ⊕⊕⊕ (–1 for risk of bias) **Study withdrawal due to AE** 4 533 participants, 9 RCTs Tramadol: 194/1000 Placebo: 73/1000 Risk ratio: 2.64 (95% CI, 2.17 to 3.20) GRADE: ⊕⊕⊕ (–1 for risk of bias) **Serious adverse events** 3612 participants, 7 RCTs Tramadol: 34/1000 Placebo: 19/1000 Risk ratio: 1.78 (95% CI, 1.11 to 2.84) GRADE: ⊕⊕ (–1 for risk of bias, –1 for imprecision)	Study eligibility criteria: *Low* Identification and selection of studies: *Unclear (*incomplete search strategy) Data collection and study appraisal: *Low* Synthesis and findings: *Low* Overall risk of bias: *Low*

				SD of the scale (in the control group at baseline) as suggested by the Cochrane Handbook for Systematic Reviews of Interventions		

AE = adverse events; **CI** = confidence interval; **COX** = cyklooxygenas; **GRADE** = The Grading of Recommendations Assessment, Development and Evaluation; **HIV** = human immunodeficiency virus; **I^2** = measure of heterogeneity; **n** = number; **NNH** = numbers needed to harm treat; **NNT** = numbers needed to treat; **NSAID** = Non steroidal anti-inflammatory drugs; **OA** = osteoarthritis; **p** = p-value; **RCT** = randomized controlled trial; **RR** = risk ratio; **SD** = standard deviation; **SMD** = standardized mean difference; **VAS** = visual analog scale; **vs** = versus; **WOMAC** = Western Ontario and McMaster Universities Osteoarthritis Index

Primary studies

Primary studies were considered for relevance if they were published after search in each systematic review was performed. Two primary studies [6,7] were included.

Table 3 Included primary studies on pharmacological treatment of osteoarthritis.

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group Comparison group Participants Drop-out rate	Outcome - efficacy	Outcome - safety
Verkleij et al 2015 [7] Netherlands **Risk of bias** Moderate	**Design** Open label, active control, randomized, prospective study **Aim** To assess the effectiveness of diclofenac compared with paracetamol over a period of 12 weeks in patients with knee osteoarthritis. **Time to follow-up** 12 weeks	**Participants** *Inclusion*: ≥45 years of age New episode of knee OA. Pain ≥2 (0–10) *Exclusion:* Contraindication for NSAIDs and/or paracetamol use. Arthroplasty or osteotomy of the knee, use of NSAIDs or paracetamol. Surgery or major trauma of the affected joint. n=104 63% women Mean age: 64 years old (SD 9 years)	**Intervention** Diclofenac flexible dose maximum 50 mg t.i.d. *Participants* n=52 *Drop-out rate* n=4 (7.7%) Mean age: 64 years (SD 9 years) **Comparison** Paracetamol flexible dose maximum dose 1000 mg t.i.d. *Participants* n=52 *Drop-out rate* n=3 (5.8 %) Mean age: 64 years (SD 9 years)	**Primary endpoints** *Change in Knee pain from baseline over 4 weeks on NRS 0–10, ITT-analysis; mean difference in change vs paracetamol (95% CI):* Diclofenac: –0.2 (–1.0 to 0.7) *Change in Knee pain and function from baseline over 12 weeks in KOOS-score (0–100), ITT-analysis; mean difference in change vs paracetamol (95% CI):* Pain, diclofenac: –2.8 (–10.7 to 5.1) Function, diclofenac: –2.7 (–10.6 to 5.0) **Secondary endpoints** *Quality of life assessed with the EuroQol instrument EQ-5D (0–1 where 1 is full health), ITT-analysis; mean difference in change vs paracetamol (95% CI):* Diclofenac: 0.0 (–0.05 to 0.1) *Compliance after 2 weeks:* Diclofenac: 44/52 Paracetamol: 45/52	**Study withdrawal because of AE** No data **Serious adverse events** No data **Three most common AEs (paracetamol vs diclofenac)** Psychiatric: 15 (28.8%) vs 20 (38.5%) Respiratory, thoracic, and connective tissue: 8 (15.4%) vs 18 (34.6%) Gastrointestinal: 7 (13.5%) vs 19 (36.5%)

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group Comparison group Participants Drop-out rate	Outcome - efficacy	Outcome - safety
Serrie et al 2017 [6] Europe **Risk of bias** Moderate	**Design** Double-blind, placebo- and active-controlled, randomized trial **Aim** To assess the efficacy and safety of tapentadol prolonged release (PR) for moderate-to-severe Chronic osteoarthritis knee pain **Time to follow-up** 12 weeks	**Participants** *Inclusion*: Age ≥40 years Knee OA requiring analgesic medication ≥3 months Pain ≥5 on NRS 0–10 *Exclusion:* Clinically significant medical or psychiatric illnesses or required painful procedures during the study that might affect efficacy or safety assessments. History of substance abuse. Hepatitis B or C or HIV infection. Seizure disorder/epilepsy, traumatic brain injury, stroke, transient ischemic attack, brain neoplasm, malignancy, uncontrolled hypertension, severe renal impairment, moderate or severe hepatic impairment n=990	**Intervention** Tapentadol PR 100–250 mg b.i.d. *Participants* n=319 *Drop-out rate* n=133 (41.7%) Mean age: 62 years (SD 9 years) **Comparison** Oxycodone CR 20–50 mg b.i.d. *Participants* n=331 *Drop-out rate* n=210 (63.4%) Mean age: 62 years (SD 9 years) Placebo *Participants* n=337 *Drop-out rate* n=116 (34.4%) Mean age: 62 years (SD 9 years)	**Primary endpoints** *Change from baseline to week 12 in average pain intensity on NRS 0–10, ITT-analysis;* *LS mean difference vs placebo (95% CI):* Tapentadol: –0.3 (–0.61 to 0.09) Oxycodone: 0.2 (–0.16 to 0.54) **Secondary endpoints** *Change from baseline to week 12 in WOMAC score:* No significant differences in changes from baseline to week 12 in the WOMAC sub-scales or global scores between the two active treatments and placebo. *PGIC, percentage of patients who rated their overall helath status as "very much improved" or "much improved" at the end of treatment:* Tapentadol: 56%, p=0.015 vs placebo Oxycodone: 42.5%, N.S. vs placebo Placebo: 43.2% *Weighted EQ-5D health status index (0–1, 1=full health), difference in LS mean change vs placebo, mean (95% CI):* Tapentadol: 0.03 (–0.01 to 0.07) Oxycodone: –0.04 (0.08 to –0.00) *SF-36 health survey* No significant differences between tapentadol and placebo regarding both mental and physical component scores, but	**Study withdrawal because of AE** Placebo: 28/337 Tapentadol: 60/319 Oxycodone: 141/331 **Serious adverse events** Placebo: 4/337 Tapentadol: 2/319 Oxycodone: 13/331 **Three most common AEs (**Placebo vs tapentadol vs oxycodone) Dizziness: 29/337 vs 70/319 vs 89/331 Nausea: 21/337 vs 65/319 vs 124/331 Constipation: 31/337 vs 57/319 vs 116/331

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group Comparison group Participants Drop-out rate	Outcome - efficacy	Outcome - safety
		72% women Mean age: 62 years old (SD 9 years)		a significant difference in favor of placebo compared to active treatment in the mental component score.	

AE = adverse events; **b.i.d.** = bis in diē. (twice a day); **CI** = confidence interval; **CR** = controlled release; **HIV** = human immunodeficiency virus; **ITT** = Intention to treat; **KOOS** = Knee Injury and Osteoarthritis Outcome Score; **LS mean** = Least Squares Means; **n** = number; **NRS** = numerical rating scale; **NSAID** = Non steroidal anti-inflammatory drugs; **OA** = osteoarthritis; **p** = p-value; **PGIC** = Patient Global Impression of Change; **SD** = standard deviation; **SF-36** = The Short Form (36) Health Survey; **t.i.d**. = ter in die (three times a day); **vs** = versus; **WOMAC** = Western Ontario and McMaster Universities Osteoarthritis Index

Part II. Diabetic polyneuropathy

Systematic reviews

No relevant systematic reviews on pharmacological treatment of Diabetic polyneuropathy (DPN) with low risk of bias according to ROBIS were identified.

Primary studies

35 relevant primary studies [8-42] were included.

Table 4 Included primary studies on pharmacological treatment of Diabetic polyneuropathy.

Author Year Reference Country Risk of bias	Design Aim Treatment duration	Participants Women/men Age	Intervention group Comparison group Participants Drop-out rate	Outcome - efficacy	Outcome - safety
Anticonvulsants versus placebo					
Pregabalin versus placebo					
Freynhagen et al 2005 [15] Europe **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of pregabalin in patients with diabetic polyneuropathy (DPN) or post-herpetic neuralgia (PHN) **Treatment duration** 12 weeks	**Participants** *Inclusion*: ≥18 years of age DPN ≥6 months VAS or SF-MPQ ≥40/100 mm *Exclusion:* Clinically significant or unstable medical or psychiatric condition, malignancy within the past 2 years, anticipated need for surgery during the study, abnormal ECG, CrCl <60 mL/min, abused drugs or alcohol within the last 2 years, history of hepatitis or HIV infection, amputations other than toes n=338 45.9% women Mean age: 62 years (SD 11 years)	**Intervention** Pregabalin flexible dose 150–600 mg/day n=141 *Drop-out rate* n=49 (34.8%) Mean age: 62 years (SD 11 years) Pregabalin 600 mg/day n=132 *Drop-out rate* n=50 (37.9%) Mean age: 62 years (SD 11 years) **Comparison** Placebo n=65 *Drop-out rate* n=30 (46.2%) Mean age: 62 years (SD 13 years)	**Primary endpoints** *Change in the mean daily NRS (numerical rating scale)-score from baseline to the mean value over the last week compared with placebo, ITT-analysis;* *Baseline value (SD), change from baseline (SD), reproduced from figure:* Placebo: 6.6 (1.7), –2.0 (N/A) Pregabalin flexible dose: 6.7 (1.6), –3.4 (N/A), p<0.01 vs placebo Pregabalin 600: 6.7 (1.5); –3.6 (N/A), p<0.01 vs placebo *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 24.2% Pregabalin flexible dose: 48.2% (p<0.001 vs placebo) Pregabalin 600: 52.3% (p<0.001 vs placebo) **Secondary endpoints** *Patient Global Impression of Change (PGIC), proportion of patients reporting ”much” or ”very much” improved:* Placebo: 30.5% Pregabalin flexible dose: 52.0% (p<0.05 vs placebo)	**Study withdrawal because of AE** Placebo: 7.7% Pregabalin flexible dose: 17.0% Pregabalin 600: 25.0% **Serious adverse events** N/A **Three most common AEs (pregabalin 600 vs placebo)** Dizziness 28.8% vs 4.6% Weight gain 13.6% vs 3.1% Somnolence 12.9% vs 0.0%

				Pregabalin 600: 53.6% (p<0.05 vs placebo)	
Guan et al 2011 [22] China **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim**	**Participants** *Inclusion*: ≥18≤75 years of age Polyneuropathy ≥1 and ≤5 years HbA_{1c} <11% VAS or SF-MPQ ≥40/100 mm	**Intervention** Pregabalin flexible dose 150–600 mg/day n=206 *Drop-out rate* n=24 (11.7%)	**Primary endpoints** *Change in the mean daily NRS-score from baseline to follow-up, ITT-analysis; Baseline value (SD), follow-up value (SD); 95% CI:* Placebo: 6.4 (1.53), 4.3 (0.19); 4.0, 4.7 Pregabalin: 6.3 (1.58), 3.7 (0.14); 3.4, 4.0; p=0.005 vs placebo	**Study withdrawal because of AE** Placebo: 4 Pregabalin: 11 **Serious adverse events** Placebo: 2 (2.0%) Pregabalin: 3 (1.5%)

	Evaluate the efficacy and safety of pregabalin in patients with diabetic polyneuropathy (DPN) or post-herpetic neuralgia (PHN) **Treatment duration** 8 weeks	*Exclusion:* Clinically significant or unstable medical or psychiatric condition, abnormal ECG, CrCl <60 mL/min n=309 Approximately 53% women Mean age: 60 years (SD 9 years) 70% had DPN	Mean age: 60 years (SD 9 years) **Comparison** Placebo n=102 *Drop-out rate* n=17 (16.7%) Mean age: 60 years (SD 10 years)	*Endpoint LS (Least square) mean difference pregabalin – placebo (95% CI):* –0.6 (–1.1 to –0.2), p=0.05 **Secondary endpoints** *Patients who achieved ≥30% reduction in pain scores from baseline to endpoint:* Placebo: 52.0% Pregabalin: 64.0% (p=0.041 vs placebo) *Clinical Global Impression of Change (CGIC) score (0–7):* Any improvement (from ”minimally” to ”very much”): Placebo: 69.2% Pregabalin: 85.2% (p<0.05 vs placebo) Difference in LS means: –0.39, 95% CI, –0.63 to –0.16; p=0,001 *Patient Global Impression of Change (PGIC) score (0–7):* Difference in LS means: –0.33, 95% CI, –0.55 to –0.11; p=0,004	**Three most common AEs (pregabalin vs placebo)** Dizziness 11.2% vs 6.9% Lethargy 7.8% vs 2.9% Somnolence 4.9% vs 1.0%
Huffman et al 2015 [25] USA, Czech Republic, South Africa, Sweden **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, cross over study **Aim** Evaluate the efficacy and safety of pregabalin in patients with	**Participants** *Inclusion*: ≥18 years of age DPN ≥3 months. NRS pain ≥4 (out of 10) Able to walk >15 m unassisted. Pain on walking > prewalk resting pain HbA_{1c} <11% *Exclusion:*	**Intervention** Pregabalin 150 mg–300 mg/day (83% on 300 mg/day) n=198 *Drop-out rate* n=22 (11.1%) Mean age: not shown **Comparison** Placebo	**Primary endpoints** *Change in the mean daily NRS-score from baseline to the end of each treatment period, compared with placebo, ITT-analysis;* *Baseline value (SD):* Placebo → pregabalin: 6.52 (1.32) Pregabalin → placebo: 6.32 (1.36) *Endpoint, LS mean (SE):* Placebo: 4.96 (0.14), 95% CI, 4.67 to 5.24 Pregabalin: 4.73 (0.14), 95% CI, 4.46 to 5.01)	**Study withdrawal because of AE** Placebo: 2.7% Pregabalin: 6.6% **Serious adverse events** Placebo: 1.1% Pregabalin: 4.5% **Three most common treatment related AEs (pregabalin vs placebo)** Somnolence: 6.1% vs 2.2% Dizziness: 5.1% vs 2.7% Fatigue: 5.1% vs 1.1%

	diabetic polyneuropathy (DPN) who experienced pain while walking **Treatment duration** 6 weeks, 2 weeks wash-out, 6 weeks	Fluctuation >4 points on daily pain diary; failed pregabalin treatment; were intolerant to pregabalin; aid while walking; other condition that could cause pain on walking; unstable diabetes; CrCL <60 mL/min; amputation of lower extremities n=205 30–40% women Mean age: 59 years (SD 9 years)	n=186 *Drop-out rate* n=10 (5.4%) Mean age: not shown	*Endpoint LS mean difference (SE) pregabalin - placebo:* –0.22 (0.12), 95% CI, –0.46 to 0.01, p=0.0659 **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to the end of each treatment period:* Placebo period 1: 13.7%, period 2: 32.1% Pregablin period 1: 23.8%, period 2: 27.8%. OR pregabalin vs placebo 1.38 (95% CI, 0.8 to 2.38). *Patient Global Assessment (PGIC), proportion of patients reporting "much" or "very much" improved:* Placebo: 31.4% Pregabalin: 51.0% (p=0.002 vs placebo) *Nine other secondary end-points was also assessed. No significant differences was detected for those end-points.*	
Lesser et al 2004 [26] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized study **Aim** Evaluate the efficacy and safety of pregabalin in patients with diabetic	**Participants** *Inclusion*: ≥18 years of age DPN ≥1 year ≤5 years Pain NRS ≥4 (0–10) VAS or SF-MPQ ≥40/100 mm HbA_{1c} <11% *Exclusion:* Clinically significant or unstable hepatic, respiratory, or hematologic illnesses.	**Intervention** Pregabalin 75 mg n=77 *Drop-out rate* n=10 (13%) Mean age: 61 years (SD 11 years) Pregabalin 300 mg n=81 *Drop-out rate* n=5 (6.2%)	**Primary endpoints** *Change in the mean daily NRS-score from baseline to the mean value over the last week compared with placebo;* *Baseline mean (SD), endpoint LS mean (SE):* Placebo: 6.6 (1.5), 5.06 (0.21) Pregabalin 75: 6.7 (1.3), 4.91 (0.24) Pregabalin 300: 6.2 (1.4), 3.80 (0.23) Pregabalin 600: 6.2 (1.5), 3.60 (0.23) *Difference vs placebo, ITT-analysis (95% CI):* Pregabalin 75: –0.15 (–0.76 to 0.46), p=0.63	**Study withdrawal because of AE** Not shown **Serious adverse events** Placebo: 3.1% Pregabalin 75: 1.3% Pregabalin 300: 0.0% Pregabalin 600: 4.9% **Three most common AEs (pregabalin 600 vs placebo)** Dizziness 39.0% vs 5.2% Somnolence 26.8% vs 4.1% Peripheral edema 13.4% vs 2.1%

	polyneuropathy (DPN) **Treatment duration** 5 weeks	Unstable cardiovascular disease. Symptomatic peripheral vascular disease. CrCL <60 mL/min Any condition that might confound pain assessment. Failure to respond to previous treatment with gabapentin at doses ≥1.200 mg/day n=338 40.1% women Mean age: 60 years (SD 10.5 years)	Mean age: 59 years (SD 9 years) Pregabalin 600 mg n=82 *Drop-out rate* n=12 (14.6%) Mean age: 62 years (SD 10 years) **Comparison** Placebo n=97 *Drop-out rate* n=8 (8.2%) Mean age: 58 years (SD 12 years)	Pregabalin 300: –1.26 (–1.86 to –0.65), p=0.0001 Pregabalin 600: –1.45 (–2.06 to –0.85), p=0.0001 *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 18% Pregabalin 75: not shown Pregabalin 300: 46% (p<0.05 vs placebo) Pregabalin 600: 48% (p<0.05 vs placebo) **Secondary endpoints** *Patient Global Impression of Change (PGIC), proportion of patients reporting "much" or "very much" improved:* Placebo: 24.2% Pregabalin 75: not shown Pregabalin 300: 55.7% (p=0.001 vs placebo) Pregabalin 600: 69.2% (p=0.001 vs placebo) *Health related quality of life, measured by SF-36* Statistically significant improvements in pregabalin 300 mg and 600 mg vs placebo, data not shown.	
Mu et al 2018 [27] China **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim**	**Participants** *Inclusion*: ≥18 years of age DPN ≥6 months ≤5 years Pain on VAS ≥40/100 *Exclusion:*	**Intervention** Pregabalin (300 mg/day n=314 *Drop-out rate* n=29 (9.2%) Mean age: 60 years (SD 10 years)	**Primary endpoints** *Change in the mean daily pain NRS-score from baseline to the mean value over the last week compared with placebo;* *Baseline mean (SD), endpoint mean (SD):* Placebo: 6.67 (1.15), 4.74 (2.05) Pregabalin: 6.65 (1.12), 4.45 (2.00)	**Study withdrawal because of AE** Placebo: 2.9% Pregabalin: 3.5% **Serious adverse events** Placebo: 1.6% Pregabalin: 2.2%

	Evaluate the efficacy and safety of pregabalin in patients with diabetic polyneuropathy (DPN) **Treatment duration** 11 weeks	Neurologic disorder, pain, or skin conditions likely to interfere with the evaluation of pain. High variability in daily pain scores Concomitant use of treatments for diabetic neuropathy. n=623 53% women Mean age: 61 years (SD 10 years)	**Comparison** Placebo n=309 *Drop-out rate* n=36 (11,7%) Mean age: 61 years (SD 10 years)	*LS mean difference vs placebo, ITT-analysis (95% CI):* Pregabalin: –0.28 (–0.58 to 0.01), p=0.0559 **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 24.1% Pregabalin: 31.1% (p=0.0384 vs placebo) *Patient Global Impression of Change (PGIC)and Clinical Global Impression of Change on a 7-point NRS, LS mean treatment difference pregabalin vs placebo (95% CI)* PGIC –0.14 (–0.28 to 0.01), p=0.0602 CGIC –0.15 (–0.29 to 0.00), p=0.0431	**Three most common AEs (pregabalin vs placebo)** Dizziness 9.6% vs 3.9% Somnolence 5.7% vs 1.9% Peripheral edema 3.2% vs 0.3%
Rosenstock et al 2004 USA [30] **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of pregabalin in patients with diabetic polyneuropathy (DPN) **Treatment duration** 8 weeks	**Participants** *Inclusion*: ≥18 years of age DPN ≥1 year ≤5 years VAS or SF-MPQ ≥40 mm HbA_{1c} <11% *Exclusion:* CrCl ≤60 ml/min Serious or unstable medical conditions. Conditions confounding evaluation of DPN. Patients who had failed to respond to treatment with gabapentin at doses ≥ 1200 mg/day for treatment of DPN	**Intervention** Pregabalin (300 mg/day n=76 *Drop-out rate* n=11 (14.5%) Mean age: 59 years (SD 12 years) **Comparison** Placebo n=70 *Drop-out rate* n=8 (11.4%) Mean age: 60 years (SD 10 years)	**Primary endpoints** *Change in the mean daily pain NRS-score from baseline to the mean value of last week of follow-up; Baseline mean (SD), endpoint LS mean (SE):* Placebo: 6.1 (N/A), 5.46 (0.28) Pregabalin: 6.5 (N/A), 3.99 (0.26) *Difference vs placebo, ITT-analysis (95% CI):* Pregabalin: –1.47 (–2.19 to –0.75), p=0.0001 *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 14.5% Pregabalin: 40.0% (p=0.001 vs placebo) **Secondary endpoints**	**Study withdrawal because of AE** Placebo: 3% Pregabalin: 11% **Serious adverse events** Not shown **Three most common AEs (pregabalin vs placebo)** Dizziness: 35.5% vs 11.4% Somnolence: 19.7% vs 2.9% Infection: 14.5% vs 5.7%

		n=146 43.8% women Mean age: 60 years (SD 10.5 years)		Any improvement (from ”minimally” to ”very much”) *on:* *Patient Global Impression of Change, PGIC:* Placebo: 39% Pregabalin: 67% (p=0.001 vs placebo) *CGIC:* Placebo: 39% Pregabalin: 59% (p=0.004 vs placebo) *Health related quality of life, measured by SF-36* Significant difference in the Bodily pain domain only, favouring pregabalin (p<0.03).	
Satoh et al 2011 [32] Japan **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of pregabalin in Japanese patients with diabetic polyneuropathy (DPN) **Treatment duration** 14 weeks	**Participants** *Inclusion*: ≥18 years of age DPN pain on VAS ≥40/100 *Exclusion:* CrCl ≤30 ml/min. Malignant tumour within the past 2 years. Pain or skin conditions that may affect the evaluation of pain. n=317 25% women Mean age: 61 years (SD 10 years)	**Intervention** Pregabalin (pre) 300 mg/day: n=134 *Drop-out rate* n=20 (14.7%) Mean age: 61 years (SD 10 years) Pregabalin (pre) 600 mg/day: n=45 *Drop-out rate* n=13 (28.9%) Mean age: 62 years (SD 10 years) **Comparison** Placebo: n=135	**Primary endpoints** *Change in the mean daily pain NRS-score from baseline to the mean value of last week of follow-up; Baseline mean (SD), endpoint LS mean change (SE) reproduced from figure:* Placebo: 6.1 (1.4), –1.2 (N/A) Pregabalin 300: 6.0 (1.4), –1.8 (N/A) Pregabalin 600: 6.1 (1.3), –1.9 (N/A) *Difference vs placebo, ITT-analysis (95% CI):* Pregabalin 300: –0.63 (–1.09 to –0.17), p=0.0075 Pregabalin 600: –0.74 (–1.39 to –0.09), p=0.0254 **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 21.5% Pregabalin 300: 29.1% (n.s. vs placebo) Pregabalin 600: 35.6% (n.s. vs placebo)	**Study withdrawal because of AE** Placebo: 5.2% Pregabalin 300: 12.7% Pregabalin 600: 28.9% **Serious adverse events** Placebo: 2.2 Pregabalin 300: 3.0% Pregabalin 600: 4.4% **Three most common AEs (pregabalin 600 vs placebo)** Somnolence 40.0% vs 8.1% Dizziness 37.8% vs 6.7% Peripheral edema 13.3% vs 4.4%

			Drop-out rate n=16 (11.8%) Mean age: 61 years (SD 10 years)	*Patient Global Impression of Change scores:* Placebo: no data shown Pregabalin 300: no data shown (n.s. vs placebo) Pregabalin 600: no data shown (p=0.0075 vs placebo, favouring pregabalin 600) *Clinical Global Impression of Change scores:* Placebo: no data shown Pregabalin 300: no data shown (p=0.0148 vs placebo, favouring pregabalin 300) Pregabalin 600: no data shown (p=0.0063 vs placebo, favouring pregabalin 600) *Health related quality of life, measured by SF-36:* Placebo: no data shown Pregabalin 300: no data shown (n.s. vs placebo) Pregabalin 600: no data shown, pregabalin 600 superior to placebo on social functioning and vitality (p<0.05)	
Tölle et al 2008 [39] Europe, Australia, South Africa **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of pregabalin in	**Participants** *Inclusion*: ≥18 years of age DPN ≥1 year VAS or SF-MPQ ≥40 mm HbA_{1c} <11%. *Exclusion:* CrCl ≤30 ml/min Clinically significant or unstable hepatic,	**Intervention** Pregabalin 150 mg: n=99 *Drop-out rate* n=17 (17.2%) Mean age: 59 years (SD 12 years) Pregabalin 300 mg: n=99	**Primary endpoints** *Change in the mean daily NRS-score from baseline to the mean value over the last week compared with placebo:* Placebo: Baseline 6.4; change –1.9 (SD N/A) Pregabalin 150: Baseline 6.2; change –2.1 (SD N/A) Pregabalin 300: Baseline 6.4; change –2.1 (SD N/A) Pregabalin 600: Baseline 6.6; change –3.0 (SD N/A)	**Study withdrawal because of AE** Placebo: 3.1% Pregabalin 150: 5.1% Pregabalin 300: 11.1% Pregabalin 600: 12.9% **Serious adverse events** Placebo: 2.1% Pregabalin 150: 4.0% Pregabalin 300: 3.0% Pregabalin 600: 5.9%

	patients with diabetic polyneuropathy (DPN) **Treatment duration** 12 weeks	respiratory, or hematologic illnesses. Unstable cardiovascular disease or symptomatic peripheral vascular disease. Severe pain or a skin condition in the area affected by neuropathy. Patients who had failed to respond to treatment with gabapentin at doses ≥1200 mg/day for treatment of DPN n=396 44,6% women Mean age: 59 years (SD 12 years)	*Drop-out rate* n= 20 (20.2%) Mean age: 57 years (SD 11 years) Pregabalin 600 mg: n=101 *Drop-out rate* n=23 (22.8%) Mean age: 60 years (SD 11 years) **Comparison** Placebo n=96 *Drop-out rate* n=17 (17.7%) Mean age: 59 years (SD 12 years)	*Difference vs placebo, ITT-analysis (95% CI):* Pregabalin 150: –0.27 (–0.87 to 0.34) Pregabalin 300: –0.10 (–0.70 to 0.50) Pregabalin 600: –0.91 (–1.51 to –0.31) *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 30.1% Pregabalin 150: 34.4% (n.s. vs placebo) Pregabalin 300: 33.3% (n.s. vs placebo) Pregabalin 600: 45.9% (p=0.036 vs placebo) **Secondary endpoints** *Patient Global Impression of Change (PGIC), proportion of patients reporting "much" or "very much" improved:* Placebo: 33.3% Pregabalin 150: 45.8% (n.s. vs placebo) Pregabalin 300: 42.5% (n.s. vs placebo) Pregabalin 600: 50.5% (p=0.021 vs placebo) *EuroQoL Health Utilities Index (EQ-5D), difference vs placebo, MITT-analysis (95% CI):* Pregabalin 150: 0.10 (0.03 to 0.16) Pregabalin 300: 0.08 (0.01 to 0.14) Pregabalin 600: 0.14 (0.07 to 0.20)	**Three most common AEs (pregabalin 600 vs placebo)** Dizziness 13.9% vs 2.1% Peripheral edema 9.9% vs 2.1% Somnolence 7.9% vs 1.0%
Oxcarbazepine versus placebo					

Beydoun et al 2006 [9] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of oxcarbazepine (oxc) in patients with diabetic polyneuropathy (DPN) **Treatment duration** 16 weeks	**Participants** *Inclusion*: >18 years with DPN >6 months <5 years >50 units on a 100-unit visual analog scale (VAS) HbA_{1c} <11% Pain for >3 months *Exclusion:* Patients with other types of pain, clinically significant medical or psychiatric illnesses. n=347 44% women Mean age: 61 years ±10 years	**Intervention group** Oxc 600 mg: n=83 *Drop-out rate* n=16 (19.3%) Mean age: 61±11 Oxc 1200 mg: n=87 *Drop-out rate* n=34 (39.1%) Mean age: 60±10 Oxc 1800 mg: n=88 *Drop-out rate* n=48 (54. %) Mean age: 59±9 **Comparison group** Placebo n=89 *Drop-out rate* n=17 (19.1%) Mean age: 62±10	**Primary endpoint** *Average daily pain, VAS score, 0–100 units (SD); ITT-analysis:* Placebo: Baseline 70.8 (13.2) change – 19.1 (no SD) oxc 600 mg: Baseline 76.9 (14.2) change -25.9 (no SD) n.s. vs placebo oxc 1200 mg: Baseline 75.7 (13.8) change -29.0 (no SD) n.s. vs placebo oxc 1800 mg: Baseline 71.3 (15.6) change -26.5 (no SD) n.s. vs placebo **Secondary endpoints** *Patients Global Assessment of Therapeutic Effect (GATE)* Percentage of patients feeling ”much” or ”very much” improved compared with baseline: Placebo: 36.4% oxc 600 mg: 37.3% n.s. vs placebo oxc 1200 mg: 50.0% n.s. vs placebo oxc 1800 mg: 49.3% n.s. vs placebo *Quality of life (SF-36 Health Survey and the Profile of Mood States (POMS)* No significant differences between the oxcarbazepine groups and placebo	**Study withdrawal because of AE** oxc 1 800 mg 41.4% oxc 1 200 mg 23.5% oxc 600 mg 11% placebo 7% **Serious adverse events** oxc 1 800 mg 11.5% oxc 1 200 mg 10.6% oxc 600 mg 2.4% placebo 1.1% **Three most common AEs (oxc 1800 mg vs placebo)** Dizziness 34.5% vs 2.2% Nausea 19.5% vs 5.6% Fatigue 14.9% vs 6.7%
Dogra et al 2005 [12] USA and Canada **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim**	**Participants** *Inclusion*: >18 years with DPN >6 months <5 years VAS >50/100 units HbA_{1c} <11% *Exclusion:*	**Intervention** Oxcarbazepine (oxc) 600 mg/day, titrated up to maximum dose of 1800 mg/day (mean	**Primary endpoints** *Average daily VAS score (0–100 units) for pain severity (SD); ITT-analysis:* Placebo: Baseline 74.3 (13.7) change – 14.7 (26.4) Oxc: Baseline 71.5 (15.8) change –24.3 (27.2) p=0.0108	**Study withdrawal because of AE** Placebo 7.8% oxc 27.5% **Serious adverse events** placebo 4% oxc 10%

	Evaluate the efficacy and safety of oxcarbazepine in patients with diabetic polyneuropathy (DPN) **Treatment duration** 18 weeks	Patients with other types of pain, CrCl <30 mL/min n=146 42% women Mean age: 60 years (SD 9 years)	maintenance dose 1445 mg/day) n=69 *Drop-out rate* n=25 (36.2%) Mean age: 60 years (SD 10 years) **Comparison** Placebo n=77 *Drop-out rate* n=15 (19.5%) Mean age: 61 years (SD 8 years)	*Proportion of patients with >50% reduction from baseline in VAS score:* Placebo: 18.4% Oxc: 35.2% p=0.0156 **Secondary endpoints** *Patients Global Assessment of Therapeutic Effect (GATE)* Percentage of patients feeling ”much” or ”very much” improved compared with baseline: Placebo: 22% Oxc: 48% p=0.025 *Quality of life (SF-36 Health Survey and the Profile of Mood States (POMS)* No significant differences between the oxcarbazepine groups and placebo	**Three most common AEs (oxc vs placebo)** Dizziness 12.7% vs 1.4% Headache 9.0% vs 1.4% Somnolence 9.0% vs 0.0%
Grosskopf et al 2006 [21] USA, Germany and UK **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of oxcarbazepine in patients with diabetic	**Participants** *Inclusion*: >18 years with DPN >6 months <5 years >50 units on a 100-unit visual analog scale (VAS). VAS >40 units over 4 of the last 7 days prior to randomization. HbA_{1c} <11% *Exclusion:* Patients with other types of pain, skin	**Intervention** Oxcarbazepine (oxc) 300 mg/day, titrated to tolerability or a maximum dose of 1200 mg/day (mean maintenance dose 1091 mg/day) n=71 *Drop-out rate* n=29 (40.8%)	**Primary endpoints** *Average daily VAS score (0–100 units) for pain severity (SD); ITT-analysis:* Placebo: Baseline 70.7 (13.6) change –22.0 (SD N/A) Oxc: Baseline 72.0 (14.2) change –20.1 (SD N/A) (n.s. vs placebo) The percentage reductions in average VAS scores were 27.9% and 31.1% for the oxcarbazepine and placebo groups respectively. **Secondary endpoints** *Patients Global Assessment of Therapeutic*	**Study withdrawal because of AE** Placebo 5.9% oxc 25.4% **Serious adverse events** placebo 3% oxc 7% **Three most common AEs (oxc vs placebo)** Dizziness 8% vs 2% Nausea 6% vs 0% Headache 4% vs 1%

	polyneuropathy (DPN) **Treatment duration** 16 weeks	conditions that could affect assessment of pain, amputations (other than toes), renal insufficiency. n=141 45% women Mean age: 61 years (SD 10.5 years)	Mean age: 61 years (SD 11 years) **Comparison** Placebo n=70 *Drop-out rate* n=17 (24.3%) Mean age: 61 years (SD 11 years)	*Effect (GATE)* No significant differences between the oxcarbazepine groups and placebo *Quality of life (SF-36 Health Survey and the Profile of Mood States (POMS)* No significant differences between the oxcarbazepine groups and placebo	
Other anticonvulsants versus placebo					
Shaibani et al 2009 [34] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of oral lacosamide in patients with diabetic polyneuropathy (DPN) **Treatment duration** 18 weeks	**Participants** *Inclusion*: >18 years with DPN >6 months <5 years Pain >4 on an 11-point numerical rating scale HbA_{1c} <12% *Exclusion:* Patients with other types of pain, use of certain drugs, major skin ulcers, amputations (other than toes), history of certain cardiovascular disease, CrCl <50 mL/min. n=468 43.5% women Mean age: 60 years (SD 10 years)	**Intervention** Lacosamide (Lac) 200, 400 or 600 mg/day n=403 *Drop-out rate* n=191 (47,4%) Mean age: 59–60 years (SD 10–11 years) **Comparison** Placebo n=65 *Drop-out rate* n=20 (30.7%) Mean age: 60 years (SD 8 years)	**Primary endpoints** *Change in daily NRS-score from baseline to the mean value over weeks 15–18, ITT-analysis; mean difference vs placebo ± SD (95% CI):* Lac 200: –0.33±0.31 (–0.94 to 0.27), p=0.28 Lac 400: –0.61±0.31 (–1.23 to 0.00), p=0.05 Lac 600: –0.56±0.31 (–1.17 to 0.05), p=0.07 **Secondary endpoints** *50% reduction in NRS-score:* Placebo: 27% Lac 200: 27% Lac 400: 44% Lac 600: 30% *Patient's Global Impression of Change (PGIC),* Percentage of patients feeling "better": Placebo: 71% Lac 200: 65% Lac 400: 82% p=0.05 vs placebo Lac 600: 79%	**Study withdrawal because of AE** Placebo: 13.8% Lac 200: 12.1% Lac 400: 24% Lac 600: 42.3% **Serious adverse events** Placebo: 6.2% Lac 200: 5% Lac 400: 4.8% Lac 600: 6.6% **Three most common AEs (Lac 600 mg vs placebo)** Dizziness: 28.5% vs 4.6% Nausea: 18.2% vs 6.2% Tremor: 14.6% vs 0.0%

Thienel et al 2004 [38] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study. Three similar studies reported altogether. **Aim** Evaluate the efficacy and tolerability of topiramate in patients with diabetic polyneuropathy (DPN) **Treatment duration** 18–22 weeks	**Participants** *Inclusion*: 18–75 years with DPN ≥6 months. Antidiabetic regimens stable ≥3 months before study entry. HbA_{1c} ≤11% *Exclusion:* Other polyneuropathies; ulceration of extremities; amputation; significant history of unstable medical disease; history of alcohol or drug abuse; previous treatment with topiramate; patients requiring chronic use of analgesics to control pain. n=1259 43% women Mean age: 58 years (SD 10 years)	**Intervention** Topiramate (Top) 100 mg/day, 200 mg/day or 400 mg/day n=878 *Drop-out rate* n=464 (53%) Mean age: 58 years (SD 9–10 years) **Comparison** Placebo n=381 *Drop-out rate* n=156 (41%) Mean age: 59 years (SD 10 years)	**Primary endpoints** *Pain reduction based on change in 100 mm VAS scores from baseline to final visit, mean values (95% CI), ITT-analysis:* **NP 001** Top 100: Change vs placebo –9.4 (–12.1 to –0.18) Top 200: Change vs placebo –2.9 (–10.4 to 1.45) Top 400: Change vs placebo –2.0 (–7.46 to 4.40) **NP 002** Placebo: Top 200: Change vs placebo –4.3 (–10.7 to 2.76) Top 400: Change vs placebo –2.6 (–8.88 to 4.20) **NP 003** Placebo: Top 100: Change vs placebo + 1.8 (–1.88 to 11.63) Top 200: Change vs placebo + 2.9 (–1.03 to 12.46) **Secondary endpoints** *Change from baseline in Categorical Pain Score and Sleep Disruption Scale:* No significant differences between topiramate and placebo except in one comparison in one study, favoring placebo *Change from baseline in SF-36 quality-of-life:* Data not shown	**Study withdrawal because of AE** Placebo: 8% Top 100: 16% Top 200: 25% Top 400: 31% **Serious adverse events** Placebo: 8% Top (all doses): 7% **Three most common AEs (Top 400 mg vs placebo)** Fatigue 7.7% vs 2.9% Nausea 5.0% vs 1.8% Paresthesia 4.6% vs 1.3%
Antidepressants versus placebo					
Duloxetine versus placebo					

Gao et al 2010 [17] China **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Evaluate the efficacy and safety of duloxetine in Chinese patients with diabetic peripheral neuropathic pain (DPNP) **Treatment duration** 12 weeks	Participants Inclusion: ≥18 years of age DPNP ≥6 months Pain on BPI ≥4/10 Exclusion: HbA1c >12% Any condition that could compromise participation. Mania, bipolar disorder. psychosis, at risk for suicide, depression. History of hepatic dysfunction or othcr serious medical conditions n=215 53% women Mean age: 59 years (SD 10 years)	**Intervention** Duloxetine flexible dose (60 mg–120 mg per day) n=106 *Drop-out rate* n=19 (17.9%) Mean age: 59 years (SD 10 years) **Comparison** Placebo: n=109 *Drop-out rate* n=17 (15.6%) Mean age: 60 years (SD 10 years)	**Primary endpoints** *Change in BPI 24 h average pain (0–10) from baseline to endpoint; Baseline mean (SD), LS mean change (SE):* Placebo: 5.5 (1.4), –2.31 (0.18) Duloxetine: 5.5 (1.3), –2.69 (0.19) *Mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine: –0.38 (not shown), p=0.124 (n.s.) **Secondary endpoints** *Patients who achieved ≥50% reduction in BPI average pain from baseline to endpoint:* Placebo: 50.5% Duloxetine: 54.8% (p=0.584 vs placebo) *PGI-I, Patient Global Impression of Improvement (7-items, 7=very much worse"); LS mean change (SE):* Placebo: 2.64 (0.10) Duloxetine: 2.32 (0.11) *Mean difference duloxetine vs placebo, ITT-analysis:* –0.32, p=0.028 *EQ-5D (US), mean change (SE):* Placebo: 0.10 (0.02) Duloxetine: 0.12 (0.02) *Mean difference duloxetine vs placebo, ITT-analysis:* 0.02, p=0.207 (n.s.)	**Study withdrawal because of AE** Placebo: 3.7% Duloxetine: 16.7% **Serious adverse events** Not shown **Three most common AEs (duloxetine vs placebo)** Nausea 30.2% vs 11.9% Somnolence 16.0% vs 5.5% Dizziness 15.1% vs 11.0%
Gao et al 2015 [16] China **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study	**Participants** *Inclusion*: ≥18 years of age DPN pain on BPI-severity ≥4/10	**Intervention** Duloxetine 60 mg n=203 *Drop-out rate* n=30 (14.8%)	**Primary endpoints** *Change in mean weekly pain on Likert scale (0–10) from baseline to follow-up; Baseline mean (SD), LS mean change (SE):* Placebo: 5.7 (1.7), –1.97 (0.14) Duloxetine: 5.6 (1.7), –2.40 (0.14)	**Study withdrawal because of AE** Placebo: 4.0% Duloxetine: 8.4% **Serious adverse events** Placebo: 1.0%

	Aim Evaluate the efficacy and safety of duloxetine in Chinese patients with diabetic polyneuropathy (DPN) **Treatment duration** 12 weeks	*Exclusion:* HbA_{1c} >12% Major depressive disorder, mania, bipolar disorder, dysthymia, anxiety disorders, alcohol or eating disorders, psychosis, risk for suicide. Serious or unstable cardiovascular, hepatic, renal, respiratory, or haematological illness, symptomatic peripheral vascular disease, or the presence of other serious medical conditions. n=405 55% women Mean age: 61 years (SD 10 years)	Mean age: 62 years (SD 10 years) **Comparison** Placebo: n=202 *Drop-out rate* n=26 (12.9%) Mean age: 61 years (SD 9 years)	*LS mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine: –0.43 (–0.82 to –0.04), p=0.030 **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 28.8% Duloxetine: 42.0% (p=0.006 vs placebo) *Patients experiencing "much better" improvement on PGI, Patient Global Impression of Improvement:* Placebo: 33.9% Duloxetine: 47.2% Difference vs placebo –0,21 (–0.4, –0.02) (p=0.034) *BPI-interference, average of 7 items ranging 0–10 (worst interference); Baseline mean (SD), LS mean change (SE):* Placebo: 4.1 (2.3), –1.82 (0.14) Duloxetine: 4.4 (2.3), –2.42 (0.13) *LS mean difference duloxetine vs placebo, ITT-analysis (95% CI)*: –0.60 (–0.96 to –0.24), p=0.001 *Sheehan Disability Scale (SDS) measuring function, 5 items ranging 0–10 (extremely impaired; Baseline mean total score (SD), LS mean change (SE):* Placebo: 11.2 (7.6), –5.09 (0.42) Duloxetine: 10.5 (7.3), –6.36 (0.40) *LS mean difference duloxetine vs placebo, ITT-analysis (95% CI):* –1.26 (–2.33 to –0.2), p=0.02	Duloxetine: 1.5% **Three most common AEs (duloxetine vs placebo)** Nausea 10.4% vs 3.5% Somnolence 8.4% vs 0.5% Dizziness 8.4% vs 4.5%

Goldstein et al 2005 [20] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Describe the efficacy and safety of duloxetine in reducing pain in patients with diabetic peripheral neuropathic pain (DPNP) **Treatment duration** 12 weeks	**Participants** *Inclusion*: ≥18 years of age DPNP ≥6 months Pain on 24 h average pain score ≥4/10 (Likert scale) *Exclusion:* Depression, dysthymic disorder, generalized anxiety disorder, alcohol or eating disorders, mania, bipolar disorder, pain that could interfere with the assessment of DPNP, history of substance abuse n=457 39% women Mean age: 60 years (SD 11 years)	**Intervention** Duloxetine (dul) 20 mg n=115 *Drop-out rate* n=24 (20.9%) Mean age: 60 years (SD 11 years) Duloxetine 60 mg n=114 *Drop-out rate* n=28 (24.6%) Mean age: 59 years (SD 12 years) Duloxetine 120 mg n=113 *Drop-out rate* n=33 (29.2%) Mean age: 61 years (SD 11 years) **Comparison** Placebo: n=115 *Drop-out rate* n=28 (24.3%) Mean age: 60 years (SD 11 years)	*Primary endpoints* *Change in mean weekly pain on Likert scale (0–10) from baseline to follow-up; Baseline mean (SD), LS mean change (SE):* Placebo: 5.8 (1.5), –1.91 (0.22) Duloxetine 20: 5.9 (1.6), –2.36 (0.21) Duloxetine 60: 6.0 (1.7), –2.89 (0.22) Duloxetine 120: 5.9 (1.4), –3.24 (0.23) *LS mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 60: –1.17 (–1.84 to –0.50) Duloxetine 120: –1.45 (–2.13 to –0.78) *Secondary endpoints* *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 26% Duloxetine 20: 41%, p<0.05 vs placebo Duloxetine 60: 49%, p<0,05 vs placebo Duloxetine 120: 52%, p<0,05 vs placebo *Patient Global Impression of Improvement; Mean change (SE):* Placebo: 2.91 (0.12) Duloxetine 20: 2.68 (0.12), n.s vs placebo Duloxetine 60: 2.21 (0.12), p≤0.001 vs placebo Duloxetine 120: 2.24 (0.12), p≤0.01 vs placebo *Euro Quality of Life, EQ-5D; Mean change (SE):* Placebo: 0.08 (0.02) Duloxetine 20: 0.1 (0.02) Duloxetine 60: 0.13 (0.02) p<0.05 vs placeo	**Study withdrawal because of AE** Placebo: 6/115 Duloxetine 20: 5/115 Duloxetine 60: 15/114 Duloxetine 120: 22/113 **Serious adverse events** Not shown **Three most common AEs (duloxetine 120 mg vs placebo)** Nausea: 27.4% vs 9.6% Somnolence: 28.3% vs 7.8% Dizziness: 23% vs 7%

				Duloxetine 120: 0.13 (0.02) p<0.05 vs placebo *CGI-severity; Mean change (SE):* Placebo: –0.83 (0.12) Duloxetine 20: –1.28 (0.11), p≤0.05 vs placebo Duloxetine 60: –1.42 (0.12), p≤0.001 vs placebo Duloxetine 120: 1.70 (0.12), p≤0.01 vs placebo	
Raskin et al 2005 [28] USA and Canada **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Assess the efficacy and safety of duloxetine in patients with diabetic peripheral neuropathic pain (DPNP) **Treatment duration** 12 weeks	**Participants** *Inclusion*: ≥18 years of age DPNP ≥6 months Pain on 24 h average pain score ≥4/10 (Likert scale) *Exclusion:* Prior renal transplant or current renal dialysis, serious or unstable illness, or other condition that might compromise participation in the study. Current major depressive disorder, dysthymia, generalized anxiety disorder, alcohol or eating disorders. Previous diagnosis of mania, bipolar disorder, or psychosis.	**Intervention** Duloxetine 60 mg n=116 *Drop-out rate* n=15 (13%) Mean age: 58 years (SD 11 years) Duloxetine 120 mg n=116 *Drop-out rate* n=21 (18%) Mean age: 59 years (SD 10 years) **Comparison** Placebo: n=116 *Drop-out rate* n=16 (14%) Mean age: 59 years (SD 10 years)	**Primary endpoints** *Change in mean weekly pain on Likert scale (0–10) from baseline to follow-up; Baseline mean (SD), Mean change (SE):* Placebo: 5.5 (1.3), –1.6 (0.18) Duloxetine 60: 5.5 (1.1), –2.5 (0.18), p<0,001 vs placebo Duloxetine 120: 5.7 (1.3), –2.47 (0.18), p<0,001 vs placebo *Mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 60: –0.9 (–1.39 to –0.42) Duloxetine 120: –0.87 (–1.36 to –0.39) *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 30% Duloxetine 60: 50% Duloxetine 120: 39% **Secondary endpoints** *BPI-interference, average of 7 items ranging 0–10 (worst interference); Mean change (SE):* Placebo: –1.56 (0.18)	**Study withdrawal because of AE** Placebo: 2.6% Duloxetine 60: 4.3% Duloxetine 120: 12.1% **Serious adverse events** Placebo: 3.4% Duloxetine 60: 3.4% Duloxetine 120: 1.7% **Three most common AEs (duloxetine 120 mg vs placebo)** Not shown

		n=348 53% women Mean age: 59 years (SD 10 years)		Duloxetine 60: –2.43 (0.18), p<0,001 vs placebo Duloxetine 120: –2.54 (0.18), p<0,001 vs placebo *Mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 60: –0.88 (–1.38 to –0.38) Duloxetine 120: –0.98 (–1.49 to –0.47) *Patient Global Impression of Improvement (7-items, 7=very much worse"), Mean change (SE):* Placebo: 3.04 (0.10) Duloxetine 60: 2.5 (0.10), p<0.001 vs placebo Duloxetine 120: 2.54 (0.10), p<0,001 vs placebo *LS mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 60: –0.53 (–0.81 to –0.26) Duloxetine 120: –0.49 (–0.77 to –0.21)	
Wernicke et al 2006 [40] USA and Canada **Risk of bias** Moderate	**Design** Double-blind, randomized, study **Aim** To assess the efficacy of duloxetine on the reduction of pain severity, as well as secondary outcome measures in patients with	**Participants** *Inclusion*: ≥18 years of age DPNP ≥6 months Pain ≥4 (0–10) HbA1c ≤12% *Exclusion:* Pregnancy, breast feeding, renal transplant, renal dialysis. Serious or unstable cardiovascular, hepatic, renal, respiratory or hematologic illness.	**Intervention** Duloxetine 60 mg n=114 *Drop-out rate* n=29 (25.4%) Mean age: 60 years (SD 11 years) Duloxetine 120 mg n=112 *Drop-out rate* n=34 (30.4%) Mean age: 62 years (SD 10 years)	**Primary endpoint** *Change in weekly mean pain on Likert scale (0–10) from baseline to follow-up; Baseline mean (SD), Mean change (SE):* Placebo: 5.9 (1.4), –1.39 (0.23) Duloxetine 60: 6.1 (1.6), –2.72 (0.22), p<0,001 vs placebo Duloxetine 120: 6.2 (1.5), –2.84 (0.23), p<0,001 vs placebo *Mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 60: –1.32 (–1.95 to –0.69) Duloxetine 120: –1.44 (–2.08 to –0.81) **Secondary end-points**	**Study withdrawal because of AE** Placebo: 8/108 Duloxetine 60: 17/114 Duloxetine 120: 20/112 **Serious adverse events** Placebo: 5/108 Duloxetine 60: 5/114 Duloxetine 120: 2/112 **Three most common AEs** (Placebo vs duloxetine 60 vs duloxetine 120): Nausea: 6.5% vs 28.1% vs 32.1% Dizziness: 5.6% vs 15.8% vs 10.7% Headache: 6.5% vs 10.5% vs 13.4%

	diabetic peripheral neuropathic pain (DPNP). **Treatment duration** 12 weeks	Symptomatic peripheral vascular disease, or other conditions that might compromise participa- tion in the study. Dysthymia, generalized anxiety disorder, alcohol, or eating disorders. Mania, bipolar disorder or psychosis. n=334 39% women Mean age: 61 years (SD 11 years)	**Comparison** Placebo: n=108 *Drop-out rate* n=23 (21.3%) Mean age: 61 years (SD 11 years)	*Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 27% Duloxetine 60: 43% Duloxetine 120: 53% *Euro Quality of Life, EQ-5D; Mean change (SE):* Placebo: 0.08 (0.02) Duloxetine 60: 0.15 (0.02) Duloxetine 120: 0.15 (0.02) *SF 36, physical functioning; Mean change (SE):* Placebo: 3.64 (1.90) Duloxetine 60: 11.96 (1.81) Duloxetine 120: 11.20 (1.86) *BPI-interference, average of 7 items ranging 0–10 (worst interference), LS mean change (SE):* Placebo: –1.72 (0.19) Duloxetine 60: –2.36 (0.19) Duloxetine 120: –2.79 (0.19)	

Yasuda et al 2011 [42] Japan **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** Describe the efficacy and safety of duloxetine in reducing pain in Japanese patients with diabetic neuropathic pain (DNP) **Treatment duration** 12 weeks	**Participants** *Inclusion*: 20–80 years of age DNP ≥6 months Pain on 24 h average pain score ≥ 4/10 on NRS scale HbA_{1c} ≤9.4% *Exclusion:* Current or past mania, bipolar disorder, depression, anxiety disorders or eating disorders. A complication that might affect assessment of DNP. n=339 24% women Mean age: 61 years (SD 10 years)	**Intervention** Duloxetine (dul) 40 mg: n=85 *Drop-out rate* n=13 (15.1%) Mean age: 62 years (SD 9 years) Duloxetine 60 mg: n=86 *Drop-out rate* n=16 (18.6%) Mean age: 60 years (SD 12 years) **Comparison** Placebo: n=167 *Drop-out rate* n=17 (10.2%) Mean age: 61 years (SD 9 years)	**Primary endpoints** *Change in mean weekly pain on NRS (0–10) from baseline to follow-up; Baseline mean (SD), mean change (SE):* Placebo: 5.78 (1.17), –1.61 (0.18) Duloxetine 40: 5.79 (1.23), –2.41 (0.21) Duloxetine 60: 5.76 (1.17), –2.53 (0.21) *Mean difference vs placebo, ITT-analysis (95% CI):* Duloxetine 40: –0.8 (–1.18 to –0.43) Duloxetine 60: –0.92 (–1.30 to –0.56) **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 33/167 (19.8%) Duloxetine 40: 32/85 (37.6%) Duloxetine 60: 35/86 (40.7%) *Patient Global Impression of Improvement (7-items, 7=very much worse"); mean change (SE):* Placebo: 3.18 (0.12) Duloxetine 40: 2.53 (0.14) Duloxetine 60: 2.52 (0.14) *BPI-interference, average of 7 items ranging 0–10 (worst interference); Baseline mean (SD), mean change (SE):* Placebo: 3.75 (2.15), –1.56 (0.20) Duloxetine 40: 3.88 (2.25), –2.00 (0.24) Duloxetine 60: 4.09 (2.13), –2.08 (0.24)	**Study withdrawal because of AE** Placebo: 9/167 (5.4%) Duloxetine 40: 9/85 (10.6%) Duloxetine 60: 12/86 (14.0%) **Serious adverse events** Placebo: 0/167 Duloxetine 40: 3/85 Duloxetine 60: 2/86 **Three most common AEs (duloxetine 60 mg vs placebo)** Somnolence 24.4% vs 8.4% Nausea 16.3% vs 1.8% Nasopharyngitis 16.3% vs 14.4%
Other antidepressants versus placebo					
Rowbotham et al 2004 [31]	**Design** Double-blind, placebo	**Participants** *Inclusion*: ≥18 years of age	**Intervention** Venlafaxine 75 mg:	**Primary endpoints**	**Study withdrawal because of AE** Placebo: 3/81 Ven 75: 6/81

USA **Risk of bias** Moderate	controlled, randomized, study **Aim** To evaluate the efficacy, safety, and tolerability of various doses of venlafaxine ER in alleviating the pain associated with diabetic neuropathy. **Treatment duration** 6 weeks	Metabolically stable diabetes Pain on 24 h average pain score ≥40/100 on VAS pain intensity (VAS-PI) scale *Exclusion:* Clinically significant psychiatric disorders, cardiovascular, renal, or hepatic disease. History of recent drug or alcohol abuse. History of seizure disorders. Clinically significant abnormalities in physical examination results. n=244 41% women Mean age: 59 years (SD 10 years)	n=82 *Drop-out rate* n=13 (15.8%) Mean age: 59 years (SD 9 years) Venlafaxine 150–225 mg: n=82 *Drop-out rate* n=18 (22%) Mean age: 58 years (SD 12 years) **Comparison** Placebo: n=81 *Drop-out rate* n=12 (15%) Mean age: 60 years (SD 10 years)	*Change in mean weekly VAS-PI (0–100) from baseline to follow-up; Baseline mean (SD), mean change (SE):* Placebo: 68.8 (n/a), –18.7 (n/a) Ven 75: 69.9 (n/a), –22.4 (n/a) Ven 150–225: 67.3 (n/a), –33.8 (n/a) *Mean difference vs placebo, ITT-analysis (95% CI):* Ven 75: –3.7 (not shown) n.s vs placebo Ven 150–225: –15.1 (not shown) p<0.001 vs placebo **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint, LOCF:* Placebo: 34% Ven 75: 39%, n.s vs placebo Ven 150-225: 56%, p<0.001 vs placebo *CGI-S, CGI-I, Patient global pain relief not extracted due to lack of description of scales and/or lack of baseline values.*	Ven 150-225: 8/82 **Serious adverse events** Placebo: 10% Ven 75: 9% Ven 150-225: 12% **Three most common AEs (venlafaxine 150-225 mg vs placebo)** Somnolence 15/82 vs 1/81 Nausea 10/82 vs 5/81 Dyspepsia 10/82 vs 1/81
Opioids versus placebo					
Oxycodone versus placebo					
Gimbel et al 2003 [19] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim**	**Participants** *Inclusion*: DPN pain >5/10 on NRS HbA_{1c} ≤11%. *Exclusion:* Unstable diabetes. Chronic pain unrelated to DPN. History of	**Intervention** Oxycodone ER, maximum 60 mg bid. Mean average daily dose 42 mg. n=82 *Drop-out rate* n=19 (23%)	**Primary endpoints** *Change in daily pain NRS-score; Baseline mean scores (SD):* Placebo: 6.8 (1.3) Oxycodone: 6.9 (1.4) LS mean change from baseline (SE), *ITT-analysis:* Placebo: –1.0 (0.23)	**Study withdrawal because of AE** Placebo: 4/77 Oxycodone: 7/82 **Serious adverse events** Data not shown **Three most common AEs (placebo vs oxycodone)**

	Evaluate the efficacy and safety of controlled-release oxycodone in subjects with moderate to severe pain due to diabetic neuropathy (DPN) **Treatment duration** 6 weeks	substance or alcohol abuse. Serum creatinine ≥2.5 mg/dL. Hepatic dysfunction. History of active cancer. Rapidly escalating pain. Recent neurologic deficit. Autonomic neuropathy or gastrointestinal dys-function. Need for surgery during the study period. n=159 48% women Mean age: 59 years (SD 11 years)	Mean age: 59 years (SD 10 years) **Comparison** Placebo n=77 *Drop-out rate* n=25 (32%) Mean age: 59 years (SD 12 years)	Oxycodone: –2.0 (0.23), p<0.001 vs placebo **Secondary endpoints** *Physical functioning (Sickness Impact Profile)* No data shown (No significant differences were observed) *General health status (SF-36 Health Survey)* No data shown (No significant differences were observed)	Constipation: 11/77 (14%) vs 35/82 (42%) Somnolence: 1/77 (1%) vs 33/82 (40%) Nausea: 6/77 (8%) vs 30/82 (36%)
Hanna et al 2008 [23] Europe and Australia **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** To assess the potential benefit of adding oxycodone to gabapentin in painful diabetic neuropathy (PDNP) patients **Treatment duration** 12 weeks	**Participants** *Inclusion*: PDNP ≥3 months Stable dose of gabapentin ≥1 month but still had pain ≥5/10 on NRS HbA_{1c} ≤11% *Exclusion:* Non stated n=338 36% women Mean age: 60 years (SD 10 years)	**Intervention** Gabapentin plus oxycodone ER max 80 mg bid. n=169 *Drop-out rate* n=42 (26%) Mean age: 60 years (SD 11 years) **Comparison** Gabapentin plus placebo bid. n=169 *Drop-out rate* n=37 (22%) Mean age: 61 years (SD 10 years)	**Primary endpoints** *Change in mean BS-11 pain score (0–10); Baseline mean (SD), mean change (SD):* Placebo: 6.5 (1.71), –1.5 (2.38) Oxycodone: 6.4 (1.76), –2.1 (2.61) *Difference vs placebo (95%CI), ITT-analysis:* Oxycodone: –0.55 (0.15, 0.95), p=0.007 vs placebo **Secondary endpoints** *Global assessment of pain relief; patients rating their overall treatment as "good" or "very good":* Placebo: 51/169 (40%) Oxycodone: 72/169 (60%)	**Study withdrawal because of AE** Placebo: 9/169 Oxycodone: 27/169 **Serious adverse events** Data not shown **Three most common AEs (placebo vs oxycodone)** Constipation: 10/167 (6%) vs 45/168 (27%) Nausea: 18/167 (11%) vs 43/168 (26%) Somnolence: 9/167 (5%) vs 37/168 (22%)

Tramadol versus placebo					
Harati et al 1998 [24] USA **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim** To evaluate the efficacy and safety of tramadol in treating the pain of diabetic neuropathy (DNP) **Treatment duration** 6 weeks	**Participants** *Inclusion*: Age ≥18 years Moderate DNP pain on likert pain rating scale HbA_{1c} <14% *Exclusion:* Neuropathy other than diabetic**,** pain more severe than the neuropathic pain, severe depression, CrCl <30 mL/min, clinically significant medical conditions, profound autonomic dysfunction, brittle diabetes, history of narcotic or alcohol abuse, amputations (including toes), open ulcers, or Charcot joint. n=131 41% women Mean age: 59 years (SD not shown)	**Intervention** Tramadol 100–400 mg/day. Mean dose 210 mg (SD 113 mg) n=65 *Drop-out rate* n=22 (34%) Mean age: 59 years (SD not shown) **Comparison** Placebo n=66 *Drop-out rate* n=27 (41%) Mean age: 59 years (SD not shown)	**Primary endpoints** *Change in daily pain intensity score on a 5 point Likert scale (0–4, 4= extreme pain) from baseline to day 42;* *Baseline mean (SD), end-point mean (SD):* Placebo: 2.6 (0.1), 2.2 (0.1) Tramadol: 2.5 (0.1), 1.4 (0.1), p<0.001 vs placebo *Mean difference vs placebo (SD):* Tramadol: –0.7 (not shown) *Mean change not shown* **Secondary endpoints** *Physical functioning (1 out of 6 items in Health and daily activities evaluation), mean score at end-point (SD):* Placebo: 55.1 (4.0) Tramadol: 64.3 (3.8), p=0.02 vs placebo	**Study withdrawal because of AE** Placebo: 1/66 Tramadol: 9/65 **Serious adverse events** Data not shown **Three most common AEs (placebo vs tramadol)** Nausea: 2/66 (3%) vs 15/65 (23%) Constipation: 2/66 (3%) vs 14/65 (22%) Headache: 3/66 (4%) vs 11/65 (17%)
Buprenorphine versus placebo					
Simpson et al 2016 [36] Australia **Risk of bias** Moderate	**Design** Double-blind, placebo controlled, randomized, study **Aim**	**Participants** *Inclusion*: DPN pain ≥6 months DPN pain ≥4/10 on NRS *Exclusion:* Eczema, cutaneous atrophy, dermatological	**Intervention** Flexible dose transdermal buprenorphine 5–40 µg/h n=93 *Drop-out rate*	**Primary endpoints** *Proportion of patients with ≥30% reduction in average pain intensity (NRS 0–10) from baseline to week 12, ITT-analysis*: Placebo: 38/92 (41.3%) Buprenorphine: 46/89 (51.7%), N.S. vs placebo	**Study withdrawal because of AE** Placebo: 6/93 Buprenorphine: 28/93 **Seroius adverse events** Placebo: 4/93 Buprenorphine: 7/93

	To evaluate the efficacy and safety of transdermal buprenorphine in patients with diabetic peripheral neuropathic pain (DPNP) **Treatment duration** 12 weeks	disorder that may preclude correct use of the patch. Hypersensitivity to opioids or patch adhesives. Need for treatment with external heat sources. n=186 33% women Mean age: 63 years (SD 10 years)	n=37 (39.8%) Mean age: 63 years (SD 10 years) **Comparison** Placebo n=93 *Drop-out rate* n=24 (25.8%) Mean age: 63 years (SD 9 years)	**Secondary endpoints** *Proportion of patients with ≥ 50% reduction in average pain intensity (NRS 0–10) from baseline to week 12, ITT-analysis*: Placebo: 19/92 (20.7%) Buprenorphine: 31/89 (34.8%), p<0.05 vs placebo *Change from baseline in HRQOL (SF-36), ITT-analysis:* Non-significant changes vs placebo in all items, with exception of "Bodily pain" which favored buprenorphine (p<0.05) *Change from baseline to week 12, ITT-analysis* PGIC: Buprenorphine better than placebo, p<0.05. CGIC: Buprenorphine vs placebo N.S.	**Three most common AEs** Data not shown
Capsaicin comparisons					
Capsaicin versus vehicle					
Donofrio et al 1991 [13] USA **Risk of bias** Moderate	**Design** Double blind, vehicle controlled, randomized study **Aim** Establish the effects of topically applied capsaicin on daily activities in patients with painful diabetic neuropathy.	**Participants** *Inclusion*: >18<85 years Pain of moderate to severe intensity daily interfering with daily activities or sleep. *Exclusion:* Other skin condition in the area affected by the neuropathy. HbA_{1c} >11%. Other organic disease or disorder not under long-term concrol.	**Intervention** 0.075% capsaicin cream q.i.d n=138 *Drop-out rate* n=38 (28%) Mean age: 60 years (SD not shown) **Comparison** Vehicle cream q.i.d n=139 *Drop-out rate* n=20 (14%)	**Endpoints** *Change in pain, VAS (0–100) from baseline to follow-up; Baseline mean (SD), mean reduction (SD):* Vehicle: 76 (n/a), –21.1 (n/a) Capsaicin: 76 (n/a) –30.5 (n/a), p=0.014 vs vehicle. *Mean difference capsaicin vs vehicle (95% CI):* –9.4 (n/a) *Physicians global evauation (PGE), change in pain status during the study, on a scale -2 – +3 (+3= pain completely gone), % of patients improved:* Vehicle: 53.4%	**Study withdrawal because of AE** Vehicle: 5/139 Capsaicin: 18/138 **Serious adverse events** Not shown **Three most common AEs (Vehicle vs capsaicin)** Burning: 23/139 vs 87/138 Coughing/sneezing:2/139 vs 16/138 Rash/erythema: 4/139 vs 10/138

	Treatment duration 8 weeks	n=277 50% women Mean age: 60 years (SD not shown)	Mean age: 60 years (SD not shown)	Capsaicin: 69.5%, p=0.012. No baseline data shown. *Data from Dailey 1992 et al* [43] *(double publication of data): Functional capacity scale. Interference of pain for 6 items on a scale 1–4 (4=severe interference).* No data extracted due to no average of interference data was shown	
Capsaicin versus placebo					
Simpson et al 2017 [35] USA **Risk of bias** Moderate	**Design** Double blind, placebo controlled, randomized study **Aim** To evaluate the efficacy and safety of capsaicin 8% patch versus placebo patch in painful diabetic peripheral neuropathy (PDPN) of the feet. **Treatment duration** 8 weeks	**Participants** *Inclusion*: Age>18 years HbA_{1c} ≤11% <1% difference in HbA_{1c} between screening and prescreening Pain on NRS ≥4/10 *Exclusion:* DPN pain in the ankles or above. Conditions that might interfere with, the assessment of DPN. Current or previous foot ulcer. Clinically significant cardiovascular disease within 6 months before screening. Significant peripheral vascular disease. Clinically significant foot deformities. Any amputation of lower extremity. Body mass index ≥40.	**Intervention** 8% capsaicin patch n=186 *Drop-out rate* n=9 (5%) Mean age: 64 years (SD 11 years) **Comparison** Placebo patch n=183 *Drop-out rate* n=8 (4%) Mean age: 62 years (SD 11 years)	**Primary endpoint** *Change in mean 24 h pain on NRS (0–10) from baseline to follow-up; Baseline mean (SD), end-point mean (SD), mean change from baseline:* Placebo: 6.4 (1.5), 5.0 (2.2), –1.34 Capsaicin: 6.6 (1.4), 4.9 (2.2), –1.81 *Mean difference vs placebo, re-calculated from percentage values, ITT-analysis (95% CI):* Capsaicin: –0.47 (–0.88 to –0.26), p=0.025 vs placebo **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Placebo: 18.0% Capsaicin: 21.0%, n.s vs placebo *Patient Global Impression of change, percentage of patients reporting ”much” or ”very much” improved:* Placebo: 30.2% Capsaicin: 39.4%, n.s vs placebo *Euro Quality of Life, EQ-5D*	**Study withdrawal because of AE** Not shown **Serious adverse events** Capsaicin: 2 (1.1%) Placebo: 7 (3.8%) **Most common AEs (Placebo vs capsaicin)** Application site TEAE: 8.2% vs 33.9%

		n=369 42% women Mean age: 63 years (SD 11 years)		No notable differences observed at any time point for the change from baseline in EQ-5D total score	
Capsaicin versus standard of care					
Vinik et al 2016 [41] Europe **Risk of bias** Moderate	**Design** Open label, controlled, randomized study **Aim** To evaluate the long-term safety	**Participants** *Inclusion*: Age >18 years HbA_{1c} ≤9 % Stable glycaemic control for ≥6 months prior to screening visit Pain on NRS ≥4/10	**Interventions** 8% capsaicin patch 30 min + SOC n=156 *Drop-out rate* n=24 (15%) Mean age: 61 years (SD 11 years)	**Primary endpoint** *Percentage change from baseline to end of study in the Norfolk QOL-DN total score, mean percentage difference vs SOC, ITT-analysis (95% CI):* Capsaicin 30: –20.9 (–31.7 to –10.1) Capsaicin 60: –26.1 (–36.8 to –15.4) **Secondary endpoints**	**Study withdrawal because of AE** SOC: 3/155 Capsaicin 30: 7/156 Capsaicin 60: 8/157 **Severe adverse events** SOC: 6.5% Capsaicin 30: 12.2% Capsaicin 60: 7.6%

	and tolerability of capsaicin 8% patch versus standard of care (SOC) in painful diabetic peripheral neuropathy (PDPN) **Treatment duration** 52 weeks	*Exclusion:* DPN pain in the ankles or above. Significant pain due to an aetiology other than PDPN. Any amputation of lower extremity. Clinically significant cardiovascular disease. Active signs of skin inflammation around onychomycosis sites. BMI ≥40 kg/m^2. Conditions that might interfere with the assessment of PDPN. CrCl <30 mL/min. Significant peripheral vascular disease. n=468 53% women Mean age: 61 years (SD 10 years)	8% capsaicin patch 60 min + SOC n=157 *Drop-out rate* n=29 (18%) Mean age: 61 years (SD 10 years) **Comparison** SOC alone n=155 *Drop-out rate* n=27 (17%) Mean age: 59 years (SD 10 years)	*Utah Early Neuropathy Scale (UENS). A 4 point reduction represent a clinical significant improvement. Mean difference vs SOC, ITT-analysis (95% CI):* Capsaicin 30: –0.9 (–1.8 to 0.1) Capsaicin 60: –1.7 (–2.7 to –0.8) *Pain score, pain severity index, pain interference index measured on NRS 0–10:* Data not shown *Patient Global Impression of change, percentage of patients reporting "much" or "very much" improved:* Data not shown	**Most common AEs (Capsaicin 30 vs Capsaicin 60)** *SOC frequencies not shown*: Application site pain: 28.2% vs 29.3% Burning sensation: 9.0% vs 9.6% Application site erythema: 7.7% vs 8.9%
Head to head comparisons					
Antidepressants versus anticonvulsants					
Boyle et al 2012 [11] UK **Risk of bias** Moderate	**Design** Double-blind, active treatment controlled, randomized, study **Aim**	**Participants** *Inclusion*: ≥18 years of age and DPN with LANS score >12. *Exclusion:* Cognitive impairment, end-stage disease of a	**Intervention/comparison groups:** Pregabalin 300–600 mg/day n=27 *Drop-out rate* n=8 (30%)	**Primary endpoint** *Subjective pain assessed by the Brief Pain Inventory (BPI*), *ITT-analysis, mean value baseline (SE), mean value after 2 weeks (SE*): *mean value after 4 weeks (SE)*: Pregabalin: 3.1 (0.4), 2.3 (0.4), 2.4 (0.4) Duloxetine: 3.4 (0.5), 2.5 (0.4), 2.2 (0.4) Amitryptiline: 3.5 (0.4), 2.7 (0.4), 2.6 (0.4)	**Study withdrawal because of AE** Pregabalin: 6 (22%) Duloxetine: 3 (11%) Amitryptiline: 1 (4%) **Serious adverse events** Data not shown

	To compare the analgesic efficacy of pregabalin, amitriptyline, and duloxetine, and their effect on polysomnographic sleep, daytime functioning, and quality of life in patients with diabetic polyneuropathy (DPN). **Treatment duration** 4 weeks. Two weeks of low dose followed by two weeks of high dose.	major system, evidence of a recurrent and/or severe hypoglycemic event in the last 3 years, recent cardiac or cerebral ischemic event. n=83 31% women Mean age: 65 years (SD 9 years) Total drop out in all three arms n=18 (22%)	Mean age: 66 years (SD 8 years) Duloxetine 60–120 mg/day n=28 *Drop-out rate* n=5 (18%) Mean age: 65 years (SD 10 years) Amitryptiline 25–50 mg/day n=28 *Drop-out rate* n=5 (18%) Mean age: 65 years (SD 9 years)	**Secondary endpoints** *Quality of life using SF-36, ITT-analysis, mean value baseline (SD), mean value after 4 weeks (SD):* *SF-36 mental component summary:* Pregabalin: 52.8 (9.3), 52.4 (10.0) Duloxetine: 50.2 (9.0), 51.0 (8.8) Amitryptiline 50: 51.1 (7.3), 51.7 (8.0) *SF-36 physical component summary:* Pregabalin: 34.2 (8.2), 31.1 (10.9) Duloxetine: 37.8 (10.0), 36.6 (9.4) Amitryptiline: 39.5 (9.3), 38.5 (8.8) *No statistically significant differences between treatment arms in any outcome.*	**Three most common treatment emergent AEs with pregabalin** Fatigue *no frequency data* Dizziness *no frequency data* Somnolence *no frequency data*
Gilron et al 2009 [18] Canada **Risk of bias** Moderate	**Design** Double-blind, active treatment controlled, randomized, cross-over trial **Aim** To assess the efficacy and tolerability of combined nortriptyline and	**Participants** *Inclusion*: ≥18 years of age and Pain ≥ 4/10 on NRS for ≥6 months ASAT/ALAT ≤120% of upper limit (UL) CrCL ≤150% of UL HbA_{1c} ≤13% *Exclusion:* Patient history of	**Intervention/comparison groups:** Gabapentin. Mean MTD 2433 mg/day (first cycle) n=19 *Drop-out rate* n=4 (21%) Mean age: not shown	**Primary endpoint** *Daily pain intensity (NRS 0–10) per treatment cycle; mean value baseline (95% CI), all groups:* 5.4 (5.0 to 5.8). *For patients with diabetic polyneuropathy, mean value at MTD period in each cycle (95% CI)*: Gabapentin: 3.1 (2.4 to 3.7) Nortriptyline: 2.9 (2.3 to 3.6) Combination: 2.2 (1.5 to 2.8) **Secondary endpoints**	**Study withdrawal because of AE (treatment in first cycle)** Gabapentin: 0/19 Nortriptyline: 2/18 Combination: 3/19 **Serious adverse events** No serious adverse events were recorded for any patients during the trial. **Three most common AEs at MTD**

	gabapentin compared with each drug given alone in patients with diabetic polyneuropathy (DPN, 70%) or postherpetic neuralgia. **Treatment duration** 18 weeks, 6 weeks per treatment cycle. Evaluation of effect at maximum tolerated dose (MTD) period (day 25–31 in each cycle).	neuropathy attributable to other causes. Any major organ system disease. Cardiovascular autonomic neuropathy. Postural hypotension of more than 20 mm Hg. Sedation or ataxia. Symptoms attributable to benign prostatic hypertrophy. Psychiatric or substance abuse disorder. Coexisting disorder causing pain as severe as the neuropathic pain. n=56 38% women Mean age: 65 years (SD 8 years)	Nortriptyline. Mean MTD 60 mg/day (first cycle) n=18 *Drop-out rate* n=3 (17%) Mean age: not shown Gabapentin plus nortriptyline. Mean MTD 2180 and 50 mg/day, respectively (first cycle) n=19 *Drop-out rate* n=4 (21%) Mean age: not shown	*SF-36 Total score (0–100, 100= good health)* *per treatment cycle; mean value baseline (SD), all groups:* 56.8 (2.1) *All grous, mean value at MTD period in each cycle (SD)*: Gabapentin: 65.4 (1.8) Nortriptyline: 63.1 (1.8) Combination: 66.3 (1.8) No statistically significant differences between groups in SF-36 total scores.	*Gabapentin, nortriptyline and combination, respectively:* Dry mouth: 8/46 (17%), 29/46 (58%), 30/50 (60%) Fatigue: 2/46 (4%), 6/46 (12%), 4/50 (8%) Dizziness: 4/46 (9%), 2/46 (4%), 4/50 (8%)
Tanenberg et al 2011 [37] Canada, Germany, USA, Puerto Rico **Risk of bias** Moderate	**Design** Open label, active treatment controlled, randomized, study **Aim** To determine whether duloxetine is noninferior to Pregabalin in the treatment of	**Participants** *Inclusion*: ≥18 years of age and Treated with stable gabapentin dose ≥900 mg/day and DPN pain ≥4/10 on NRS HbA_{1c} ≤12% *Exclusion:* Past or current diagnosis of mania, bipolar disorder, obsessive-compulsive disorder, or	**Intervention/comparison groups:** Duloxetin 60 mg/day n=138 *Drop-out rate* n=51 (37%) Mean age: 61 years (SD 10 years) Pregabalin 300 mg/day n=134	**Primary endpoint** *Change on BPI (0–10) from baseline to week 12 in weekly mean of 24-hour pain, ITT-analysis, mean value baseline (SD), mean change at week 12 (SD)*: Duloxetine: 5.7 (1.7), –2.4 (0.2) Pregabalin: 5.6 (1.9), –1.8 (0.2) *Mean difference vs pregabalin (95% CI), ITT-analysis:* Duloxetine: –0.49 (n.s.) **Secondary endpoints** *Patients who achieved ≥50% reduction in pain scores from baseline to endpoint:* Duloxetine: 50/120 (41.7%)	**Study withdrawal because of AE** Duloxetine: 19.6% Pregabalin: 10.4%, p=0.04 vs duloxetine **Serious adverse events** Duloxetine: 3/138 (2.2%), Pregabalin: 6/134(4.5%) Combination: 5/135 (3.7%) *No significant differences* **Three most common treatment emergent AEs (duloxetine vs pregabalin)**

	pain associated with diabetic peripheral neuropathy (DPN). **Treatment duration** 12 weeks.	posttraumatic stress disorder or were judged to beat risk of suicide. Historical exposure to drugs known to cause neuropathy. n=407 41% women Mean age: 62 years (SD 11 years)	*Drop-out rate* n=38 (28%) Mean age: 62 years (SD 11 years) Combination n=135 *Drop-out rate* n=36 (27%) Mean age: 62 years (SD 11 years)	Pregabalin: 48/127 (37.8%), n.s. vs duloxetine *ClinicalGlobal Impression of Severity* No significant differences *Sheehan Disability Scale* No significant diffeernces	*Nausea:* 19 (13.8%) vs 2 (1.5%), p<0.001 *Fatigue:* 16 (11.6%) vs 7 (5.2%), n.s *Peripheral edema*: 2 (1.4%) vs 18 (13.4%), p<0.001
Shahid et al 2019 [33] Pakistan **Risk of bias** Moderate	**Design** Open label, active treatment controlled, randomized study **Aim** To compare the efficacy of duloxetine with pregabalin in patients with painful diabetic neuropathy in a tertiary care hospital **Treatment duration** 12 weeks.	**Participants** *Inclusion*: Diagnosis of diabetes. History of pain and numbness in hands and Feet. Biothesiometer score of 16 volts or above. *Exclusion:* Diabetes-related foot injuries, ulcers, and/or any other painful wound/lesion. n=173 42% women Mean age: 63 years (SD 7 years)	**Intervention/comparison groups:** Duloxetin 60 mg/day n=87 *Drop-out rate* n=5 (37%) Mean age: not shown Pregabalin 300 mg/day n=86 *Drop-out rate* n=7 (28%) Mean age: not shown	**Primary endpoint** *Change on VAS (0–10) from baseline to week 12. Mean value baseline (SD), mean value at week 12 (SD)*: Duloxetine: 6.8 (0.9), 4.0 (1.1) Pregabalin: 7.0 (1.1), 4.9 (0.8) *Mean difference vs pregabalin (95% CI), ITT-analysis:* Duloxetine: –0.72 (no CI shown), p=0.90	**Study withdrawal because of AE** Duloxetine: 0/87 Pregabalin: 2/86 **Serious adverse events** Data not recorded/shown **Three most common treatment emergent AEs (pregabalin vs duloxetine)** *Somnolence:* 7 (8.1%) vs 1 (1.1%) *Peripheral edema:* 3 (3.4%) vs 0 *Constipation*: 3 (3.4%) vs 6 (6.9%)
Enomoto et al 2018 [14] Japan	**Design** Double blind, active treatment controlled,	**Participants** *Inclusion*:	**Intervention/comparison groups:** Duloxetin 20–60 mg/day. Average	**Primary endpoint** *Change on NRS (0–10) from baseline to week 12. Mean value baseline (SD), mean value at week 12 (SD)*:	**Study withdrawal because of AE** Duloxetine: 10/152 Pregabalin: 12/151

Risk of bias Moderate	randomized study **Aim** To assess the noninferiority of duloxetine compared with pregabalin after 12 weeks of treatment in adult patients with DPNP in Japan **Treatment duration** 12 weeks.	≥20 and <80 years with diabetic polyneuropathy. Duloxetine and Pregabalin naive. score of ≥4 on NRS 0–10. HbA1c ≤9.4% *Exclusion:* Poor glycemic control last 70 days. Psychiatric diseases including MDD. Complications of diseases that could affect the assessment of DPNP. Neuropathic pain suspected to be caused by alcohol. n=303 27% women Mean age: 59 years (SD 9 years)	dose approx. 60 mg/day. n=152 *Drop-out rate* n=15 (10%) Mean age: 59 years (SD 8 years) Pregabalin 150–600 mg/day. Average dose approx. 300 mg/day. n=151 *Drop-out rate* n=21 (14%) Mean age: 60 years (SD 10 years)	Duloxetine: 5.38 (1.079), 3.09 (not shown) Pregabalin: 5.35 (1.129), 2.99 (not shown) *LS mean change (SE) at week 12:* Duloxetine: –2.286 (0.133) Pregabalin: –2.358 (0.133) *Mean difference vs pregabalin (95% CI), ITT-analysis:* Duloxetine: 0.072 (–0.295 to 0.439) **Secondary endpoints** *Euro Quality of Life, EQ-5D* *LS mean change (SE) at week 12:* Duloxetine: 0.1144 (0.0112) Pregabalin: 0.1004 (0.0112) *Mean difference vs pregabalin (95% CI), ITT-analysis:* Duloxetine: 0.0140 (–0.0161 to 0.0441)	**Serious adverse events** Duloxetine: 1/152 Pregabalin: 6/151 **Three most common treatment emergent AEs (pregabalin vs duloxetine)** *Somnolence:* Duloxetine: 18/152 Pregabalin: 22/151 *Dizziness:* Duloxetine: 6/152 Pregabalin: 16/151 *Nausea*: Duloxetine: 11/152 Pregabalin: 5/151
Other head to head comparisons					
Baron et al 2009 [8] Europe **Risk of bias** Moderate	**Design** Randomized study **Aim** To compare efficacy and safety of 5% lidocaine medicated plaster with pregabalin in patients with post-herpetic	**Participants** *Inclusion*: >18 years pain intensity of >4 on NRS HbA_{1c} <11%. Pain for >3 months. *Exclusion:* Venous insufficiency, post-thrombotic syndrome, ulcers on lower extremities, CrCl of <30 mL/min,	**Intervention** 5% lidocaine medicated plaster *DPN participants* n=105 *Drop-out rate* n=6 (5.7%) Mean age: 61 years (SD 10 years) **Comparison** Pregabalin 150 mg/day week 1,	**Primary endpoint** *Response rate* (at least 2 points change or a value of 4 or less on NRS-3 scale) *Response rates in DPN patients; Full analysis set:* Lidocaine patch 68%, pregabalin, 68.3% (n.s.) **Secondary endpoints** *NRS-3 changes in DPN patients from baseline (SD):* Lidocaine patch baseline 6.6 (1.32), change –2,4 (2,07)	**Study withdrawal because of AE** Lidocaine patch 5.8% pregabalin 25.5% **Serious adverse events** Lidocaine patch 1.8% pregabalin 0.7% **Three most common AEs (Lidocaine vs pregabalin)** Dizziness 11.8% vs 0.0% Fatigue 8.5% vs 0.0% Vertigo 7.8% vs 0.0%

	neuralgia (PHN) or DPN **Treatment duration** 4 weeks	concomitant use of adjuvant drugs for neuropathic pain. n=311 48% women Mean age: 62 years (SD 10 years)	300 mg/day week 2. If NRS-3 ≥4, titration to 600 mg/day. *DPN participants* n=105 *Drop-out rate* n=11 (10.4%) Mean age: 61 years (SD 9 years)	Pregabalin baseline 6.7 (1.26), change –2.0 (2.24) *Proportion of patients with 50% reductions from baseline in NRS-3 score* Lidocaine patch n=59 (59.6%) Pregabalin n=53 (56.4%) **EQ-5D estimated health in DPN patients** Lidocaine patch baseline 0.49 (0.29), change 0.13 (0.245) Pregabalin baseline 0.56 (0.249), change 0.06 (0.211)	
Bisbroeck et al 1995 [10] USA and Canada **Risk of bias** Low	**Design** Double blind, double dummy, active treatment controlled randomized study **Aim** To compare the safety and effectiveness of topical capsaicin with oral amitriptyline in diabetic patients with pain associated with sensory polyneuropathies involving the feet.	**Participants** *Inclusion*: ≥21≤ 85 years Painful DPN in feet ≥4 months *Exclusion:* Non stated n=235 44% women Mean age: 60 years (SD not shown)	**Intervention** 0.075% capsaicin cream qid + placebo capsules n=118 *Drop-out rate* n=14 (13%) Mean age: 60 years (SD not shown) **Comparison** Amitriptyline 25-125 mg/day + vehicle cream qid n=117 *Drop-out rate* n= 9 (8%) Mean age: 60 years (SD not shown)	**Primary endpoint** *Physicians global evaluation (PGE) of change in pain severity from –2 (much worse) to +3 (completely gone), patients reporting at least "better".* Capsaicin: 73% Amitriptyline: 73% **Secondary endpoints** *Patient reported change in pain, VAS (0–100) from baseline to follow-up; Baseline mean (SD), mean change (SD):* Capsaicin: 62.1 (n/a), –26.1 (2.9) Amitriptyline: 66.4 (n/a), –29.1 (3.0) *No significant between treatment difference was noted* *QoL, pain interference with daily activities:* No significant between treatment differences were noted.	**Study withdrawal because of AE** Not shown **Serious adverse events** Not shown **Three most common AEs (Capsaicin vs amitriptyline):** Burning: 44% vs 0% Somnolence: 0% vs 46% Dry mouth: 0% vs 33%

	Treatment duration 8 weeks				
Raskin et al 2006 [29] Australia, Canada, South America and Taiwan **Risk of bias** Moderate	**Design** Open label, randomized, study **Aim** Assess the safety and tolerability of duloxetine in patients with diabetic peripheral neuropathic pain (DPNP). Evaluation of efficacy was a secondary objective. **Treatment duration** 28 weeks	**Participants** *Inclusion*: ≥18 years of age DPNP ≥6 months HbA_{1c} ≤12%. *Exclusion:* Previous or current diagnosis of mania, bipolar disorder, psychosis, substance abuse or dependence. Judged to be at risk for suicide. Serious or unstable cardiovascular, hepatic, renal, respiratory, or hematologic illness. Symptomatic peripheral vascular disease or other conditions that would compromise study participation. Elevated ALT, AST or serum creatinine. Renal transplants or renal dialysis. n=449 48% women Mean age: 60 years (SD 11 years)	**Intervention** Duloxetine 60 mg twice daily n=334 *Drop-out rate* n=121 (36.2%) Mean age: 60 years (SD 10 years) **Comparison** Duloxetine 120 mg once daily n=115 *Drop-out rate* n=43 (37.4%) Mean age: 60 years (SD 11 years)	**Primary endpoint** *Percentage of patients who discontinued the study prematurely:* Duloxetine 60 x 2: 36.2% Duloxetine 120 x 1: 37.4% (p=0.823 n.s) *≥1 Treatment-emergent adverse events:* Duloxetine 60 x 2: 96.1% Duloxetine 120 x 1: 92.2% (p=0.129 n.s) **Secondary endpoints** (data reproduced from figure): *BPI-severity (0–10); Mean change from baseline (SD):* Duloxetine 60: –2.8 (2.7) Duloxetine 120: –2.8 (2.7) *Mean difference (95% CI):* Duloxetine 120: 0.0 (not shown) *BPI-interference w function, ranging 0–10 (worst interference); Mean change (SD):* Duloxetine 60: –2.9 (2.7) Duloxetine 120: –3.0 (3.1) *Mean difference (95% CI):* Duloxetine 120: 0.1 (not shown)	**Study withdrawal because of AE** Duloxetine 60 x 2: 20.1% Duloxetine 120 x 1: 27.0% **Serious adverse events** Duloxetine 60 x 2: 7.5% Duloxetine 120 x 1: 8.7% **Three most common AEs** **(**Duloxetine 60 x 2 vs Duloxetine 120): Nausea: 40.4% vs 42.6% Somnolence: 33.5% vs 36.5% Dizziness: 19.5% vs 16.5%

AE = adverse events; **ALT** = alanine aminotransferase; **AST** = aspartate aminotransferase; **BPI** = Brief Pain Inventory; **CI** = confidence interval; **CGIC** = Clinical Global Impression of Change controlled release; **CGI-S** = Clinical Global Impression – Severity; **CGI-I** = Clinical Global Impression – Improvement scale; **DNP** = diabetic

neuropathic pain; **DPNP** = diabetic peripheral neuropathic pain; **ECG** = electrocardiogram; **HbA1c** = Hemoglobin A1c; **HIV** = human immunodeficiency virus; **HRQOL** = Health related quality of life; **ITT** = Intention to treat; **LOCF** = Last observation carried forward; **LS mean** = Least Squares Means; **MITT** = modified intention-to-treat; **n** = number; **N/A** = not applicable; **NRS** = numerical rating scale; **p** = p-value; **PGIC** = Patient Global Impression of Change; **q.i.d**. = Quater in die (four times each day); **QOL-DN** = Quality of Life Questionnaire - Diabetic Neuropathy; **SD** = standard deviation; **SF-36** = The Short Form (36) Health Survey; **SF-MPQ** = Short-form McGill Pain Questionnaire; **vs** = versus; **VAS** = visual analog scale; **VAS-PI** = visual analog scale - pain intensity;

Part III. Pain associated with spinal compression fractures

Systematic reviews

One systematic review was found [44]. This review found no studies that studied the effect or safety of the drugs in our PICO.

Primary studies

We performed a search of primary studies from January 2014 (date when Rzewuska et al performed their search) and onwards but found no relevant studies.

Part IV. NSAIDs and the risk of acute renal failure

Systematic reviews

One systematic review was found [45] that studied the correlation of the treatment with NSAIDs and the risk of acute renal failure in adult patients. Of the studies included in the review, three were considered relevant to our PICO [46-48].

Primary studies

We performed a search of primary studies from 2016 (when Zhang et al performed their search) and found one additional relevant study with low risk of bias [49].

Table 5 Included primary studies on NSAIDs and the risk of acute renal failure.

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group Participants Age	Comparison group Participants Age	Outcome
Henry et al 1997 [47] Australia **Risk of bias** Moderate	**Design** Matched case-control study **Aim** Assess the relationship between recent use of NSAIDs and the presence of functional renal impairment present at the time of hospitalisation with a range of clinical problems **Time to follow-up** Point prevalence of functional renal impairment at time of hospitalisation.	**Participants** *Cases* Consecutive patients admitted acutely to the study hospitals who had serum creatinine levels greater than or equal to 0.15 mmol/L. *Controls* Two controls to each case. Controls were subjects of the same sex and age (to within 5 years) as the cases, admitted to the same hospital, who had normal serum creatinine levels (<0.12 mmol/L) throughout their hospital stay. n=299 45% women Mean age: 76 years old (SD 7 years)	**Intervention group** Cases *Participants* n=110 Mean age: 77 years (SD 7 years) Cases more likely than controls to have a past history of malignancy, hypertension, heart disease, renal/urinary tract disease and gout/hyperuricemia ACE-I use 33.6% in cases and 20.1% in controls. High-ceiling diuretics use 34.6% in cases and 8.5% in controls	**Comparison group** Controls *Participants* n=189 Mean age: 75 years (SD 7 years)	*Consumption of NSAID use (excluding prophylactic aspirin) prior to hospitalisation and elevated serum creatinin level* *Use in the past month:* Cases 43/110 (39.1%), controls 45/189 (23.8%) OR (95% CI) 2.1 (1.3 to 3.7) Adjusted OR (95% CI) 1.8 (0.97 to 3.4) *Use in the past week:* Cases: 38/110 (34.6%) Controls: 40/189 (21.2%) OR (95% CI): 2.0 (1.2 to 3.5) Adjusted OR (95% CI) 1.5 (0.80 to 2.9) *The relationship between the odds of functional renal impairment and the half life of the NSAIDs* Half -life of NSAID — Adjusted OR (95 % CI) No NSAID — 1 ≤4 h — 1.1 (0.5 to 2.5) 4–12 h — 2.1 (0.77 to 5.9) ≥12 h — 2.9 (0.72 to 11.6) OR adjusted for age, a history of gout, a heart disease and renal disease OR not adjusted for differences in use of ACE-I or diuretics.

	Retrospective drug use assessment by structured interview.				
Griffin et al 2000 [46] USA **Risk of bias** Moderate	**Design** Nested case-control study **Aim** Evaluate the risk of important deterioration of renal function due to NSAID use **Time to follow-up** Four years of data collection. Retrospective drug use assessment, by data base prescription fillment, prior to hospitalisation with acute renal failure.	**Participants** Tennessee Medicaid enrollees aged ≥65 years who had been enrolled for at least 1 year *Cases* Hospital admissions for acute renal failure with admission creatinine level of >180 µmol/L (2 mg/dl) and either a >20% increase in creatinine from a baseline value or a >20% decline in creatinine during hospitalization. Exclusion: Patients with end-stage renal disease or hospital-acquired acute renal failure. *Controls* Randomly selected from Tennessee Medicaid database. n=11698 76% women Mean age: not shown	**Intervention group** Cases *Participants* n=1799 Mean age: not shown Cases were older, more often nursing home residents, had greater prevalence of recent hospitalization and greater use of diuretics and ACE-I, compared with controls	**Comparison group** Controls *Participants* n=9899 Mean age: not shown	**Endpoints** *Association between current use of NSAID and hospitalisation due to acute renal failure:* *Current NSAID use:* Cases: 326/1799 (18.1%) Controls: 1119/9899 (11.3%) Adjusted OR (95% CI) 1.58 (1.34 to 1.86) Current use was defined as the individuals NSAID supply included the index date. Nonuse of NSAIDs in the past year was the reference category. OR adjusted for age, gender, ethnicity, nursing home resident, recent hospitalisation, use of loop-diuretics, thiazides, ACE-inhibitors, antibiotics and six other drugs within the past 30 days
Schneider et al 2006 [48] Canada **Risk of bias** Moderate	**Design** Nested case-control study **Aim** To assess the association	**Participants** New NSAID users older than 65 years from the administrative health care databases of Quebec, Canada Exclusion: Kidney transplantation.	**Intervention group** Cases *Participants* n=4228	**Comparison group** Controls *Participants* n=84540	**Endpoints** *Association between use of NSAID and hospitalisation due to acute renal failure:* Current and recent use of NSAID (use in the past month AND the two preceeding months):

	between exposure to NSAIDs and hospitalization for acute renal failure. **Time to follow-up** Four years of data collection. Retrospective drug use assessment, by data base prescription fillment, prior to hospitalisation with acute renal failure	*Cases* Hospital admissions for acute renal failure. *Controls* Up to 20 randomly selected individulas per case from the database, matched to cases on year and month of cohort entry as well as age at cohort entry (±1 year) n=88768.	Mean age: 78 years, SD 6 years. Women: 54% Cases were more likely to be male and to have hypertension, diabetes, and preexisting renal diseases, including previous episodes of acute renal failure. In the year before the index date, cases used more health care services and required a higher number of drugs. Exposure to nephrotoxic drugs and contrast media was also more frequent in cases.	Mean age: 78 years, SD 6 years. Women: 68%	Cases: 149/4228 (3.5%) Controls: 2205/84540 (2.6%) Unadjusted RR (95% CI): 1.83 (1.47 to 2.26) Adjusted RR (95% CI): 1.62 (1.29 to 2.04) Rate ratios (RR) adjusted for age, gender, comorbidity, chronic disease score, charlson index, number of drugs, use of anticoagulants, corticosteroids, psychotropics, thyroid drugs, aspirin, nephrotoxic drugs, exposure to contrast media, health care utilisation. The risk of acute renal failure for all NSAIDs combined was highest within 30 days of treatment initiation (adjusted RR 2.05 (1.61, 2.60) and receded thereafter. The association with acute renal failure within 30 days of therapy initiation was comparable for different NSAIDs with regards to COX-selectivity.
Nash et al 2019 [49] Canada **Risk of bias** Moderate	**Design** Retrospective chort study **Aim** Quantify the 30-day risk of acute kidney injury (AKI) and hyperkalemia in older adults	**Participants** New NSAID users older than 65 years from the administrative health care databases of Ontario, Canada. Exclusion: NSAID prescription in the prior 6 months. Discharge from hospital in the 2 days prior to the index date. eGFR >150mL/min/1.73 m2. End-stage kidney disease.	**Intervention group** Cases after matching *Participants* n=46107 Mean age: 74 years, SD 7 years. Women: 58%	**Comparison group** Controls after matching *Participants* n=46107 Mean age: 74 years, SD 7 years. Women: 58%	**Endpoints** *Association between use of NSAID and 30-day risk of acute kidney injury:* Current and recent use of NSAID (use in the past month AND the two preceeding months): Cases: 380/46107 (0.82%) Controls: 272/ 46107 (0.59%) OR (95% CI): 1.41 (1.20 to 1.65)

	after NSAID initiation **Time to follow-up** Eight years of data collection. Retrospective drug use assessment, by data base prescription fillment, prior to hospital visit with acute kidney injury.	*Cases* Acute kidney injury defined as serum creatinine increase ≥50% or an absolute increase of at least 26.5 mmol/L. *Controls* Matched with cases with similar baseline health n=92214			We calculated a propensity score for the probability of receiving an NSAID prescription using a multivariable logistic regression model that incorporated >150 baseline characteristics (including indications for NSAID use and risk factors for AKI.

ACE-1 = Angiotensin-converting enzyme; **AKI** = Acute kidney injury; **CI** = confidence interval; **COX** = cyklooxygenas; **eGRF** = Estimated glomerular filtration rate; **n** = number; **NSAID** = Non steroidal anti-inflammatory drugs; **OR** = odds ratio; **RR** = relative risk; **SD** = standard deviation

Part V. NSAIDs and the risk of gastrointestinal perforations, bleeds or ulcerations

Systematic reviews

One systematic review, CNT Collaboration 2013 [50], with analysis of individual patient data in 274 RCTs was included. CNT Collaboration 2013 studied the correlation of treatment with NSAIDs and the risk of gastrointestinal perforations, bleeds or ulcerations (PUBs) in adult patients with sub-group analysis of patients younger than 60 years and patients 60 years and older.

Table 6 Table of the included systematic review on treatment with NSAIDs and the risk of PUBs.

Author Year Reference	Study design Follow up	Population	Interventions and controls	Outcome - safety	Risk of bias SBU rating of risk of bias in the review
Coxib and traditional NSAID Trialists' (CNT) Collaboration 2013 [50]	Systematic review and meta-analysis of individual patient data of cardiovascular events and symptomatic upper GI events in 280 trials of NSAIDs versus placebo (124513 participants, 68342 person-years) and 474 trials of one NSAID versus another NSAID (229296 participants, 165456 person-years). This results in a mean follow up period on an	Mean age at randomisation was 61 years, about two thirds were female, and 79% were white. 7% of the patients had a history of upper gastrointestinal peptic ulcer. Overall, the indication for treatment with an NSAID was rheumatoid arthritis or osteoarthritis in around four fifths of participants	Four comparisons was extracted: **Coxibs vs placebo** **tNSAIDs* vs placebo** **Coxibs vs tNSAIDs (naproxen excluded)** **Coxibs vs naproxen** *) traditional NSAIDs eg ibuprofen, diclofenac, naproxen. The predominant daily doses in the includes studies were diclofenac 150 mg, ibuprofen 2400	Rate ratios (RR) for symptomatic upper GI event (perforation, ulcer, obstruction, or bleed) **Coxibs vs placebo** *<60 years* 0.43% vs 0.12% (44/10233 vs 8/6667) RR 2.74 (95% CI, 1.22 to 6.12) *≥60 years* 0.74% vs 0.37% (116/15676 vs 49/13243) RR 1.77 (95% CI, 1.14 to 2.74) RR in <60 years vs ≥60 years χ^2=2.9, p=0.23 **tNSAIDs vs placebo** *<60 years* 0.80% vs 0.12% (154/19250 vs 8/6667) Adj RR 5.03 (95% CI, 2.30 to 10.97)	Study eligibility criteria: *Low* Identification and selection of studies: *Low* Data collection and study appraisal: *Unclear (no formal risk of bias assessment)* Synthesis and findings: *Low* Overall risk of bias: *Low*

	individual level of 7.9 months. Search was performed in january 2009		mg, naproxen 1000 mg, celecoxib 200–400 mg	≥*60 years* 1.24% vs 0.37% (370/29839 vs 49/13243) RR 3.12 (95% CI, 1.98 to 4.91) RR in <60 years vs ≥60 years χ^2=1.9, p=0.17 **Coxibs vs tNSAID (naproxen excluded)** *<60 years* 0.46% vs 0.80% (94/20435 vs 154/19250) RR 0.51 (95% CI, 0.36 to 0.72) ≥*60 years* 0.78% vs 1.24% (245/31410 vs 370/29839) RR 0.58 (95% CI, 0.47 to 0.72) RR in <60 years vs ≥60 years χ^2=1.3, p=0.53 **Coxibs vs naproxen** *<60 years* 1.04% vs 2.20% (77/7404 vs 126/5727) RR 0.51 (95% CI, 0.35 to 0.74) ≥*60 years* 1.35% vs 3.54% (121/8963 vs 276/7797) RR 0.4 (95% CI, 0.3 to 0.52) RR in <60 years vs ≥60 years χ^2=2.1, p=0.36	

CI = confidence interval; **CNT** = Coxib and traditional NSAID; **NSAID** = Non steroidal anti-inflammatory drugs; **tNSAID** = traditional Non steroidal anti-inflammatory drugs; **vs** = versus;

Primary studies

We performed a search of primary studies from 2009 (when CNT Collaboration 2013 performed their search) and onwards. We included three [51-53] additional primary studies.

Table 7 Included primary studies on treatment with NSAIDs and the risk of PUBs.

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group n Age	Comparison group n Age	Outcome
Non-randomized studies					
Bakhriansyah et al 2017 [51] Netherlands **Risk of bias** Moderate	**Design** Register based case-control study **Aim** Assess the risk of gastrointestinal perforation, ulcers, or bleeding (PUB) associated with the use of NSAIDs and selective COX-2 inhibitors, with or without PPIs. **Follow-up time** Study period 1998–2012.	**Participants** *Cases* Patients aged ≥18 years at first hospital admission (index date) with diagnosis of PUB in the GI tract. *Controls* Patients without any diagnoses of GI toxicity. For each case, up to four controls were matched on year of birth and sex. *Exposure to study drugs* Patients were classified as current users when the theoretical end date of the last prescription ended after the index date.	**Intervention group** Subgroup analysis of patients ≥75 years relevant to this review: Cases NSAID users=988 COX-2 users=142 Mean age in subgroup ≥75 years: not shown	**Comparison group** Subgroup analysis of patients ≥75 years relevant to this review: Controls NSAID users=1831 COX-2 users=353 Mean age in subgroup ≥75 years: not shown	**Risk of hospital admission due to a PUB in individuals ≥75 years. Adjusted OR (95% CI).** *NSAID users with PPI vs NSAID users without PPI:* Adj OR: 0.69 (0.47 to 1.03) *COX-2 users without PPI vs NSAID users without PPI:* Adj OR: 0.88 (0.64 to 1.22) *NSAID users without PPI vs COX-2 users with PPI:* Adj OR: 0.71 (0.53 to 0.97) NSAID users with PPI: *Individuals aged ≥75 years vs individuals <75 years:* Adj interaction OR: 0.79 (0.64 to 0.99) COX-2 users without PPI:

	Individual retrospective follow up from index date to date of last prescription for study drugs.	n=2634 cases and 5074 controls were users of NSAIDs or COX-2 inhibitors (with or without PPIs) at the index date 60% women Mean age: 69 years old (SD 15 years)			*Individuals aged ≥75 years vs individuals <75 years:* Adj interaction OR: 1.22 (1.01 to 1.47) COX-2 users with PPI: *Individuals aged ≥75 years vs individuals <75 years:* Adj interaction OR: 0.84 (0.7 to 1.00) *Adjusted OR for sex, concomitant drugs (acid-lowering drugs, vitamin K antagonists, platelet aggregation inhibitors, glucocorticoids, and selective serotonin receptor inhibitors), and a history of drug use (conventional NSAID, selective COX-2 inhibitors, and acid-lowering drugs).*
Chang et al 2011 [52] Taiwan **Risk of bias** Moderate	**Design** Case cross-over study **Aim** Evaluate the risks of upper (GI) adverse events of coxibs and nonselective NSAIDs in the general population of Taiwan **Follow-up time** Study period 2006.	**Participants** *Cases* Patients aged ≥20 years who were hospitalized for upper GI adverse events (peptic ulcer, bleeding, gastritis or duodenitis) *Exposure to study drugs* Outpatient pharmacy prescription database was searched for individual NSAID use during the case and control periods. n=40635 patients hospitalized for upper GI adverse events were included. 37% women	**Intervention group** Subgroup analysis of patients ≥65 years relevant to this review: The case period was defined as 1–30 days before the date of hospitalization Neither number of patients, nor the characteristics of these, were shown for this subgroup.	**Comparison group** Subgroup analysis of patients ≥65 years relevant to this review: The control period was defined as 31–60 days before the date of hospitalization Neither number of patients, nor the characteristics of these, were shown for this subgroup.	**Risk of hospital admission due to upper GI events** (peptic ulcer, bleeding, gastritis or duodenitis) **in individuals ≥65 years. Adjusted OR (95% CI).** Celecoxib users: *Case period vs control period* Adj OR 65–79 years: 1.97 (1.53 to 2.54) Adj OR ≥80 years: 1.63 (1.18 to 2.24) Oral nonselective NSAIDs *Case period vs control period* Adj OR 65–79 years: 3.42 (3.14 to 3.72) Adj OR ≥80 years: 4.35 (3.85 to 4.93) Adjusted OR for important potential time-varying confounding variables including selective serotonin reuptake inhibitors, other antidepressants, calcium channel blockers, nitrates, systemic corticosteroids, low-dose

	For each patient, the case period was defined as 1–30 days and the control period as 31–60 days before the date of hospitalization	Mean age: 61 years old (SD 18 years)			aspirin, proton pump inhibitors, histamine 2 receptor blockers, and sucralfate.
Randomized studies					
Dahlberg et al 2009 [53] Scandinavia **Risk of bias** Moderate	**Design** Double-blind, active and placebo controlled, randomized, prospective study **Aim** To compare the adverse event-related discontinuation rate with celecoxib vs. diclofenac associated with knee or hip osteoarthritis in elderly patients **Time to follow-up** 52 weeks	**Participants** *Inclusion*: ≥60 years of age OA in hip or knee Functional capacity classification of I–III according to ACR criteria *Exclusion:* History of NSAID-induced peptic ulcer, two or more episodes of peptic ulceration or GI bleeding, active GI disease or any type of malignancy, diagnos of an oesophageal, gastric, or duodenal ulcer within 30 days of randomization, history of renal or hepatic disease, clinically significant congestive heart failure, anticipated need for digoxin/digitoxin, requirement of corticosteroid or hyaluronic	**Intervention** Celecoxib 200 mg q.d. *Participants* n=458 *Drop-out rate* n=181 (39.5%) Mean age: 71 years (SD 7 years)	**Comparison** Diclofenac 50 mg b.i.d. *Participants* n=458 *Drop-out rate* n=185 (40.3%) Mean age: 71 years (SD 7 years)	**Primary endpoints** Incidence of discontinuation of study drug due to AEs: Celecoxib: 124/458 (27.1%) Diclofenac:142/458 (31.0%) *Celecoxib vs diclofenac (9 % CI):* –3.9% (–9.8 to 1.9), p=0.22 **Secondary endpoints** Time to discontinuation of study medication, log rank test Kaplan-Meier survival: p=0.23 Hazard ratio (95% CI) diclofenac vs celecoxib: 1.16 (0.91 to 1.47)

		acid within 30 days of randomization n=925 68.5% women Mean age: 71 years old (SD 7 years)			

AE = adverse events; **ACR** = American College of Radiology; **b.i.d.** = bis in diē. (twice a day); **CI** = confidence interval; **COX** = cyklooxygenas; **GI** = Gastrointestinal; **n** = number; **NSAID** = Non steroidal anti-inflammatory drugs; **OR** = odds ratio; **p** = p-value; **PPI** = proton pump inhibitor; **PUB** = peptic ulcer bleeding; **q.d** = quaque die (once a day); **SD** = standard deviation

Part VI. Opioids and the risk of falls

Systematic reviews

One systematic review, Seppala 2018 [54], was included. Seppala et al included 30 studies that investigated the correlation of treatment with opioids and the risk of falls. Eight of them were suitable for meta-analysis.

Table 8 Included systematic review on treatment with opioids and the risk of falls.

Author Year Reference	Study design Follow up	Population	Interventions and controls	Outcome – safety	Risk of bias SBU rating of risk of bias in the review
Seppala et al 2018 [54]	Systematic review and meta-analysis of 281 studies (randomized and non-randomized studies) that investigated nonpsychotropic and noncardiovascul	All settings (population-based, community dwellers, hospital wards, long-term care institutions, and outpatient clinics). Participants needed to be at least 60 years old, or the mean age of the participants had to	Use, as compared with non-use, of index drug.	The risk of falling with opioid use vs non-use in 8 non-randomized studies (total 366036 participants) with individuals 65 years or older that presented adjusted odd ratios: *Opioid use vs non-use (95% CI):* Adjusted OR 1.6 (1.35 to 1.91)	Study eligibility criteria: *Low* Identification and selection of studies: *Low* Data collection and study appraisal: *Low* Synthesis and findings: *Unclear (no information on sensitivity analysis or robustness of findings)*

	ar medications as risk factors for falls. Meta-analysis was performed using the generic inverse variance method, pooling unadjusted and adjusted odds ratio (OR) estimates separately.	be 70 years or more, or the results of the older age group needed to be reported separately.			Overall risk of bias: *Low*

CI = confidence interval; **OR** = odds ratio

Primary studies

We performed a search of primary studies from 2016 (when Seppala et al performed their search) and onwards. We included five [55-59] additional primary studies.

Table 9 Included primary studies on treatment with opioids and the risk of falls.

Author Year Reference Country Risk of bias	Design Aim Time to follow-up	Participants Women/men Age	Intervention group Participants Age	Comparison group Participants Age	Outcome
Daoust et al 2018 [55] Canada **Risk of bias** Moderate	**Design** Retrospective cohort study **Aim** To examine the association between recent opioid use and the risk, as well	**Participants** Patients aged ≥65 years who were admitted for injury in any adult trauma centres in the province of Quebec. Information on medical consultations and medications were extracted from two governmental population databases.	**Cohort** Patients who were admitted for injury sustained from a fall n=3041 78.1% women Mean age: not shown	**Control** Patients who were admitted for injury sustained from another mechanism n=85 % women: not shown	**Risk of falling with opioid use** Opioid users were 2.4 times (95% CI, 1.9 to 3.0) more likely to have suffered a fall rather than an injury via another mechanism

	as the clinical outcomes, of fall-related injuries in a large trauma population of older adults **Follow-up time** Study period 2004–2014. Individual retrospective follow up 2 weeks preceding the trauma in patients who sustained a fall	Patients with no recorded mechanism of their injury were excluded. n=67929 69% women Mean age: 81 years old (SD 8 years)		Mean age: not shown	
Grewal et al 2018 [56] Canada **Risk of bias** Moderate	**Design** Retrospective cohort study **Aim** To examine the risk of fractures in discharged Emergency Deparment (ED) patients with peripheral vertigo who were being prescribed opioids during the same time period	**Participants** Patients aged ≥65 years with index diagnos in an administrative database that contains abstracted data on all ED patient visits in the province of Ontario. Drug use was examined in the Ontario drug benefit database. Patients were excluded if they were admitted to the hospital from the ED, were from a long-term care facility/nursing home, died in the ED, or were seen in an ED that was not open 24 hours a day 68% women	**Cohort** Patients who were discharged from ED with diagnosis of peripheral vertigo 1676 (12,9%) had access to a filled opioid prescription n=13012 62% women Mean age: 76 years old (SD 7 years)	**Control group** Patients who were discharged from ED with diagnosis of urinary tract infection (UTI) 18969 (24.7%) had access to a filled opioid prescription n=76885 69% women Mean age: 78 years old (SD 8 years)	**Risk of fractures with opioid use** *Vertigo patients, adjusted hazard ratios (95% CI):* Opioid users vs non opioid users, 3.59 (1.97 to 6.13). *UTI patients, adjusted hazard ratios (95% CI):* Opioid users vs non opioid users, 1.68 (1.43 to 1.97).

	Follow-up time Study period 2006–2011. Individual retrospective opioid use 90 days preceding the ED visit/ Hospitalization for a fracture	Mean age: 78 years old (SD 8 years)			
Hunnicut et al 2018 [57] USA **Risk of bias** Moderate	**Design** Retrospective cohort study **Aim** To estimate the comparative safety of initiating commonly used opioids among older, long-stay United States nursing home residents with fracture hospitalizations **Follow-up time** Study period 2011–2013. Incident opioid users were followed for 180 days.	**Participants** Medicare beneficiaries aged ≥65 who were long-stay nursing home residents (≥120 consecutive days in facility) and who initiated short-acting oral formulations of hydrocodone, oxycodone, or tramadol. Initiation was defined as being prescribed a study drug with no prior prescriptions of any opioid in the 120 days before the initiating fill date. *Exclusion criteria:* Recently hospitalized or received skilled nursing facility care. Treatment episodes were the resident was comatose, had cancer, received hospice care, or had missing data on potential confounders. Those initiating unusually high opioid doses.	**Cohorts** *Oxycodone:* 14373 treatment episodes 72% women Mean age: 84 years (SD 9 years) *Hydrocodone:* 69182 treatment episodes 75% women Mean age: 84 years (SD 9 years) *Tramadol:* 50877 treatment episodes 79% women Mean age: 86 years (SD 8 years)		**Risk of fractures with different opioids** *Incidence of fracture hospitalizations per 100 person-years (95% CI):* Oxycodone: 9.4 (7.5 to 11.7) Hydrocodone: 7.9 (7.1 to 8.8) Tramadol: 5.0 (4.3 to 5.7) *Adjusted hazard ratio (95% CI):* Oxycodone vs hydrocodone: 1.08 (0.79 to 1.48)

		n=110862 residents contributed to 134432 treatment episodes. 76% women Mean age: 85 years (SD 9 years)			
Krebs et al 2016 [58] USA **Risk of bias** Moderate	**Design** Prospective cohort study **Aim** To examine longitudinal relationships between opioid use and falls, clinical fractures, and changes in physical performance **Follow-up time** Participants completed baseline visits from 2000 to 2002 and were followed for 9.1 (SD 4.0) years.	**Participants** Community dwelling men ≥65 years of age included in the Osteoporotic Fractures in Men Study (MrOS), a large prospective longitudinal cohort study. MrOS enrolled 5994. The present study included 2902 participants with back, hip, or knee pain most or all of the time at baseline. Medication exposure and covariate data were collected from participants at baseline and two follow-up visits. Opioid use was defined as participant-reported daily or near-daily use of any opioid analgesic. 0% women Mean age: 74 years old (SD 6 years)	**Cohort** Patients with opioid use n=129 0% women Mean age: 75 years old (SD 6 years)	**Control group** Patients without opioid use n=2603 0% women Mean age: 74 years old (SD 6 years)	**Risk of falls and fractures with opioid use** *Adjusted relative risk of falls (95% CI):* Opioid users vs non opioid users: 1.10 (0.99 to 1.24) *Adjusted hazard ratio of any clinical fracture (95% CI):* Opioid users vs non opioid users: 1.13 (0.94 to 1.36) *Adjusted hazard ratio of hip fracture (95% CI):* Opioid users vs non opioid users: 1.64 (0.97 to 2.79)
Taipale et al 2018 [59] Finland	**Design** Matched cohort study **Aim**	**Participants** All community dwelling persons who were diagnosed with AD between 2005 and	**Cohort** Incident opioid users n=4750	**Matched cohort** Opioid non-users n=4750	**Risk of hip fracture** *Adjusted HR (95% CI), Incident opioid use vs non-use*:

Risk of bias Moderate	To investigate whether incident opioid use is associated with an increased risk of hip fractures among community-dwelling persons with Alzheimer disease (AD) and to assess the association in terms of duration of use and opioid strength. **Study period** Between 2005 and 2011	2011 in Finland. Incident opioid users were matched with opioid nonusers. Matching was based on age, sex, and time since AD diagnosis at opioid initiation. Data on drug use and hip fractures were retrieved from nationwide registers. Incident opioid users were identified with a 1-year washout. n=9500 67% women Mean age: 83 years old (SD 7 years)	67% women Mean age: 83 years old (SD 7 years)	67% women Mean age: 83 years old (SD 7 years)	According to duration of use: All follow-up: 1.96 (1.27 to 3.02) 1–60 days: 2.37 (1.04 to 5.41) 61–180 days: 1.79 (0.82 to 3.89) 181–365 days: 1.43 (0.61 to 3.37) >365 days: 2.59 (0.92 to 7.28) According to opioid strength: Weak opioid: 1.75 (0.91 to 3.35) Buprenorphine: 2.10 (1.41 to 3.13) Strong opioid: 2.89 (1.32 to 6.32)

CI = confidence interval; **HR** = hazard ratio; **n** = number; **SD** = standard deviation; vs = versus

Part VII – Experiences of encounters between elderly with pain and health care staff

Primary studies

We included 20 relevant primary studies [60-79].

Table 10 Included primary studies on experiences of encounters between elderly with pain and health care staff.

Author Year Ref Country	Aim	Theory or approach Competence of researchers	Setting, recruitment	Participants	Data collection	Data analysis
Baumann et al 2007 [60] France	Explore expectations of the patient-physician relationship to improve the health care provision for persons with OA	No specific theory or approach Two teams of senior academic sociologists and rheumatologists	10 pharmacies in 10 towns in 10 regions, randomly selected. The first 10 customers that purchased medication for OA were approached	n=96 elderly (81% women) Mean age: 65 years (42–89) Duration of disease: 18 years	10 focus groups with 10 participants each. Moderated by 2 teams with 2 interviewers each. Two hours duration	Not described
Berglund et al 2015 [61] Sweden	Describe HCP:s experiences of providing health care to older adults with long-term musculoskeletal pain at home to gain a deep understanding	Reflective lifeworld research (RLR), based on phenomenology Three researchers, speciality not stated	Integrated social services and medical care at home in three communities in the western region of Sweden Nomination by the heads of the health care units	n=10 registered HCP (5 nurses, 3 physiotherapists, 2 occupational therapists) (8 women) Mean age: 52 years (range 35 to 56 years) Experience of working with elderly with pain: mean 19 years (range 5 to 34 years)	Interviews grounded in the RLR approach	Grounded in the RLR approach and directed towards discovering patterns and nuances of qualitative meanings.

Blomqvist et al 2002 [63] Sweden	Explore sense of self, sense of pain, daily living with pain, sense of others and ways of handling pain	Construction of a typology One junior and one senior registered nurse	People receiving care from nursing auxiliaries in their homes or in sheltered accommodation. Invitation letters to individuals above 75 years and with persistent pain who were able to be interviewed were identified by staff	n=90 (73% women) Mean age: 85 years (SD 6.0) Duration of pain: 8 years (3–20 years)	Interviews with open and structured questions, lasting 45–90 minutes. Performed in the respondents' homes	Development of a typology based on the literature Manifest content analysis for ways of handling the pain
Blomquist 2003 [62] Sweden	Explore nursing and paramedical staff perceptions of elderly with persistent pain and the day-to-day management of pain	Not reported One senior researcher and one co-investigator	Nursing auxiliaries (NA) in their homes or in sheltered accommodation in a municipality of southern Sweden All RNs and P/OTs were included	n=52 (33 NA, 10 RN, P/OT) (46 women) Mean age: 46 years >10 years' experience of care of elderly with persistent pain: n=47	Interviews with at strategy to obtain concrete descriptions of management of all elderly whom the staff had met the previous week (n=150). The interviews lasted between 20 and 45 minutes	Manifest content analysis and construction of typology for types of elderly in pain
Bower et al 2006 [64] Canada	Explore factors that influence patients to choose coxibs	Grounded theory Four researchers in family medicine	Community, two urban areas Random selection from a sample that had completed a quantitative survey	n=16	Interviews in the homes of the participants, conducted by the principal investigator. Data collection continued until perceived saturation	Consistent with grounded theory

Carmona-Terés et al 2017 [65] Spain	Explore patient related factors that can affect the implementation of an intervention for knee OA Explore perceptions and experiences of living with knee OA	Lazarus stress model Eight researchers in primary care research, rheumatology and psychology; one specialised in interviewing	Primary care Recruitment by GPs at each of 4 PHCCs Theoretical sampling based on a priori defined patient characteristics	n=10 (70% women) with mild – moderate knee OA. Age: 60–85 years Duration of knee OA: 1–20 years	Semi-structured interviews conducted by the first author at the PHCCs and lasting 30–60 minutes. Observational field notes	Content thematic analysis
Clarke 2014 [66] UK	Explore experiences of interacting with health professionals	No specific theory or approach Seven university researchers, specialised in nursing, medicine, occupational therapy and one GP	Community Purposive sampling through media advertising	n=23 (70% women) with self-reported chronic musculoskeletal pain Median age: 73 years (66–89 years)	Two in-depth interviews with each participant: n=14 One group interview: n=7 One individual interview: n=2 Interviews lasted for one hour	Framework analysis
Davis et al 2002 [67] USA	Explore barriers to pain management	Grounded theory Three registered nurses: one professor, one doctoral student and one practitioner	Community, respondents with arthritis that lived in own homes or in retirement settings and were functioning independently Recruitment via ads and flyers	n=57 (79% women) Mean age: 79 years (SD 6.88) Arthritis: OA (63.2%), osteoporosis (33.3%), RA (29.8%), tendinitis or bursitis (19.3%)	8 focus groups (group size 5 to 9).	Open coding of data followed by axial and selective coding
Erwin et al 2018 [68] UK	Explore expectations on community-based HP to improve	Partly phenomenology	Community Recruitment through	n=25 (64% women) Age: 28 to 84 years	Four focus groups, between 4 and 8 participants. Duration: 1 hour	Deductive thematic analysis

	care of people with arthritis	Seven researchers, senior and junior with various backgrounds	advertisements and flyers to local support groups, GP surgeries and local newspapers	Arthritis: IA or OA	The approach was phenomenological	
Gudmansdottir et al 2009 [69] Iceland	Explore the lived experiences of elderly with chronic pain	Interpretive phenomenology according to the Vancouver school One professor and one junior researcher in nursing research	Nursing homes Purposeful sampling. Recruitment via head nurses	n=12 (42% women) Mean age: 86 years (74–97 years)	Open interviews, two per participant, lasting for 10–44 minutes (mean 46 minutes for both interviews)	According to the Vancouver School
Higgins 2005 [70] Australia	Explore the lived experience of being old with chronic pain	Phenomenology according to Merleau-Ponty One senior researcher in nursing sciences	Three nursing homes Recruitment via the nursing unit manager	n=13 (77% women) Age: 78–97 years Pain mostly was related to arthritis and ageing pathology like OA and vascular disease	In-depth interviews and observational field notes. Interviews lasted <1 hour and most participants were interviewed several times	Phenomenologic reduction
Hill et al 2010 [71] UK	Explore experiences of the treatment and management of hand OA	No specific theory or approach Three researchers from the Arthritis Research UK National Primary Care Centre	Primary and secondary care Purposive sampling from a longitudinal study	n=17 (82% women) Mean age: 64.9 years (51–84 years) Duration of hand OA: 1–30 years	Two focus groups in primary care and two in secondary care	Inductive thematic analysis with the constant comparison method
Kaasalainen 2010 [72] Canada	Explore barriers to pain management with qualitative and quantitative methods (only qualitative reported here)	Not reported Twelve researchers with broad expertise	Two LTC homes in the Ontario area Purposive sampling, recruited by the advance	n=53; 70% of HCP women Mean age: 49 years	Focus groups: one at each site with RNs, one with RPNs; one at each site with UCPs; and one with physicians from both sites	Content analysis for the interviews Analysis according to Duggleby [80] and Stevens [81] for the focus groups

			practice nurse at each site		Individual interviews (30 minutes) with 2 pharmacists, 2 PTs, 2 administrators, 2 directors and 2 residents	
McHugh et al 2006 [73] UK	Explore patients' experiences of management and care in order to improve care	No specific theory or approach Three senior researchers in nursing or rheumatic disease epidemiology	Primary care, persons with end-stage lower limb OA, waiting for JR Purposeful sampling from 105 randomly selected patients who were part of a longitudinal study	n=21 (80% women) Mean age: 65 years (48–86 years) Duration of OA: 7 months to 38 years	Semi-structured individual interviews in the homes of the respondents. Duration on average 45 minutes	Framework analysis
Park et al 2015 [74] South Korea	Explore barriers influencing chronic pain management of nurses providing home-visiting care for low-income elderly	No specific theory or approach Three senior researchers in nursing	Home-visiting care from four PHC in one area	n=23 Median age: 46 years (range 32–53 years) Experience: median 8 (range 1–23 years) for RN median 5.7 years (range 3–13 years) for community nurses	4 focus groups with 5–6 participants per group which lasted around 1.5 hours.	Inductive thematic analysis
Paskins et al 2015 [75] UK	Increase understanding of the consultation in order to improve the care and management of OA	No specific theory or approach The team included competencies in qualitative research, rheumatology, sociology and	Seven GP surgeries Invitation to members of local research networks. Consecutive patients >45 years	n_1=17 patients (68% women) Median age: 69 years (49 to 84 years)	Video-recorded real-life consultations and interviews after the consultation. Interviews were conducted by one investigator	Constant comparison

		epidemiology and primary care. Both senior and junior researchers	where the GP used OA or arthritis diagnostically or findings supported the diagnosis	n_2=13 GPs (3 women) Experience as GP: median 17 years (range 3 to 29)		
Rosemann et al 2006 [76] Germany	Identify health care needs of patients with OA and barriers to improvements in primary care management of OA	No specific theory or approach Six senior researchers with expertise in primary care and implementation science; two had experience from qualitative research	Unclear number of GP surgeries Unclear method for selecting GPs and nurses. Random selection of patients from the GPs computer files	n_1=20 patients (12 women) Mean age: 56 years (40–78 years) n_2=20 GPs (4 women) Mean age: 43, 5 (33–57) Years working experience: mean 11 (8–19 years) n_3=20 practice nurses (20 women) Mean age: 41 (29–56) Years working experience: 22 (13-–35)	Individual, semi-structured interviews	Unclear method, but data was analysed with Atlas.ti software and all steps in the analysis was conducted independently by four researchers followed by consensus.
Spitaels et al 2016 [77] Belgium	Explore perceived barriers and facilitators in current care of knee OA in order to improve guideline adherence	Framework for implementation by Grol and Wensing The team included one expert in qualitative research	GP practices in a region and advertisement in the national federation for patients with rheumatic diseases	n=11 (64% women) Mean age: 66.2 years (40–90 years)	Face-to-face interviews in the participants' homes, guided by the Belgian set of quality indicators	Directed content analysis

					Median duration: 52 minutes (28–88 minutes)	
Svensson et al 2016 [78] Sweden	Explore the experience of women living with VCF	Phenomenological hermeneutic approach Five researchers	One outpatient clinic in Gothenburg Purposeful selection of women one or several osteoporotic VCFs.	n=10 Mean age: 80 years	Face-toface interviews in the participants' homes, lasting between 50 and 75 minutes. Memos and field notes were taken to capture body language and emotions	Based on the theoretical approach where the interpretation was based on a dialectic dialogue between the naïve understanding and the structural analysis. Conducted by two researchers
Yates et al 1995 [79] Australia	Provide an in-depth account of the beliefs, attitudes and perceptions to pain of elderly.	No specific theory or approach Three senior researchers in nursing	Five residential care settings in Brisbane Residents able to participate were identified by the directors of nursing	n=42 (35 women) Age: 65 years or older	10 focus group interviews (4-9 participants per group), lasting around 1 hour	According to Marshall and Rossman 1989; independent coding followed by meetings to agree upon codes and categories

GP = general practitioner; **HCP** = Health care professionals; **HP** = Health Practitioners; **IA** = Inflammatory arthritis; **JR** = joint replacement; **LTC** = long-term care; **n** = number; **OA** = osteoarthritis; **PHC** = primary health care; **PHCC** = primary health care centre; **P/OT** = physiotherapists and occupational therapists; **RA** = rheumatoid arthritis; **RN** = Registered Nurses; **RPN** = Registered Practical Nurses; **SD** = standars deviation; **UCP** = Unlicensed Care Providers; **VCF** = Vertebral compression fractures

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Bilaga 4. Evidenstabeller, resultat från studier med kvantitativ metodik

Innehållsförteckning

Del I: Läkemedelsbehandling av artros hos äldre

Resultat identifierade i systematiska översikter

Fem systematiska översikter inkluderades. Sökning för primärstudier utfördes för respektive läkemedelsgrupp för perioden efter respektive översikts litteratursökning gjordes till december 2019.

Tabell 1.1 Inkluderade systematiska översikter inom området artros.

	Knä– och/eller höftartros Författare, år, referens	Tidpunkt då litteratursökning utfördes
Paracetamol	Leopoldini et al, 2019, [1]	Oktober 2017
Orala NSAID–preparat	Osani et al, 2019, [2]	Maj 2018
Topikala NSAID–preparat	Derry et al, 2016, [3]	Februari 2016
Opioids exklusive tramadol	da Costa et al, 2014, [4]	Augusti 2012
Tramadol	Toupin April et al, 2019, [5]	Februari 2018

Tabell 1.2 Paracetamol. Data i tabellen kommer från den systematiska översikten av Leopoldini och medarbetare [1].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Paracetamol 2–4 g jämfört med placebo				
Förändring i smärta på VAS (0–100 mm)	2 355 individer, 7 RCT	Paracetamol minskar smärta med i genomsnitt 3,2 mm (95 % KI, 1,0 till 5,4) mer än placebo	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[1] effekt av paracetamol vad gäller smärta	Överförbarhet[2]: –1
Förändring i funktion på en standardiserad WOMAC–skala 0–100	2 354 individer, 7 RCT	Paracetamol förbättrar funktion med i genomsnitt 2,9 skalsteg (95 % KI, 1,0 till 4,9) mer än placebo	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[3] effekt av paracetamol vad gäller funktion	Överförbarhet[2]: –1

Frekvens av biverkningar	3 252 individer, 8 RCT	Paracetamol 32,5 %, placebo 32,8 %. Riskkvot 1,01 (95% KI, 0,92 till 1,11)	⊕⊕⊕ Måttlig tillförlitlighet för en biverkningsfrekvens som är *jämförbar*[4] med placebo	Överförbarhet[2]: –1
Andel patienter som avbryter behandling p.g.a. biverkningar	3 023 individer, 7 RCT	Paracetamol 7,7 %, placebo 6,5 %. Riskkvot 1,19 (95 % KI, 0,91 till 1,55)	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[5]: –2
Frekvens av allvarliga biverkningar	3 209 individer, 6 RCT	Paracetamol 1,6 %, placebo 1,1 %. Riskkvot 1,36 (95 % KI, 0,73 till 2,53)	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[5]: –2
Frekvens av förhöjda värden av leverenzymer	1 237 individer, 3 RCT	Paracetamol 7,0 %, placebo 1,8 %. Riskkvot 3,79 (95 % KI, 1,94 till 7,39)	⊕⊕ Låg tillförlitlighet för *stor*[6] riskökning för förhöjda värden av leverenzymer	Överförbarhet[2]: –1 Precision[7]: –1

1) En förbättring med 3,2 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt. Förekommande gränser för klinisk relevans (MCID, minimally clinicirkal important difference) vad gäller smärta vid artros i litteraturen ligger mellan 8 och 30 skalstegs skillnad jämfört med placebo på en skala 0–100 [6,7].
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
3) En förbättring med 2,9 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt.
4) På grund av ett stort antal händelser, en riskkvot mycket nära ett samt ett snävt och symmetriskt konfidensintervall bedömer vi dessa biverkningsfrekvenser som *jämförbara*.
5) Bristande precision: Avdrag med två steg p.g.a. att riskkvotens konfidensintervall överlappar 1 och är dessutom brett i relation till punktestimatets storlek.
6) En riskkvot på 3,8 bedömer vi som en *stor* riskökning.
7) Bristande precision: Avdrag med ett steg p.g.a. brett konfidensintervall i relation till punktestimatets storlek.

Tabell 1.3 Perorala NSAID–preparat. Data i tabellen kommer från den systematiska översikten av Osani och medarbetare [2].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Perorala NSAIDs jämfört med placebo				
Förändring i smärta på en standardiserad VAS 0–100 mm	6 341 individer, 13 RCT	SMD –0,36 (95 % KI, –0,43 till 0,30), vilket motsvarar en minskning med 7 mm (95 % KI, 6 till 9)[1] mer än placebo	⊕⊕ Låg tillförlitlighet för en *mycket liten*[2] effekt av NSAID vad gäller smärta	Överförbarhet[3]: –1 Risk för bias[4]: –1
Förändring i funktion på en standardiserad WOMAC–skala 0–100	2 492 individer, 7 RCT	SMD –0,37 (95 % KI, –0,45 till –0,29), vilket motsvarar en minskning med NSAID på 8 skalsteg (95 % KI, 6 till 9)[1] mer än placebo	⊕⊕ Låg tillförlitlighet för en *mycket liten*[5] effekt av NSAID vad gäller funktion	Överförbarhet[3]: –1 Risk för bias[4]: –1
Frekvens av behandlingsrelaterade biverkningar	9 548 individer, 24 RCT	Riskkvot: 1,21 (95 % KI, 1,04 till 1,40)	⊕⊕ Låg tillförlitlighet för en *liten*[6] riskökning för biverkningar med NSAID	Överförbarhet[3]: –1 Risk för bias[4]: –1
Andel patienter som avbryter behandling p.g.a. biverkningar	22 993 individer, 60 RCT	Riskkvot 1,16 (95 % KI, 1,02 till 1,32)	⊕⊕ Låg tillförlitlighet för en *liten*[6] riskökning för behandlings–avbrott p.g.a. biverkningar med NSAID	Överförbarhet[1]: –1 Risk för bias[4]: –1
Frekvens av allvarliga biverkningar	17 278 individer, 40 RCT	Riskkvot: 0,90 (95 % KI, 0,68 till 1,19)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[4]: –1 Precision[7]: –1

1) Medelvärdesskillnaden på en skala (e.g. 0–100 mm, 0–1700 poäng) beräknades genom att multiplicera SMD med standardavvikelsen i placebogruppen vid baslinje, som föreslaget i Cochrane Handbook for Systematic Reviews of Interventions [8].

2) En förbättring med 7 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt. Förekommande gränser för klinisk relevans (MCID, minimally clinicirkal important difference) vad gäller smärta vid artros i litteraturen ligger mellan 8 och 30 skalstegs skillnad jämfört med placebo på en skala 0–100 [6,7].
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
4) Risk för bias: Cirka 50 procent av de ingående studierna i översikten av Osani [2] bedömdes ha en hög risk för bias vad gäller bortfall, där bortfallet oftast var större i interventionsgruppen (biverkningar) än i placebogruppen (bristande effekt). Vidare bedömdes att cirka 40 procent av de ingående studierna har hög risk för bedömningsbias, eftersom de stora bortfallen kan ha påverkat blindningen och därför också patienternas självjämfört medkattning av smärta.
5) En förbättring med 8 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt.
6) En riskkvot på cirka 1,2 bedömer vi som en *liten* riskökning.
7) Bristande precision: Riskkvotens konfidensintervall överlappar 1.

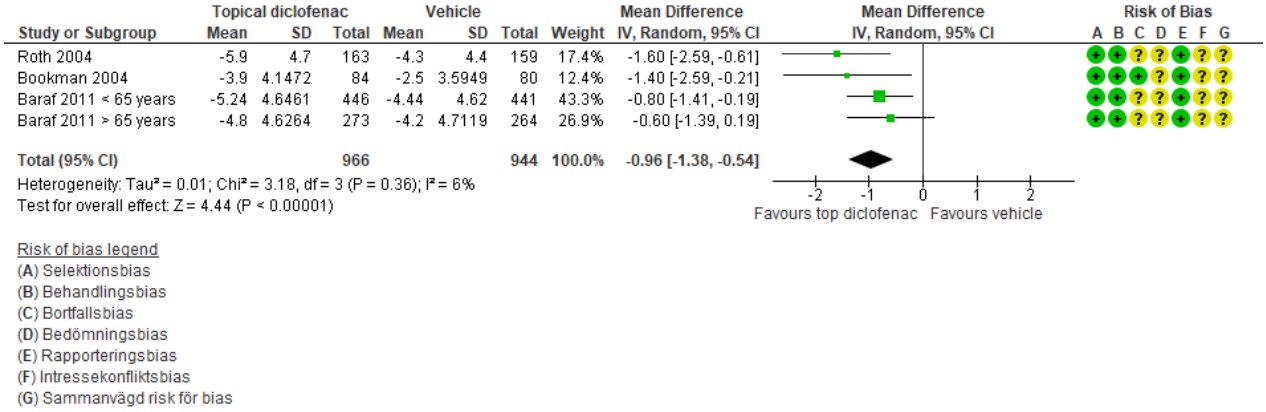
Topikala NSAID–preparat

Tabell 1.4 Topikalt diklofenak jämfört med vehikel (smärta medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt diklofenak jämfört med vehikel				
Förändring av smärta på WOMAC–skala (0–20)	3 RCT [2,9,10], 1910 individer[1]	Topikalt diklofenak förbättrar smärta med 0,96 skalsteg (95 % KI, 0,54 till 1,38) mer än vehikel, vilket motsvarar 5 skalsteg (95 % KI, 3 till 7)[2] på en skala 0–100.	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[3] effekt av topikalt diklofenak vad gäller smärta	Överförbarhet[4]: –1

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] är inte utförd med aveende på detta utfallsmått, varpå metaanalys med data som presenteras i de ingående studierna i översikten har utförts.
2) Skalan 0–20 omvandlad till en skala 0–100
3) En förbättring med 5 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt. Förekommande gränser för klinisk relevans (MCID, minimally clinicirkal important difference) vad gäller smärta vid artros i litteraturen ligger mellan 8 och 30 skalstegs skillnad jämfört med placebo på en skala 0–100 [6,7].
4) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre

Figur 1.1 Metaanalys topikalt diklofenak jämfört med vehikel (smärta medelvärdesskillnad).

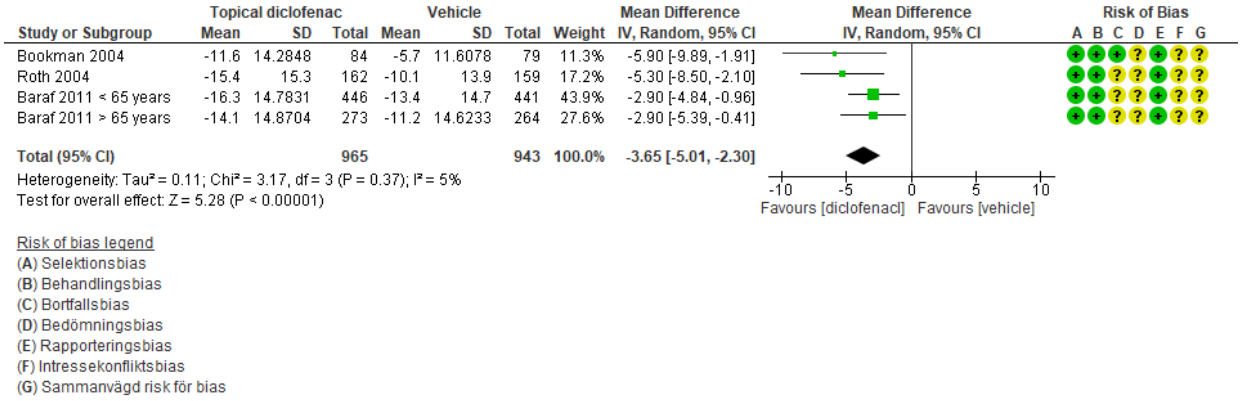


Tabell 1.5 Topikalt diklofenak jämfört med vehikel (funktion medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt diklofenak jämfört med vehikel				
Förändring av funktion på WOMAC–skala (0–68)	3 RCT [2,9,10], 1 908 individer[1]	Topikalt diklofenak förbättrar funktion med 3,7 skalsteg (95 % KI, 2,3 till 5,0) mer än vehikel, vilket motsvarar 5 skalsteg (95 % KI, 3 till 7)[2] på en skala 0–100.	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[3] effekt av topikalt diklofenak vad gäller funktion	Överförbarhet[4]: –1

1) Metaanalys i den systematiska översikten av Derry och madarbetare [3] är inte utförd på kontinuerligt utfallsmått, varpå ny metaanalys med data som presenteras i de ingående studierna i översikten har utförts.
2) Skalan 0–68 omvandlad till en skala 0–100
3) En förbättring med 5 skalsteg jämfört med vehikel på en skala 0–100 bedömer vi som en *mycket liten* effekt.
4) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre

Figur 1.2 Metaanalys topikalt diklofenak jämfört med vehikel (funktion medelvärdesskillnad).

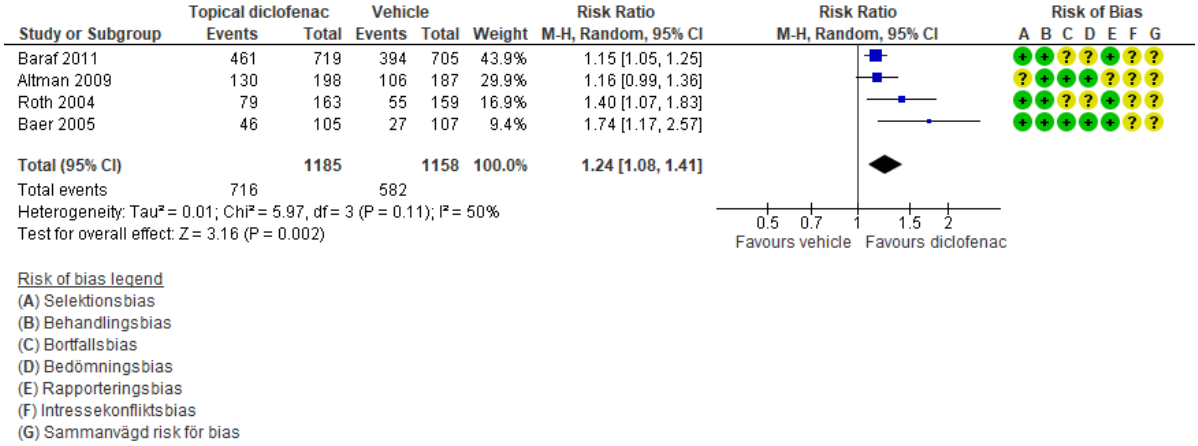


Tabell 1.6 Topikalt diklofenak jämfört med vehikel (responderanalys smärta). Data i tabellen kommer från den systematiska översikten av Derry och medarbetare [3].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt diklofenak jämfört med vehikel				
Andel patienter som når 50 procents smärtreduktion på en smärtskala	4 RCT, 2 343 individer[1]	Diklofenak 60,4 %, vehikel 50,3 %. NNT=9,8[2]. Riskkvot 1,24 (95 % KI, 1,08 till 1,41).	⨁⨁⨁ Måttlig tillförlitlighet för en *mycket liten*[3] effekt av topikalt diklofenak vad gäller smärta	Överförbarhet[4]: –1

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] är utförd med en så kallad ”fixed effects model”. Här har metaanalysen utförts med en ”random effects model” på grund av att det är önskvärt att kunna generalisera dessa data till populationer utanför de ingående studierna.
2) Data för NNT gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var fem veckor.
3) Att behandla tio patienter för att ytterligera en patient (jämfört med vehikel) ska nå en halvering av sin självjämfört medkattade smärta bedömer vi som en *mycket liten* effekt.
4) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre

Figur 1.3. Metaanalys topikalt diklofenak jämfört med vehikel (responderanalys smärta). Data i analysen kommer från den systematiska översikten av Derry och medarbetare [3].

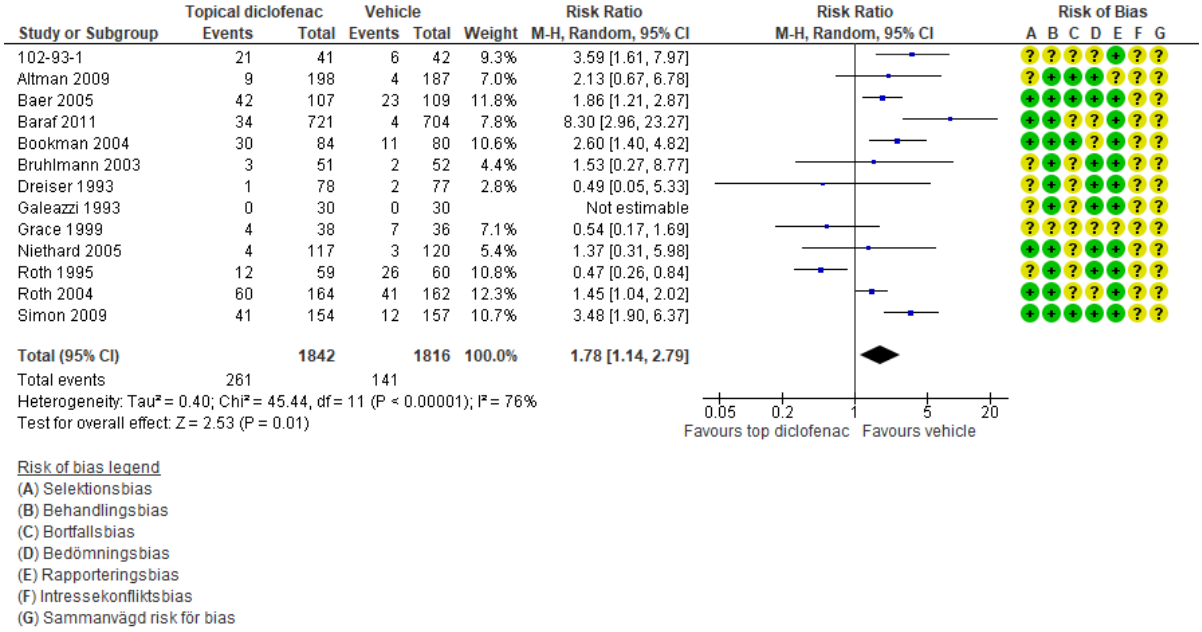


Tabell 1.7 Topikalt diklofenak jämfört med vehikel (lokala biverkningar). Data i tabellen kommer från den systematiska översikten av Derry och medarbetare [3].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt diklofenak jämfört med vehikel				
Frekvens av lokala biverkningar	3 658 individer, 13 RCT[1]	Topikalt diklofenak 14 %, placebo 8 %. NNH=16[2]. Riskkvot 1,78 (95 % KI, 1,14 till 2,79).	⨁⨁⨁ Måttlig tillförlitlighet för en *måttlig*[3] riskökning för lokala biverkningar med diklofenak	Överförbarhet[4]: –1

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] är utförd med en så kallad ”fixed effects model”. Vi har gjort om metaanalysen med en ”random effects model” på grund av att det är önskvärt att kunna generalisera dessa data till populationer utanför de ingående studierna.
2) Data för NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var fem veckor.
3) En riskkvot på cirka 1,8 bedömer vi som en *måttlig* riskökning.
4) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 1.4. Metaanalys topikalt diklofenak jämfört med vehikel (lokala biverkningar). Data i analysen kommer från den systematiska översikten av Derry och medarbetare [3].

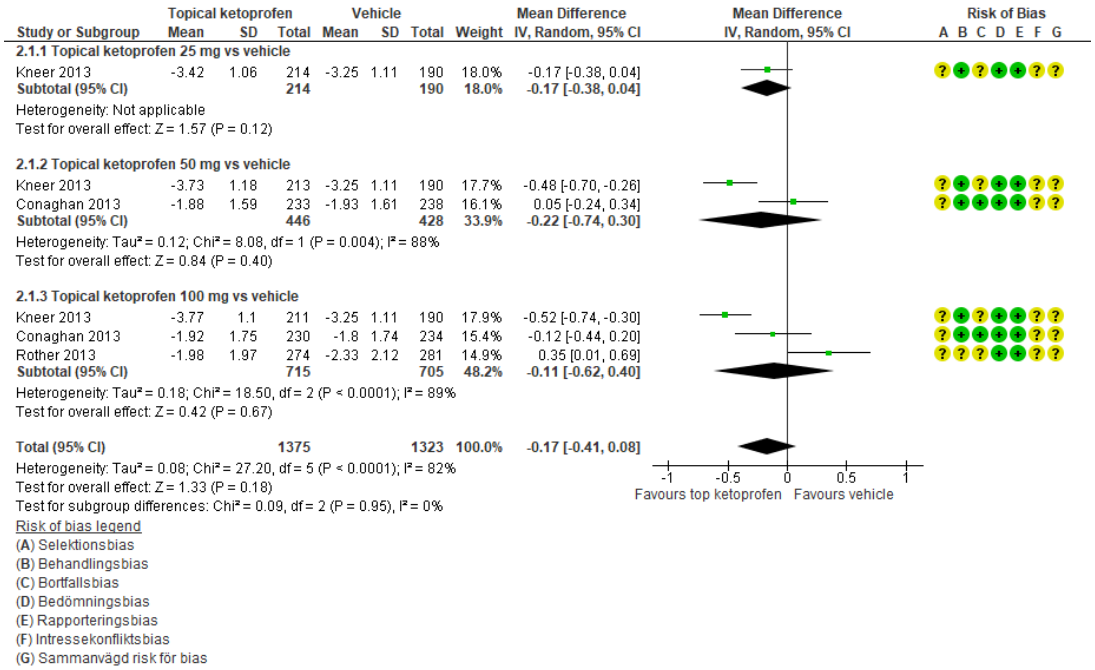


Tabell 1.8 Topikalt ketoprofen jämfört med vehikel (smärta medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt ketoprofen jämfört med vehikel				
Förändring av smärta på WOMAC–skala (0–10)	3 RCT, 2 318 individer[1] [11-13]	Skillnad mellan ketoprofen och vehikel – 0,17 skalsteg (95 % KI, –0,41 till 0,08)	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[3]: –2

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] är inte utförd på kontinuerligt utfallsmått, varpå vi har gjort en ny metaanalys med data som presenteras i de ingående studierna i översikten.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre
3) Bristande precision: Konfidensintervallet överlappar noll.

Figur 1.5 Meta-analys topikalt ketoprofen jämfört med vehikel (smärta medelvärdesskillnad).

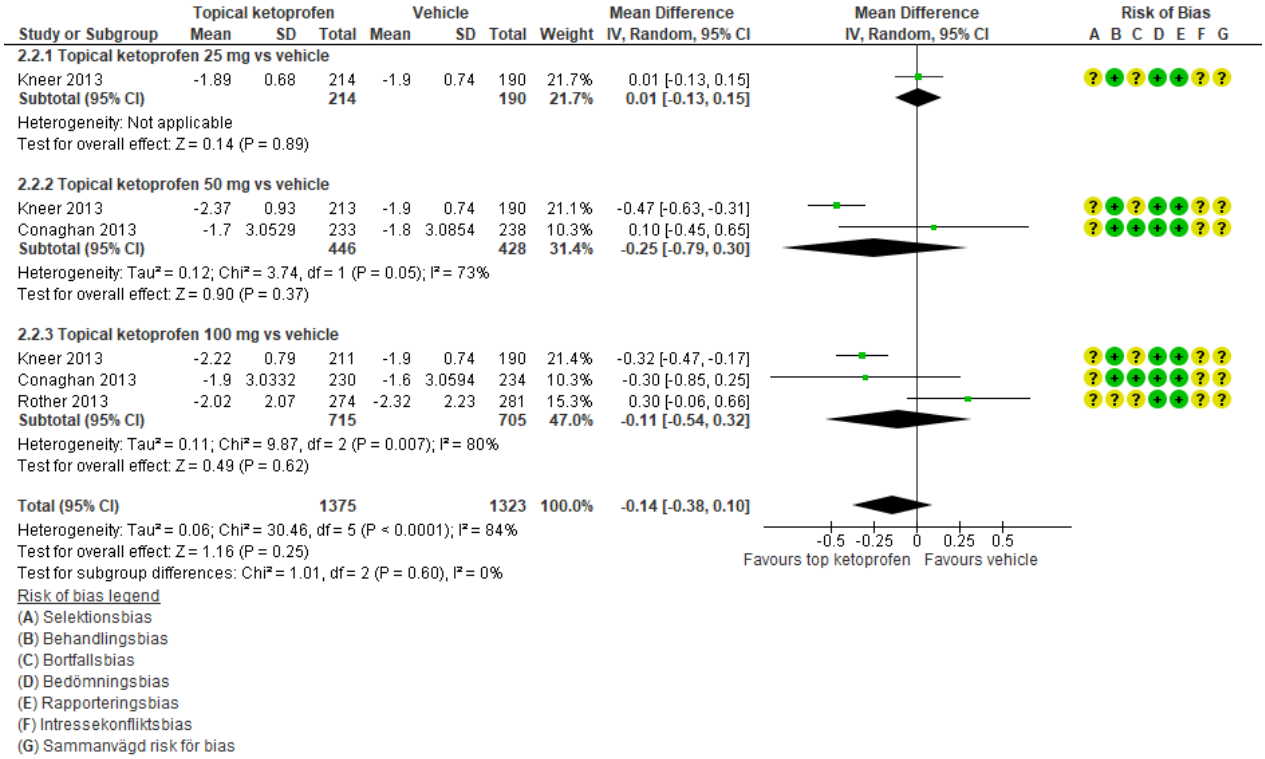


Tabell 1.9 Topikalt ketoprofen jämfört med vehikel (funktion medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt ketoprofen jämfört med vehikel				
Förändring av funktion på WOMAC–skala (0–10)	3 RCT, 2 318 individer[1] [11-13]	Skillnad mellan ketoprofen och vehikel –0,14 skalsteg (95 % KI, –0,38 till 0,10)	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[3]: –2

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] är inte utförd på kontinuerligt utfallsmått, varpå vi har gjort en ny tmetaanalys med data som presenteras i de ingående studierna i översikten.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre
3) Bristande precision: Konfidensintervallet överlappar noll.

Figur 1.6. Metaanalys topikalt ketoprofen jämfört med vehikel (funktion medelvärdesskillnad).

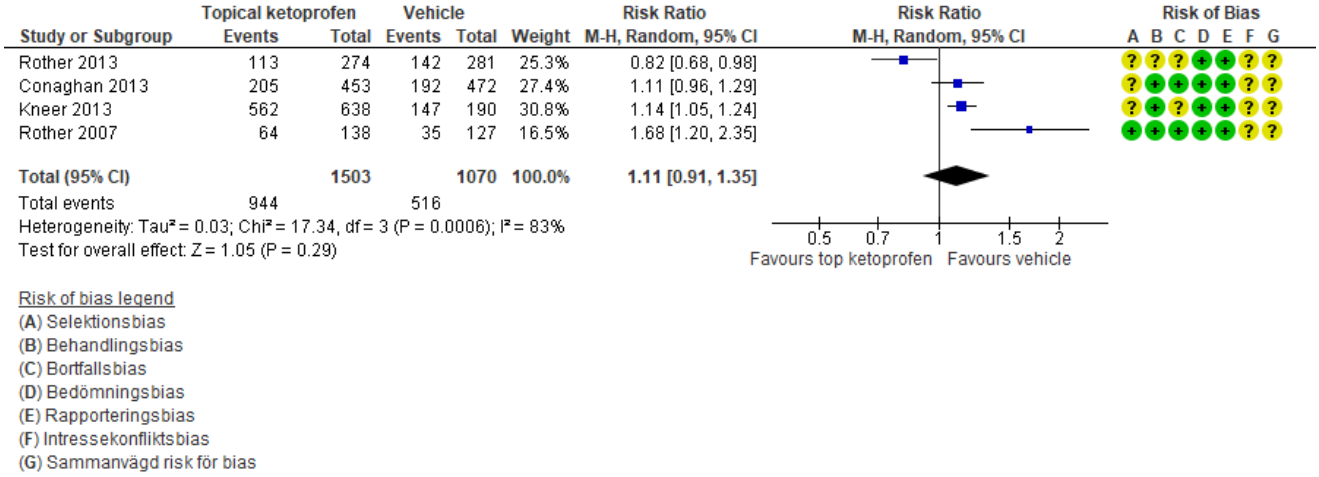


Tabell 1.10 Topikalt ketoprofen jämfört med vehikel (responderanalys smärta). Data i tabellen kommer från den systematiska översikten av Derry och medarbetare [3]

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topikalt ketoprofen jämfört med vehikel				
Andel patienter som når 50 procents smärtreduktion på en smärtskala	4 RCT, 2 573 individer[1]	Ketoprofen 62,8 %, placebo 48,2 %. Riskkvot 1,11 (95 % KI, 0,91 till 1,35).	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[3]: ⁻2

1) Metaanalysen i den systematiska översikten av Derry och medarbetare [3] var inte utförd med en så kallad ”fixed effects model”. Vi har gjort om metaanalysen med en ”random effects model” på grund av att det är önskvärt att kunna generalisera dessa data till populationer utanför de ingående studierna.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre
3) Bristande precision: Riskkvotens konfidensintervall överlappar 1 och är dessutom brett i relation till punktestimatets storlek.

Figur 1.7. Metaanalys topikalt ketoprofen jämfört med vehikel (responderanalys smärta). Data i analysen kommer från den systematiska översikten av Derry och medarbetare [3].

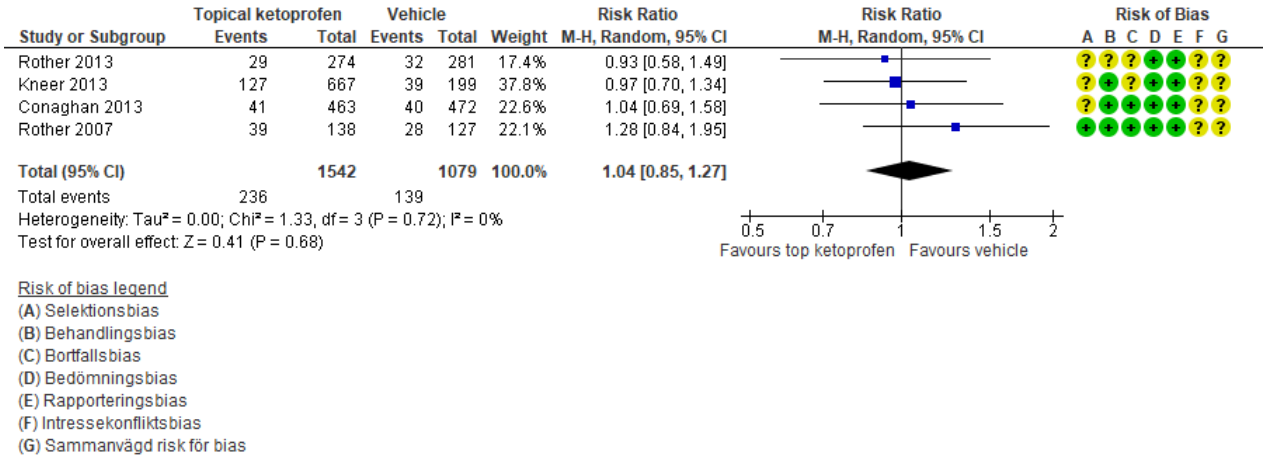


Tabell 1.11 Topikalt ketoprofen jämfört med vehikel (lokala biverkningar). Data i tabellen kommer från den systematiska översikten av Derry och medarbetare [3]

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat		Tillförlitlighet i vetenskapligt underlag	Kommentarer
	Topikalt ketoprofen jämfört med vehikel				
Frekvens av lokala biverkningar	2 261 individer, 4 RCT[1]	Ketoprofen (15 %), vehikel (13 %). Riskkvot 1,04 (95 % KI, 0,85 till 1,27).		⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Precision[3]: –2

1) Metaanalysen i den systeamtiska översikten av Derry och medarbetare [3] var inte utförd med en så kallad ”fixed effects model”. Vi har gjort om metaanalysen med en ”random effects model” på grund av att det är önskvärt att kunna generalisera dessa data till populationer utanför de ingående studierna.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
3) Bristande precision: Riskkvotens konfidensintervall överlappar 1 och är dessutom brett i relation till punktestimatets storlek.

Figur 1.8. Metaanalys topikalt ketoprofen jämfört med vehikel (lokala biverkningar). Data i analysen kommer från den systematiska översikten av Derry och medarbetare [3].



Tabell 1.12 Opioider exklusive tramadol. Data i tabellen kommer från den systematiska översikten av da Costa och medarbetare [4].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Opioider (förutom tramadol) jämfört med placebo				
Förändring i smärta på en standardiserad VAS (0–100 mm)	8 275 individer, 22 RCT	SMD –0,28 (95 % KI, –0,35 till –0,20) vilket motsvarar en minskning med 7 mm (95 % KI, 5 till 9 mm)[1] mer än placebo	⨁⨁⨁ Måttlig tillförlighet för en *mycket liten*[2] effekt av opioider vad gäller smärta	Överförbarhet[3]: –1
Förändring i funktion på en standardiserad WOMAC-skala 0–100	3 553 individer, 12 RCT	SMD –0,26 (95 % KI, –0,35 till –0,17) vilket motsvarar en förbättring med 6 skalsteg (95 % KI, 4 till 8)[1] mer än placebo	⨁⨁⨁ Måttlig tillförlighet för en *mycket liten*[4] effekt av opioider vad gäller funktion	Överförbarhet[3]: –1
Frekvens av biverkningar	4 898 individer, 9 RCT	Opioider 22 %, placebo 15 %. Riskkvot 1,49 (95 % KI, 1,35 till 1,63).	⨁⨁ Låg tillförlighet för en *måttlig*[5] riskökning för biverkningar med opioider	Överförbarhet[3]: –1 Risk för bias[6]: –1
Andel patienter som avbryter	7 712 individer,	Opioider 6,4 %, placebo 1,7 %.	⨁⨁⨁	Överförbarhet[3]: –1

behandling p.g.a. biverkningar	19 RCT	Riskkvot 3,76 (95 % KI, 2,93 till 4,82).	Måttlig tillförlitlighet för en *stor*[7] riskökning för behandlings–avbrott med opioider p.g.a. biverkningar	
Frekvens av allvarliga biverkningar	681 individer, 3 RCT	Opioider 1,3 %, placebo 0,4 %. Riskkvot 3,35 (95 % KI, 0,83 till 13,56).	⊕ Mycket låg tillförlitlighet	Överförbarhet[3]: –1 Risk för bias[6]: –1 Precision[8]: –2
Frekvens av utsättningssymtom	1151 individer, 3 RCT	Opioider 24 %, placebo 9 %. Riskkvot 2,67 (95 % KI, 2,02 till 3,77).	⊕⊕ Låg tillförlitlighet för en *stor*[7] riskökning för utsättnings–symtom med opioider	Överförbarhet[3]: –1 Risk för bias[6]: –1

1) Författarna av översikten [4] beräknade medelvärdesskillnaden på en skala (e.g. 0–100 mm, 0–1700 poäng) genom att multiplicera SMD med standardavvikelsen vid baslinjen i stora artrosstudier [14].
2) En förbättring med 7 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt. Förekommande gränser för klinisk relevans (MCID, minimally clinicirkal important difference) vad gäller smärta vid artros i litteraturen ligger mellan 8 och 30 skalstegs skillnad jämfört med placebo på en skala 0–100 [6,7].
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
4) En förbättring med 6 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt.
5) En riskkvot på cirka 1,5 bedömer vi som en *måttlig* riskökning.
6) Risk för bias: Många studier i översikten av da Costa och medarbetare [4] rapporterade inte detta utfall, vilket sannolikt innebär rapporteringsbias.
7) En riskkvot på 3,8 respektive 2,7 bedömer vi som en *stor* riskökning.
8) Bristande precision: Riskkvotens konfidensintervall är mycket brett och överlappar dessutom 1.
9) Författarna av översikten [5] beräknade medelvärdesskillnaden på en skala (e.g. 0–100 mm, 0–1700 poäng) genom att multiplicera SMD med standardavvikelsen i placebogruppen vid baslinje, som föreslaget i Cochrane Handbook for Systematic Reviews of Interventions [8].
10) Risk för bias: Alla ingående studier i översikten av Toupin April och medarbetare [5] hade hög eller oklar risk för bias i minst en domän av risk för bias.

Tabell 1.13 Tramadol. Data i tabellen kommer från den systematiska översikten av Toupin-April och medarbetare [5].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Tramadol 40–400 mg jämfört med placebo				
Förändring i smärta på VAS (0–100 mm)	3 972 individer, 8 RCT	SMD –0.25 (9 5% KI, –0,32 till –0,18) vilket motsvarar en förbättring med 4 mm (95 % KI 3 till 5 mm)[1] mer än placebo.	⊕⊕ Låg tillförlitlighet för en *mycket liten*[2] effekt av tramadol vad gäller smärta	Överförbarhet[3]: –1 Risk för bias[4]: –1
Förändring i funktion på en standardiserad WOMAC-skala 0–100	2 550 individer, 5 RCT	SMD –0.20 (95 % KI, –0,29 till –0,12) vilket motsvarar en förbättring med 4 skalsteg (95 % KI, 2 till 6)[1] mer än placebo.	⊕⊕ Låg tillförlitlighet för en *mycket liten*[5] effekt av tramadol vad gäller funktion	Överförbarhet[3]: –1 Risk för bias[4]: –1
Frekvens av biverkningar	2 039 individer, 4 RCT	Tramadol 65,9 %, placebo 49,2 %. Riskkvot 1,34 (95 % KI, 1,24 till 1,46).	⊕⊕ Låg tillförlitlighet för en *liten*[6] riskökning för biverkningar med tramadol	Överförbarhet[3]: –1 Risk för bias[4]: –1
Andel patienter som avbryter behandling p.g.a. biverkningar	4 533 individer, 9 RCT	Tramadol 19,4 %, placebo 7,3 %. Riskkvot 2,64 (95 % KI, 2,17 till 3,20).	⊕⊕ Låg tillförlitlighet för en *stor*[7] riskökning för behandlingsavbrott p.g.a. biverkningar med tramadol	Överförbarhet[3]: –1 Risk för bias[4]: –1
Frekvens av allvarliga biverkningar	3 612 individer, 7 RCT	Tramadol 3,4 %, placebo 1,9 %. Riskkvot: 1,78 (95 % KI, 1,11 till 2,84)	⊕⊕ Låg tillförlitlighet för en *måttlig*[8] riskökning för allvarliga biverkningar med tramadol	Överförbarhet[3]: –1 Risk för bias[4]: –1

1) Författarna av översikten [5] beräknade medelvärdesskillnaden på en skala (e.g. 0–100 mm, 0–1700 poäng) genom att multiplicera SMD med standardavvikelsen i placebogruppen vid baslinjen, som föreslaget i Cochrane Handbook for Systematic Reviews of Interventions [8].

2) En förbättring med 4 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt. Förekommande gränser för klinisk relevans (MCID, minimally clinicirkal important difference) vad gäller smärta vid artros i litteraturen ligger mellan 8 och 30 skalstegs skillnad jämfört med placebo på en skala 0–100 [6,7].

3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
4) Risk för bias: Alla ingående studier i översikten av Toupin April och medarbetare [5] hade hög eller oklar risk för bias i minst en domän av risk för bias.
5) En förbättring med 4 skalsteg jämfört med placebo på en skala 0–100 bedömer vi som en *mycket liten* effekt.
6) En riskkvot på cirka 1,3 bedömer vi som en *liten* riskökning.
7) En riskkvot på cirka 2,6 bedömer vi som en *stor* riskökning.
8) En riskkvot på cirka 1,8 bedömer vi som en *måttlig* riskökning.

Resultat identifierade i primärstudier

Två primärstudier [15,16] inom området artros inkluderades. Dessa publicerades efter respektive översikts litteratursökning utfördes.

Tabell 1.14 Fynd i inkluderade primärstudier inom området artros.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Diklofenak flexibel dos jämfört med paracetamol flexibel dos				
Förändring i smärta mätt med numerisk smärtskala (0–10).	104 individer, 1 RCT, [16]	Skillnad i smärta mellan diklofenak och paracetamol, –0,2 skalsteg (95 % KI, –1,0 till 0,7).	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Förändring jämfört med kvalitet mätt med EQ–5D (0–1).	104 individer, 1 RCT, [16]	Skillnad i jämfört med kvalitet mellan diklofenak och paracetamol, 0,0 skalsteg (95 % KI, –0,05 till 0,1).	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Följsamhet till behandling	104 individer, 1 RCT, [16]	Efter två veckor var 84,6 % av patienterna följsamma i diklofenak–gruppen respective 86,5 % i paracetamol–gruppen. Statistisk analys saknas.	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Tapentadol flexibel dos jämfört med oxikodon flexibel dos jämfört med placebo				
Förändring i smärta mätt med numerisk smärtskala (0–10).	990 individer, 1 RCT, [15]	Tapentadol –0,3 skalsteg (95 % KI –0,61 till 0,09). Oxikodon 0,2 skalsteg (95 % KI, –0,16 till 0,54)	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1

Förändring i funktion mätt med WOMAC funktionsskala	990 individer, 1 RCT, [15]	Tapentadol –0,1 skalsteg (95 % KI, –0,23 till 0,07). Oxikodon –0,1 skalsteg (95 % KI –0,25 till 0,08)	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Förändring jämfört med kvalitet mätt med EQ-5D (0–1).	990 individer, 1 RCT, [15]	Tapentadol 0,03 skalsteg (95 % KI –0,01 till 0,07). Oxikodon –0,04 skalsteg (95 % KI, –0,08 till 0,00).	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Andel patienter som avbryter behandling p.g.a. biverkningar	990 individer, 1 RCT, [15]	8 % med placebo, 18,8 % med tapentadol, 42,3 % med oxikodon. Statistisk analys saknas.	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Riskkvotens konfidensintervall överlappar 1 och/eller är brett i relation till punktestimatets storlek, alternativt statistisk analys saknas.
3) Risk för bias: I studierna av Verkleij och medarbetare [16] och Serrie och medarbetare [15] förelåg oklar risk för bias i fyra av sex domäner.

Del II: Läkemedelsbehandling av diabetesneuropati hos äldre

Resultat identifierade i systematiska översikter

Inga relevanta systematiska översikter med låg risk för bias identifierades.

Resultat identifierade i primärstudier

35 primärstudier [17-51] inkluderades.

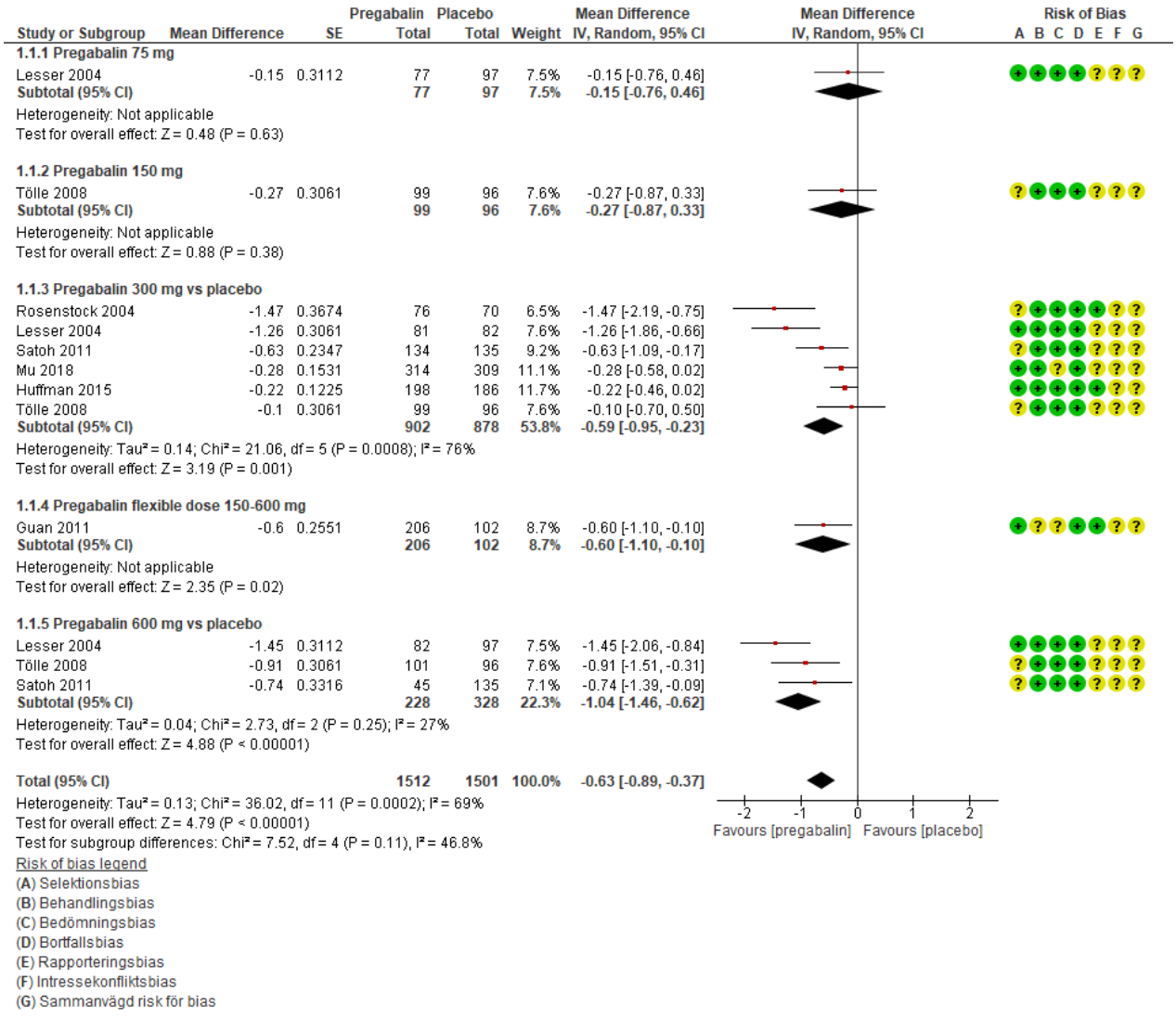
Antiepileptika

Tabell 2.1 Pregabalin jämfört med placebo (smärta medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 75–600 mg jämfört med placebo				
Förändring på numerisk smärtskala (0–10)	n=2 334 7 RCT	Pregabalin minskar smärta med i genomsnitt 0,63 skalsteg (95 % KI, 0,37 till 0,89) mer än placebo	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[1] effekt av pregabalin vad gäller smärta	Överförbarhet[2]: –1

1) En effektskillnad vad gäller smärta med cirka 0,6 skalsteg på en skala 0–10 bedömer vi som en *mycket liten* effekt.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.1 Metaanalys pregabalin jämfört med placebo (smärta medelvärdesskillnad).

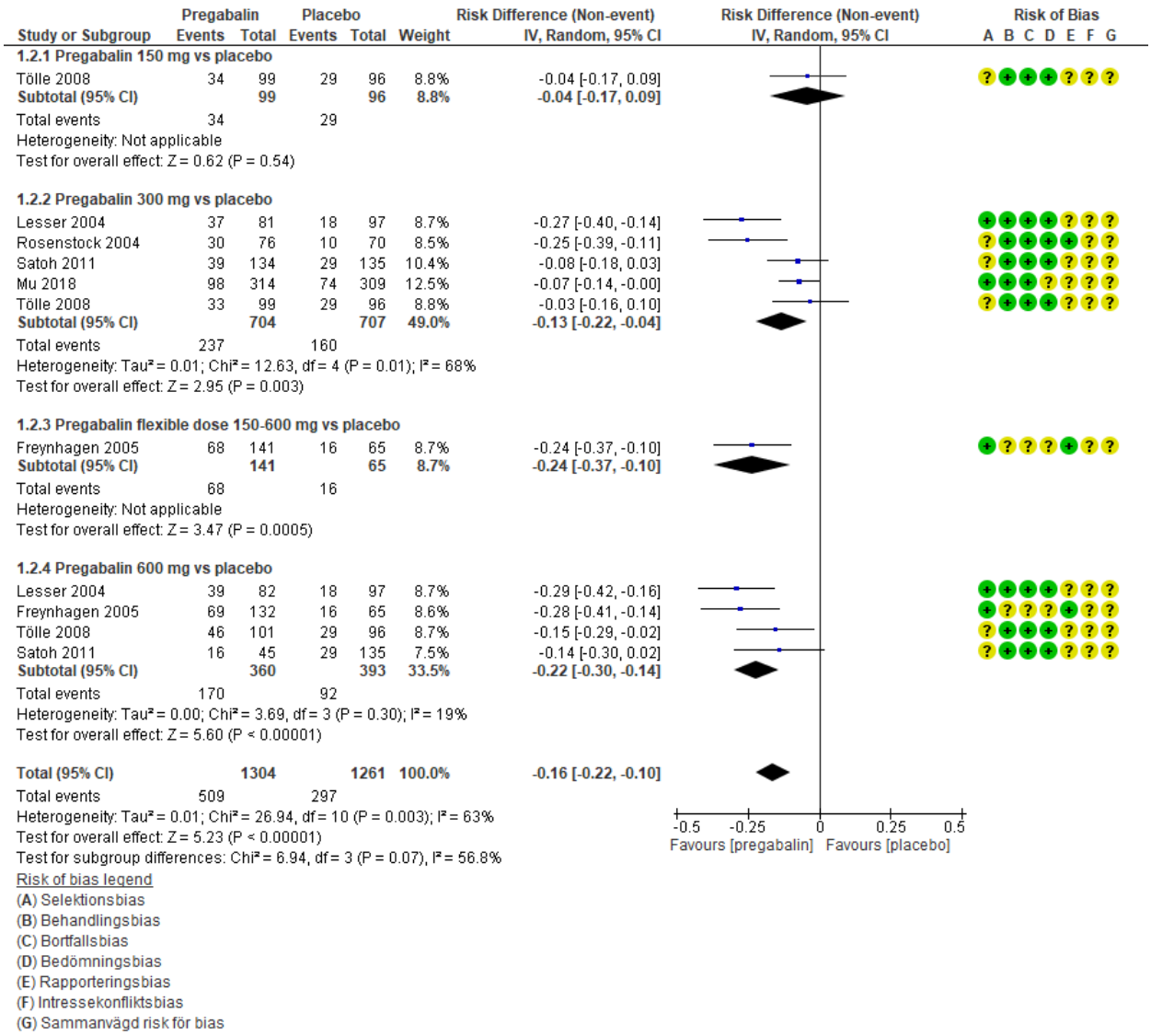


Tabell 2.2 Pregabalin jämfört med placebo (smärta responderanalys).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 150–600 mg jämfört med placebo				
Andel patienter som når 50 % smärtminskning eller mer på numerisk smärtskala (0–10)	n=2 157 6 RCT	Pregabalin 39,0 %, placebo 23,6 %. 15,5 %[1] (95 % KI, 10 till 22 %) absolut skillnad i effekt. NNT=6,5.	⊕⊕⊕ Måttlig tillförlitlighet för en mycket liten[2] effekt av pregabalin vad gäller smärta	Överförbarhet[3]: –1

1) Data för absolut skillnad i effekt och NNT gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var tio veckor.
2) Att ytterliger två av 13 patienter (jämfört med placebo) uppnår 50 % smärtreduktion bedömer vi som en mycket liten effekt.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.2 Metaanalys pregabalin jämfört med placebo (smärta responderanalys).

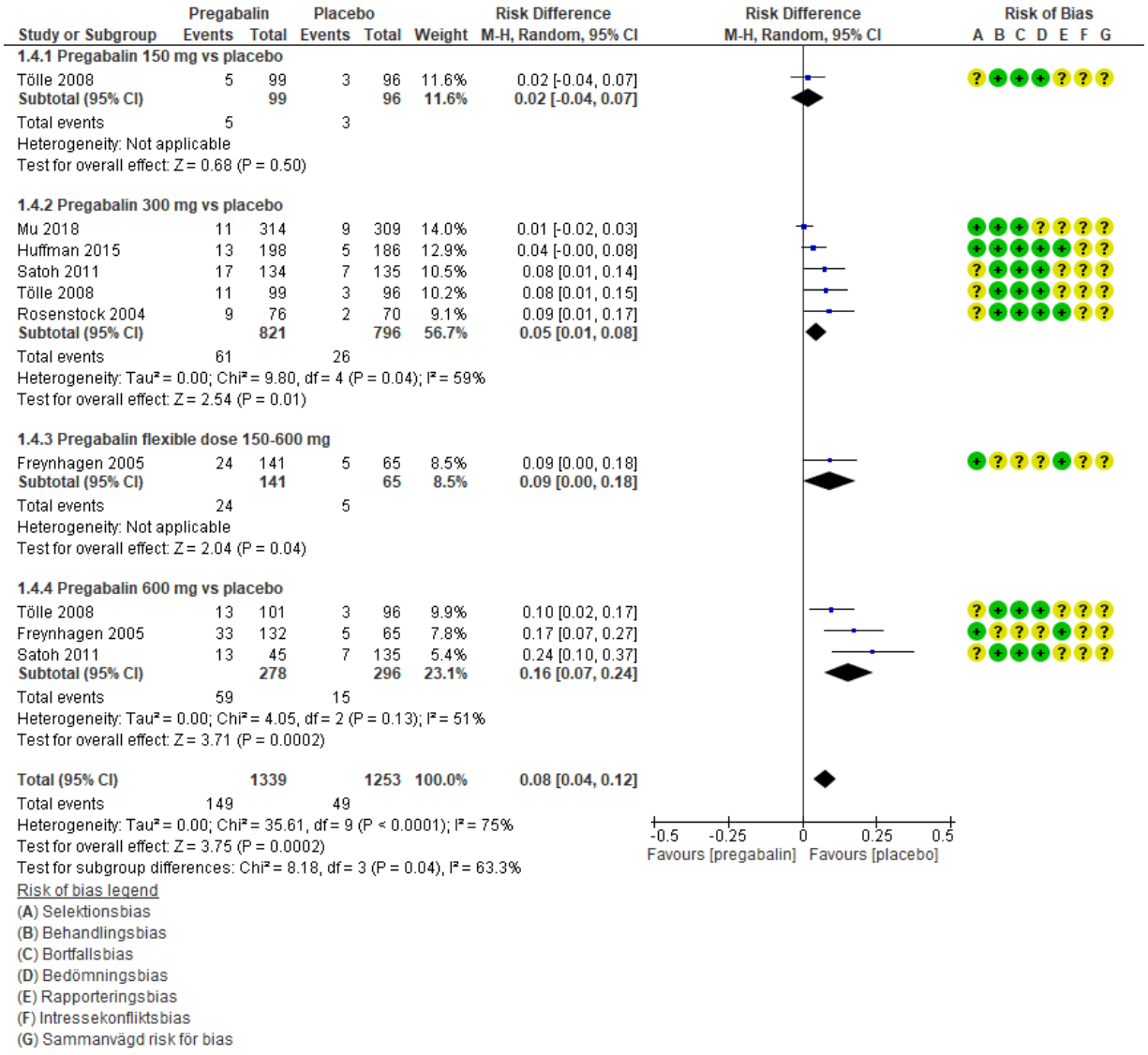


Tabell 2.3 Pregabalin jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 75–600 mg jämfört med placebo				
Andel patienter som avbryter behandling på grund av biverkningar	n=1 823 6 RCT	Placebo 3,3 %, pregabalin 10,6 %. Absolut riskökning 7,3 %[1] (95 % KI, 4 till 12 %). NNH=14.	⊕⊕⊕ Måttlig tillförlitlighet för en *måttlig*[2] riskökning för behandlingsavbrott p.g.a. biverkningar	Överförbarhet[3]: –1

1) Data för absolut riskökning och NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var tio veckor.
2) En absolut riskökning på 7 procent med 10 veckors behandling bedömer vi som en *måttlig* riskökning.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.3. Metaanalys pregabalin jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).

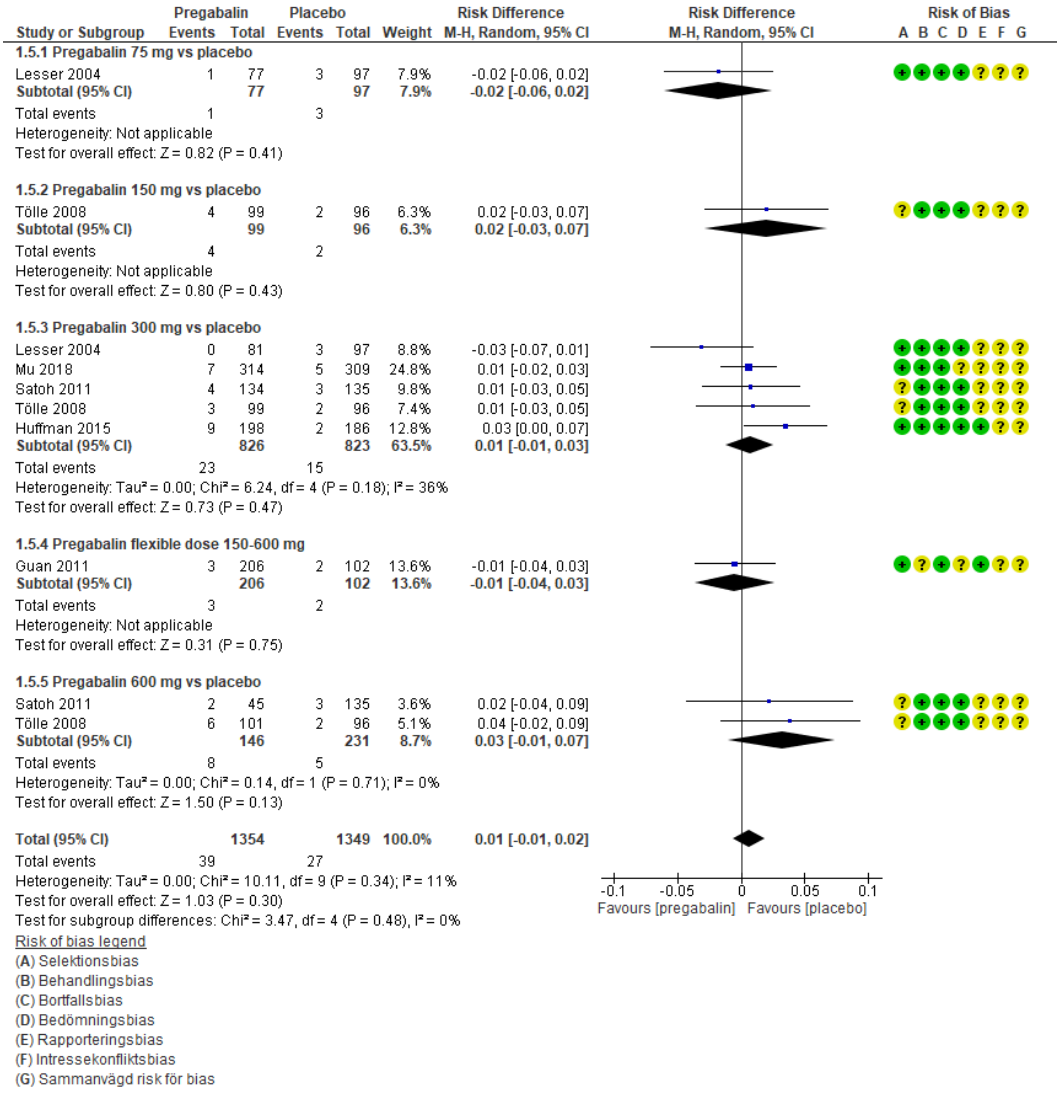


Tabell 2.4 Pregabalin jämfört med placebo (allvarliga biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 75–600 mg jämfört med placebo				
Frekvens av allvarliga biverkningar	n=2 188 6 RCT	Placebo 2,88 %, pregabalin 1,84 %. Absolut riskskillnad 1,04 %[1] (95 % KI, –1 till 2 %).	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet överlappar 0 och är brett i relation till punktestiamtets storlek.

Figur 2.4 Metaanalys pregabalin jämfört med placebo (allvarliga biverkningar).

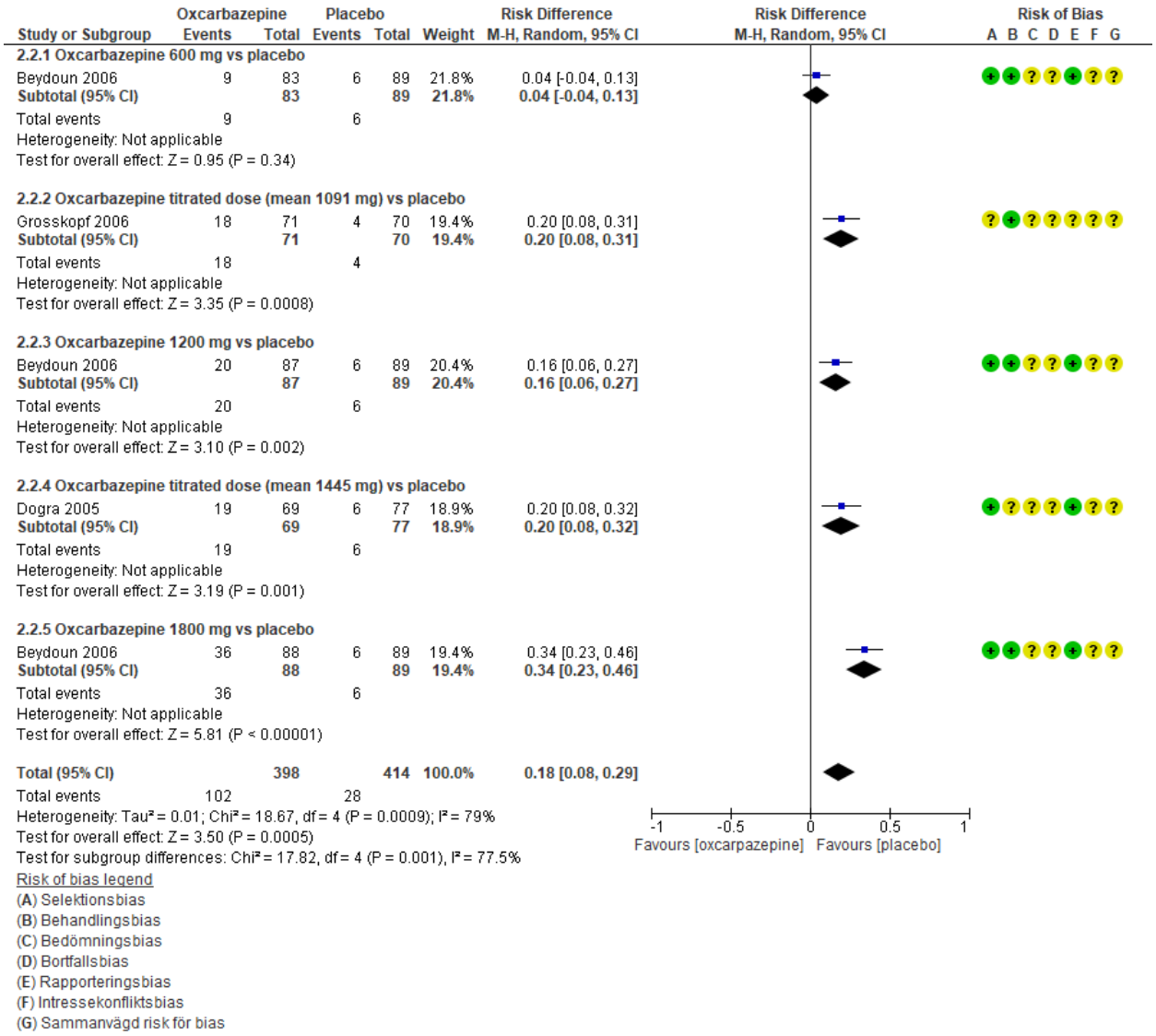


Tabell 2.5 Oxkarbazepin jämfört med placebo.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Oxkarbazepin 600–1 800 mg jämfört med placebo				
Förändring i smärta mätt med VAS-skala (0–100 mm)	n=634 3 RCT [18,21,30]	En studie visar på 9,6 mm mer smärtreduktion med oxkarbazepin jämfört med placebo, p=0,01. Två studier visar ingen statistiskt signifikant skillnad. Spridningsdata vad gäller effekt saknas i samtliga tre studier.	⊕ Mycket låg tillförlitlighet	Överförbarhet[2]: –1 Samstämmighet[3]: –1 Precision[4]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=634 3 RCT	Placebo 6,8 %, oxkarbazepin 25,6 %. Absolut riskökning 18,9 %[1] (95 % KI, 8 till 29 %). NNH=5.	⊕⊕⊕ Måttlig tillförlitlighet för en *stor*[5] riskökning för behandlings–avbrott p.g.a. biverkningar	Överförbarhet[2]: –1

1) Data för absolut riskökning och NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var 16 veckor.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
3) Bristande samstämmighet: En studie visar på en statistiskt signifikant skillnad mellan oxkarbazepin och placebo och två studier visar inte en statistiskt signifikant skillnad.
4) Bristande precision: Spridningsdata vad gäller effekt saknas i alla tre studier.
5) En absolut riskökning på 18 procent med 16 veckors behandling bedömer vi som en *stor* riskökning.

Figur 2.5. Metaanalys oxkarbazepin jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).

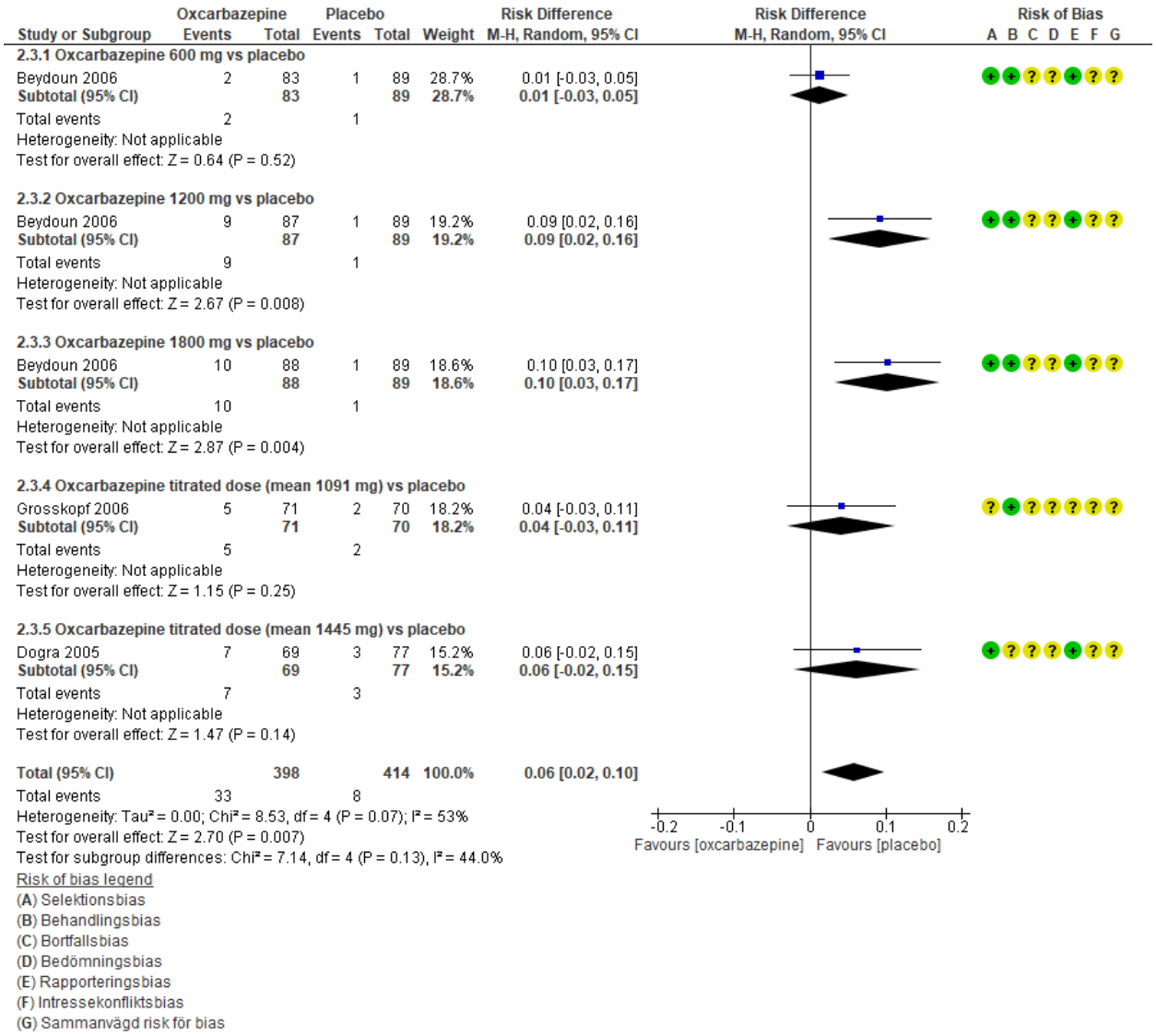


Tabell 2.5 Oxkarbazepin jämfört med placebo (allvarliga biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Oxkarbazepin 600–1 800 mg jämfört med placebo				
Frekvens av allvarliga biverkningar	n=634 3 RCT	Placebo 2,5 %, oxkarbazepin 8,3 %. Absolut riskökning 5,8 %[1] (95 % KI, 2 till 10 %). NNH=17.	⨁⨁⨁ Måttlig tillförlitlighet för en måttlig[2] riskökning för allvarliga biverkningar	Överförbarhet[3]: –1

1) Data för absolut riskökning och NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var 16 veckor.
2) En absolut riskökning på 6 procent med 16 veckors behandling bedömer vi som en *måttlig* riskökning.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.6. Metaanalys oxkarbazepin jämfört med placebo (allvarliga. biverkningar).



Tabell 2.6 Lakosamid. Data i tabellen kommer från studien av Shaibani och medarbetare [43].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Lakosamid 200–600 mg jämfört med placebo				
Förändring på numerisk smärtskala (0–10)	n=468 1 RCT	Skillnad jämfört med placebo (95 % KI): Lakosamid 200 mg –0,33 (–0,94 till 0,27), Lakosamid 400 mg –0,61 (–1,23 till 0,00) Lakosamid 600 mg –0,56 (–1,17 till 0,05)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1
Andel patienter som avbryter behandling på grund av biverkningar	n=468 1 RCT	Placebo 13,8 %, lakosamid 200 mg 12,1 %, lakosamid 400 mg 24 %, lakosamid 600 mg 42,3 %. Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[4]: –2 Risk för bias[3]: –1

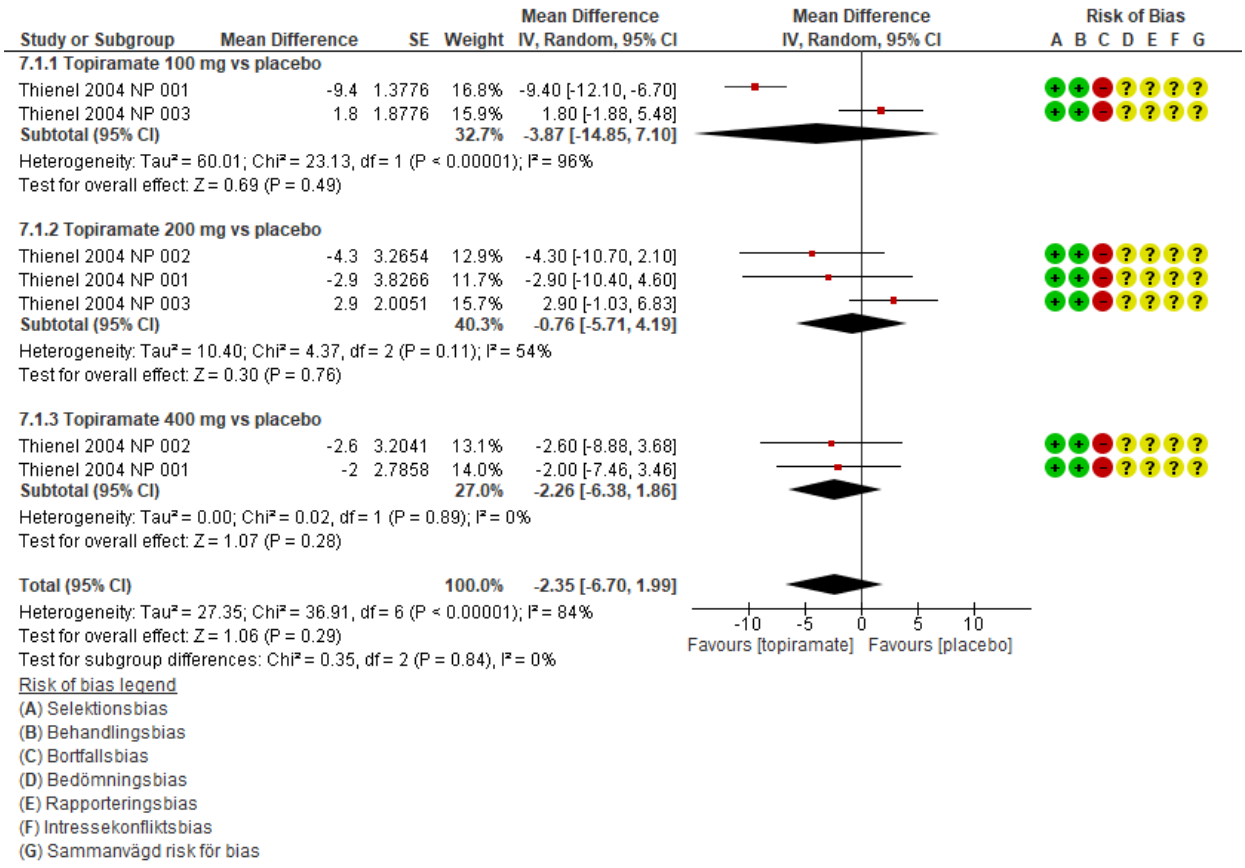
1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet överlappar 0.
3) Risk för bias: I studien av Shaibani 2009 var bortfallen mellan 30 och 66 procent i de olika armarna, vilket medför hög risk för bortfallsbias.
4) Bristande precision: Statistisk analys samt spridningsdata saknas.

Tabell 2.7 Topiramat (smärta medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topiramat 100–400 mg jämfört med placebo				
Förändring i smärta mätt med VAS-skala (0–100 mm)	n=1 259 3 RCT	Topiramat jämfört med placebo –2,35 mm (95 % KI, –6,7 till 1,99)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2 Risk för bias[3]: –1

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet överlappar 0.
3) Risk för bias: Stora bortfall i samtliga tre studier innebär hög risk för bortfallsbias.

Figur 2.7 Metaanalys topiramat jämfört med (smärta medelvärdesskillnad).

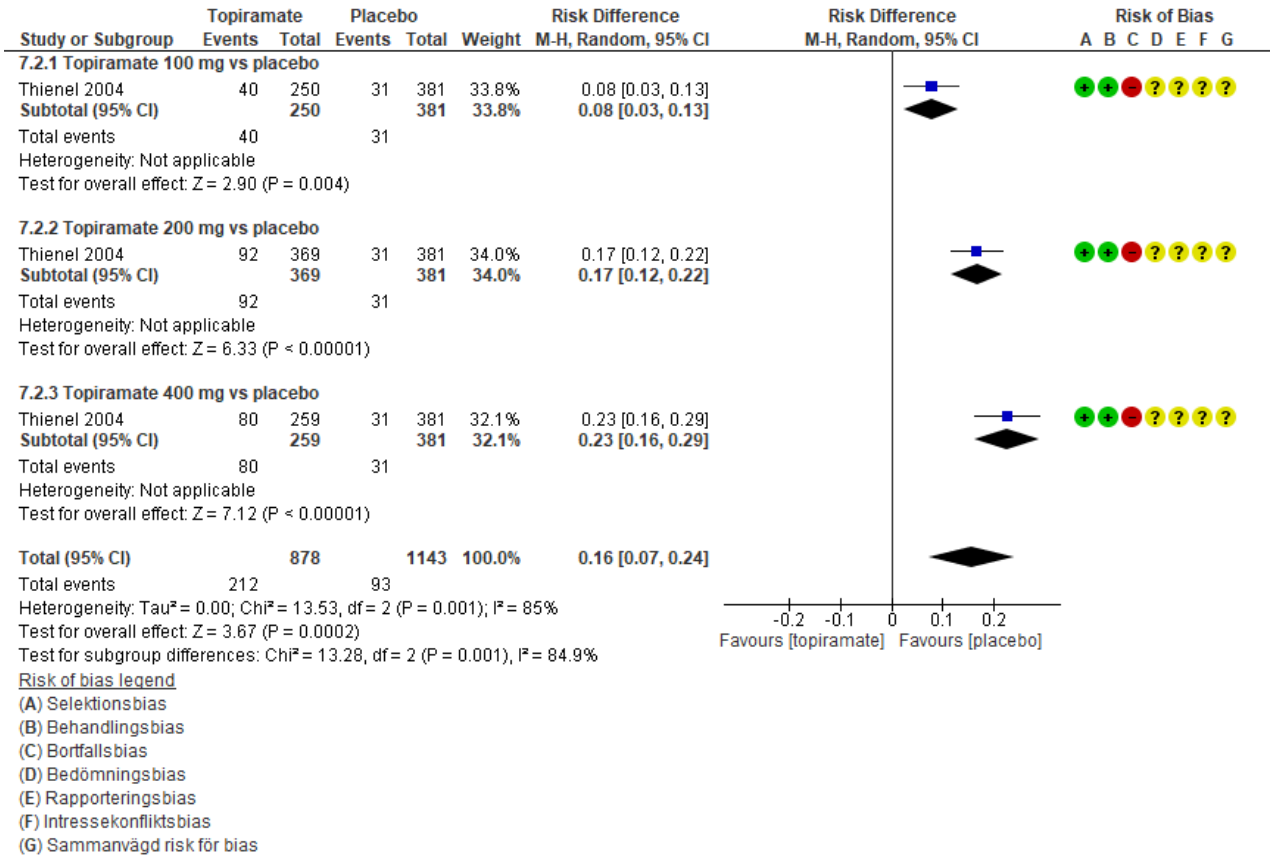


Tabell 2.8 Topiramat (behandlingsavbrott p.g.a. biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Topiramat 100–400 mg jämfört med placebo				
Andel patienter som avbryter behandling på grund av biverkningar	n=1 259 3 RCT	Placebo 8,1 %, topiramat 24,1 %. Absolut riskökning 16,0 %[1] (95 % KI, 7 till 24 %). NNH=6.	⨁⨁ Låg tillförlitlighet för en *stor*[2] riskökning för biverkningar	Överförbarhet[3]: –1 Risk för bias[4]: –1

1) Data för absolut riskökning och NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var 20 veckor.
2) En absolut riskökning på 16 procent med 20 veckors behandling bedömer vi som en *måttlig* riskökning.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
4) Risk för bias: Stora bortfall i samtliga tre studier innebär hög risk för bortfallsbias.

Figur 2.8 Metaanalys topiramat jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).



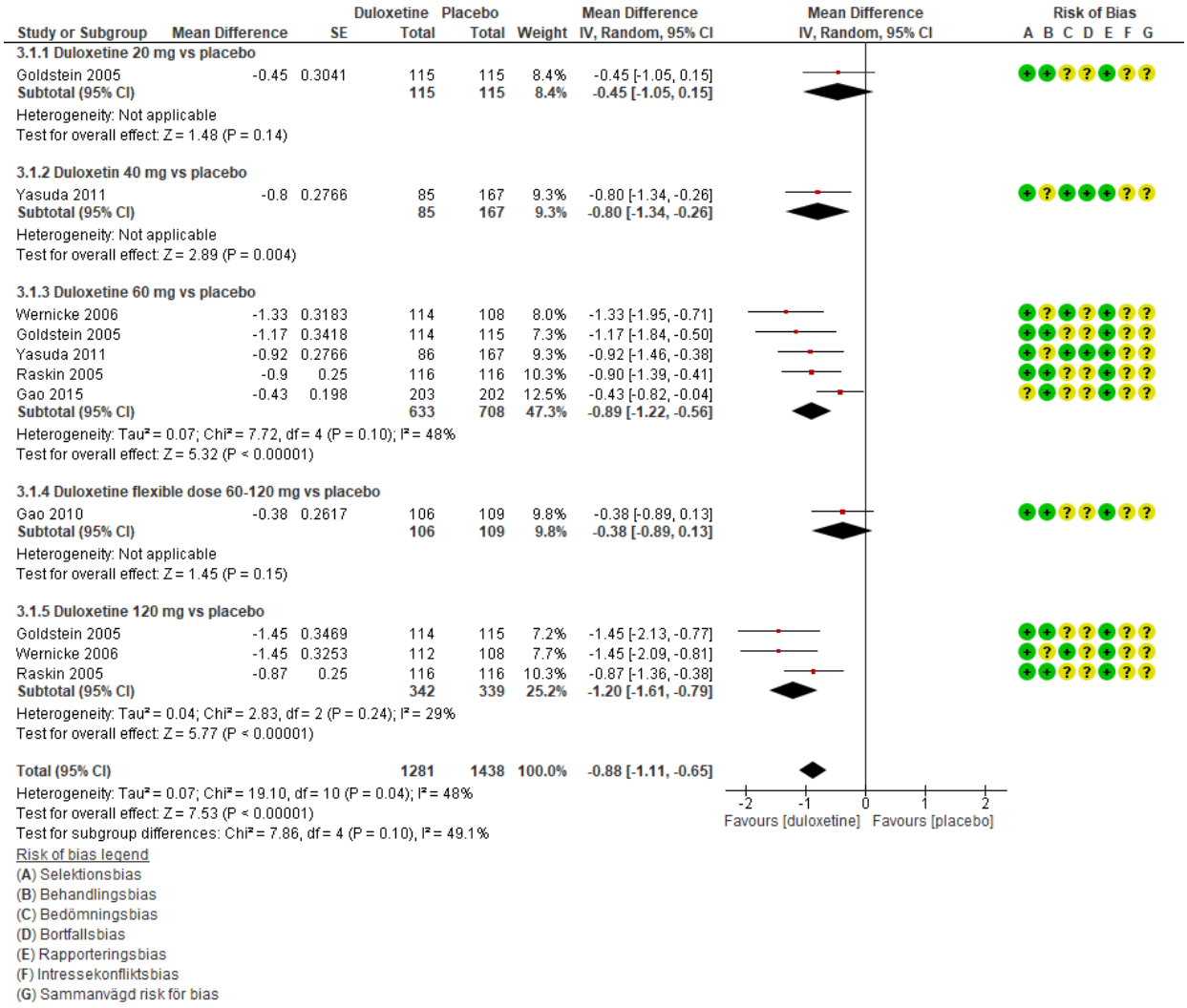
Antidepressiva läkemedel

Tabell 2.9 Duloxetin (smärta medelvärdesskillnad).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Duloxetin 20–120 mg jämfört med placebo				
Förändring på numerisk smärtskala (0–10)	n=2 098 6 RCT	Duloxetin minskar smärta med i genomsnitt 0,88 skalsteg (95 % KI, 0,65 till 1,11) mer än placebo	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[1] effekt av duloxetin vad gäller smärta	Överförbarhet[2]: –1

1) En effektskillnad vad gäller smärta med cirka 0,9 skalsteg på en skala 0–10 bedömer vi som en *mycket liten* effekt.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.9 Metaanalys duloxetin jämfört med placebo (smärta medelvärdesskillnad).

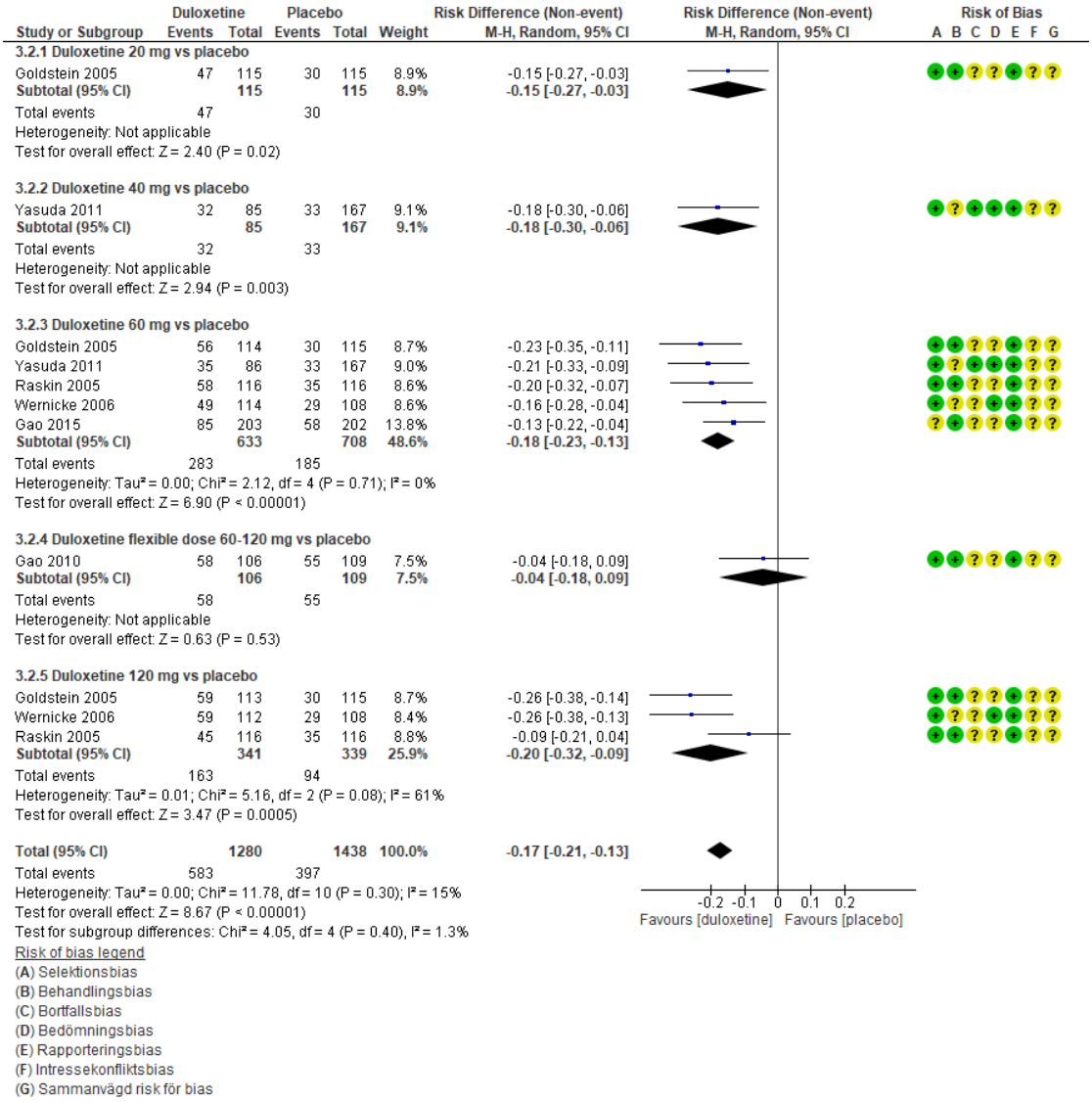


Tabell 2.10 Duloxetin jämfört med placebo (smärta responderanalys).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Duloxetin 20–120 mg jämfört med placebo				
Andel patienter med 50 % smärtminskning eller mer på numerisk smärtskala (0–10)	n=1 556 6 RCT	Duloxetin 45,5 %, placebo 28,3 %. 17 %[1] (95 % KI, 13 till 21 %) absolut skillnad i effekt. NNT=6.	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[2] effekt av duloxetin vad gäller smärta	Överförbarhet[3]: –1

1) Data för absolut skillnad i effekt och NNT gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var 14 veckor.
2) Att ytterligare en av sex patienter (jämfört placebo) uppnår 50 procent smärtreduktion bedömer vi som en *mycket liten* effekt.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.10 Metaanalys duloxetin jämfört med placebo (smärta responderanalys).

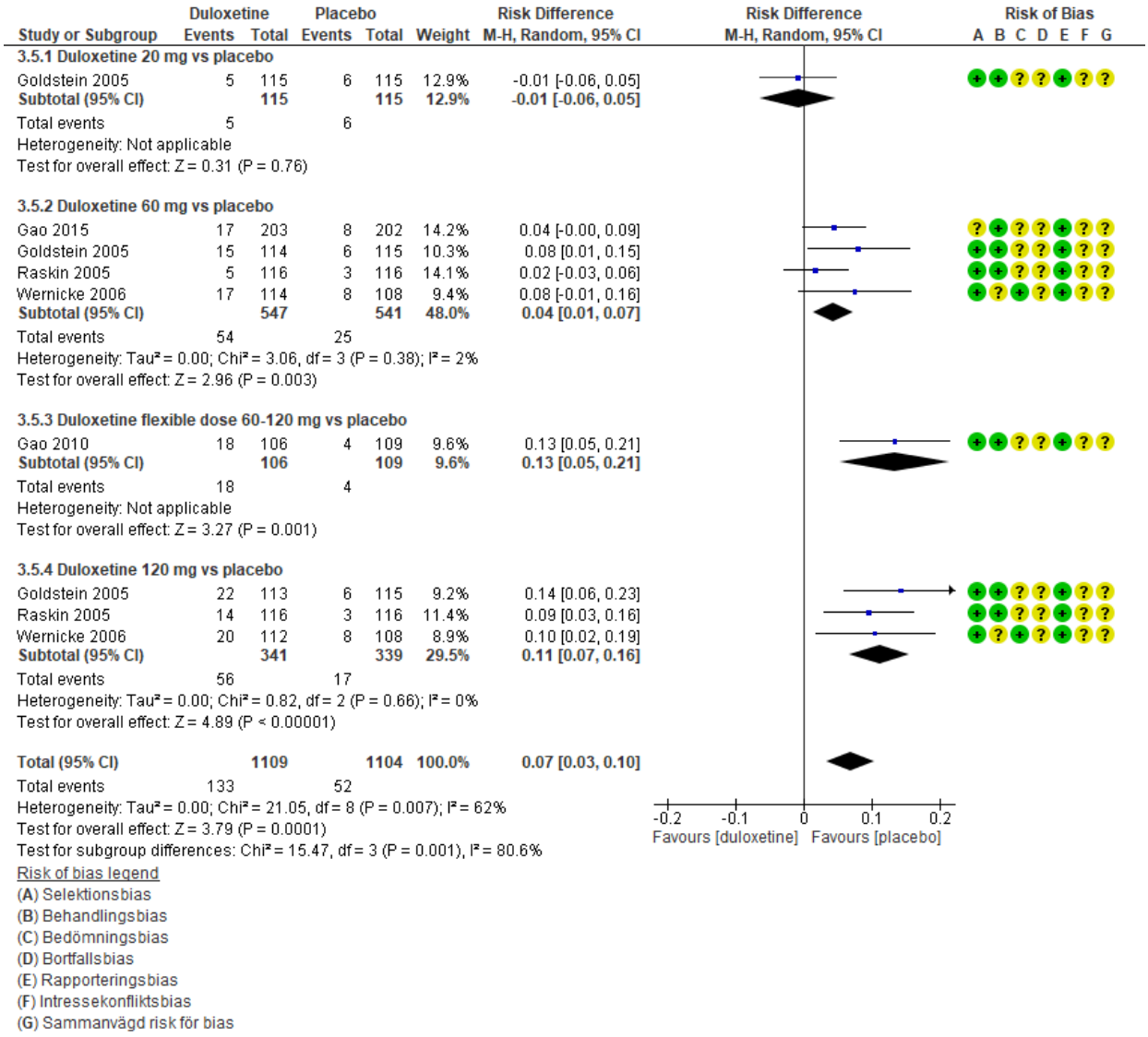


Tabell 2.11 Duloxetin jämfört med placebo (behandlingsavbrott på grund av biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Duloxetin 20–120 mg jämfört med placebo				
Andel patienter som avbryter behandling på grund av biverkningar	n=1 303 5 RCT	Placebo 4,7 %, duloxetin 12,0 %. Absolut riskökning 7,3 %[1] (95 % KI, 3 till 10 %). NNH=14.	⨁⨁⨁ Måttlig tillförlitlighet för en *måttlig*[2] riskökning för behandlingsavbrott p.g.a. biverkningar	Överförbarhet[3]: –1

1) Data för absolut skillnad i effekt och NNT gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var 14 veckor.
2) En absolut riskökning på 7 procent med 14 veckors behandling bedömer vi som en *måttlig* riskökning.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.11 Metaanalys duloxetin jämfört med placebo (behandlingsavbrott på grund av biverkningar).

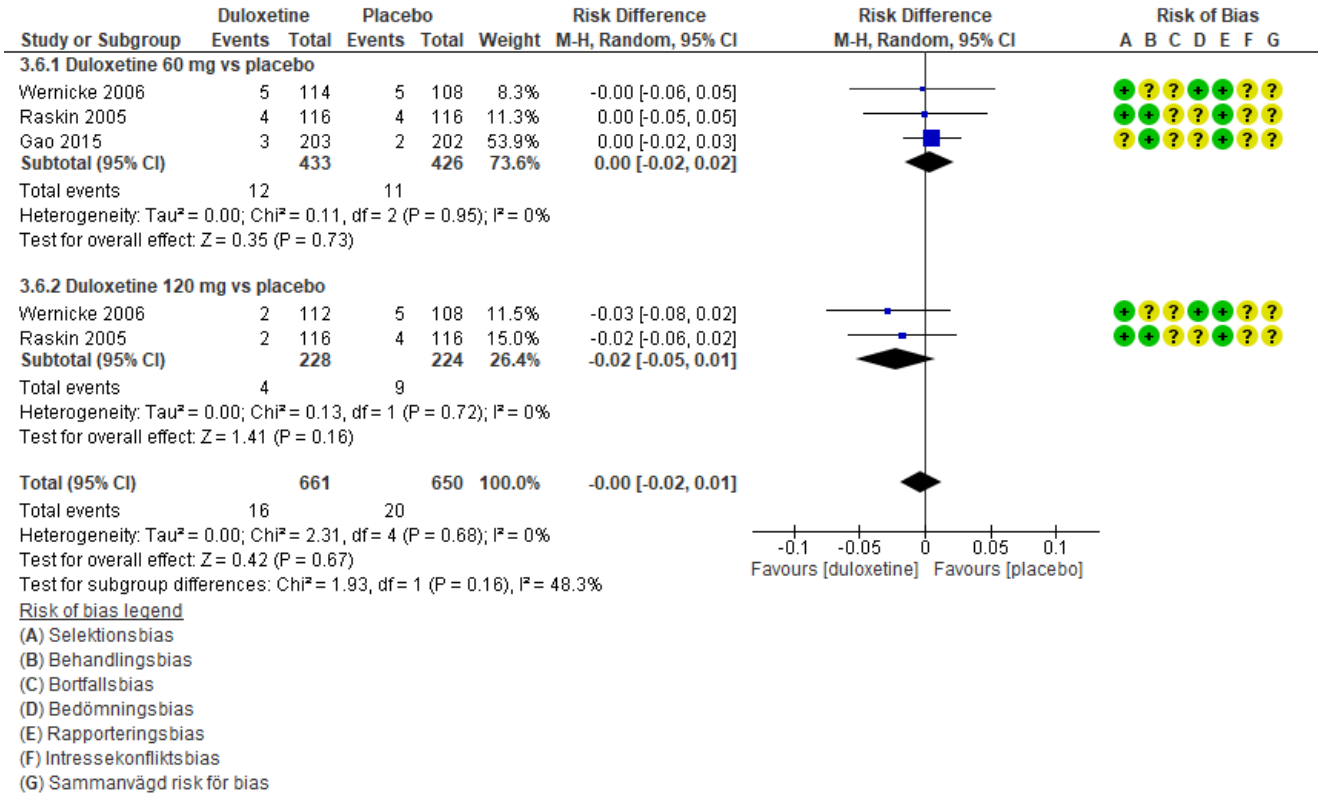


Tabell 2.12 Duloxetin jämfört med placebo (allvarliga biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Duloxetin 20–120 mg jämfört med placebo				
Frekvens av allvarliga biverkningar	n=1 087, 3 RCT	Placebo 2,6 %, duloxetin 2,4 %. Absolut riskskillnad 0,2 % (95 % KI, –2,0 till 1,0 %).	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet överlappar 0.

Figur 2.12 Metaanalys duloxetin jämfört med placebo (allvarliga biverkningar).

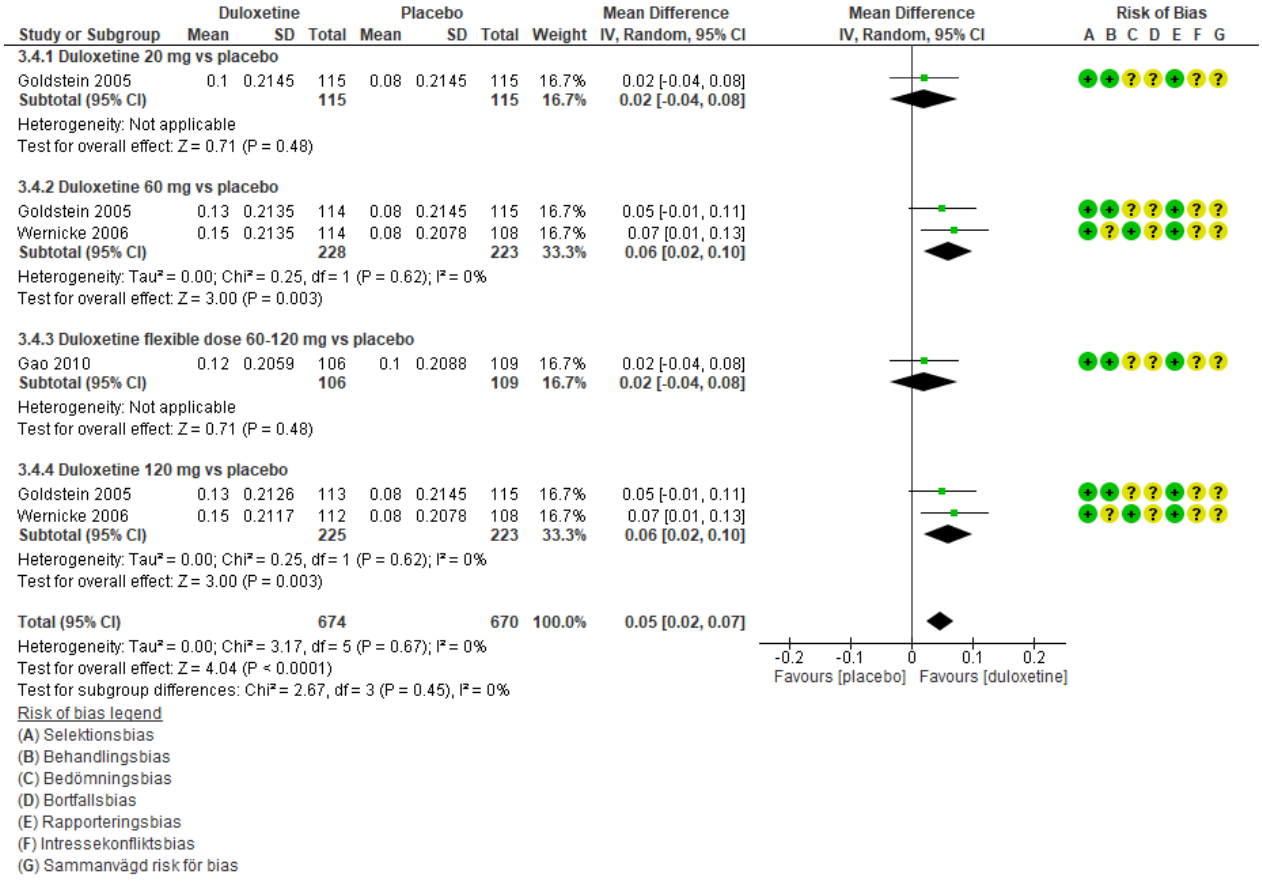


Tabell 2.13 Duloxetin jämfört med placebo (livskvalitet).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Duloxetin 20–120 mg jämfört med placebo				
Påverkan på livskvalitet mätt med EQ-5D (0–1)	n=666 3 RCT	Duloxetin förbättrar livskvaliteten med i genomsnitt 0,05 (95 % KI, 0,02 till 0,07) skalsteg enligt EQ-5D	⨁⨁⨁ Måttlig tillförlitlighet för en mycket liten[1] effekt med duloxetin vad gäller jämfört medkvalitet	Överförbarhet[2]: –1

1) En förändring med 0,05 skalsteg på EQ-5D skalan 0–1 bedömer vi som en mycket liten effekt.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.13 Metaanalys duloxetin jämfört med placebo (livskvalitet).



Tabell 2.14 Venlafaxin. Data i tabellen kommer från studien av Rowbotham och medarbetare [40].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Venlafaxin 75–225 mg jämfört med placebo				
Förändring i smärta mätt med VAS-skala (0–100 mm)	n=244 1 RCT	Venlafaxin 75 mg jämfört med placebo – 3,7 mm, icke signifikant skillnad, spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2
Förändring i smärta mätt med VAS-skala (0–100 mm)	n=244 1 RCT	Venlafaxin 150–225 mg jämfört med placebo – 15,1 mm, p<0,001, spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[4]: –1
Andel patienter som avbryter behandling på grund av biverkningar	n=244 1 RCT	Placebo (3,7 %), venlafaxin 75 mg (7,4 %), eller venlafaxin 150–225 mg (9,8 %). Icke signifikant skillnad, spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Risk för bias: Vissa utfallsmått samt spridningsdata rapporteras inte, vilket medför hög risk för rapporteringsbias.
3) Bristande precision: Ingen statistisk signifikant skillnad samt spridningsdata saknas.
4) Bristande precision: Spridningsdata saknas.

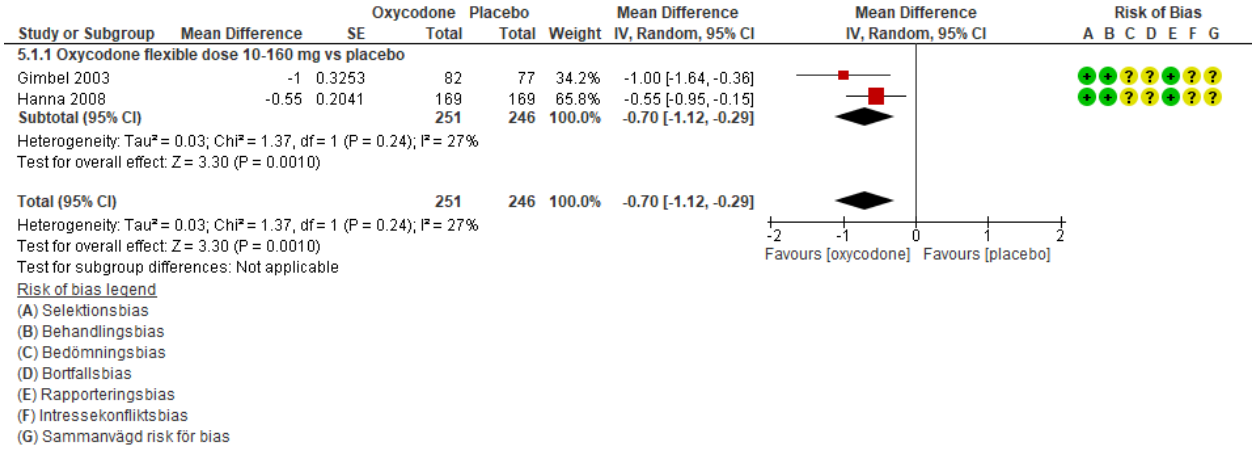
Opioider

Tabell 2.15 Oxikodon jämfört med placebo (medelvärdesskillnad smärta).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Oxikodon 10–160 mg jämfört med placebo				
Förändring på numerisk smärtskala (0–10)	n=497 2 RCT	Oxikodon minskar smärta med igenomsnitt 0,7 skalsteg (95 % KI, 0,29 till 1,12) mer än placebo	⊕⊕⊕ Måttlig tillförlitlighet för en *mycket liten*[1] effekt av oxikodon vad gäller smärta	Överförbarhet[2]: –1

1) En effektskillnad vad gäller smärta med cirka 0,7 skalsteg på en skala 0–10 bedömer vi som en *mycket liten* effekt.
2) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.

Figur 2.14 Metaanalys oxikodon jämfört med placebo (medelvärdesskillnad smärta).

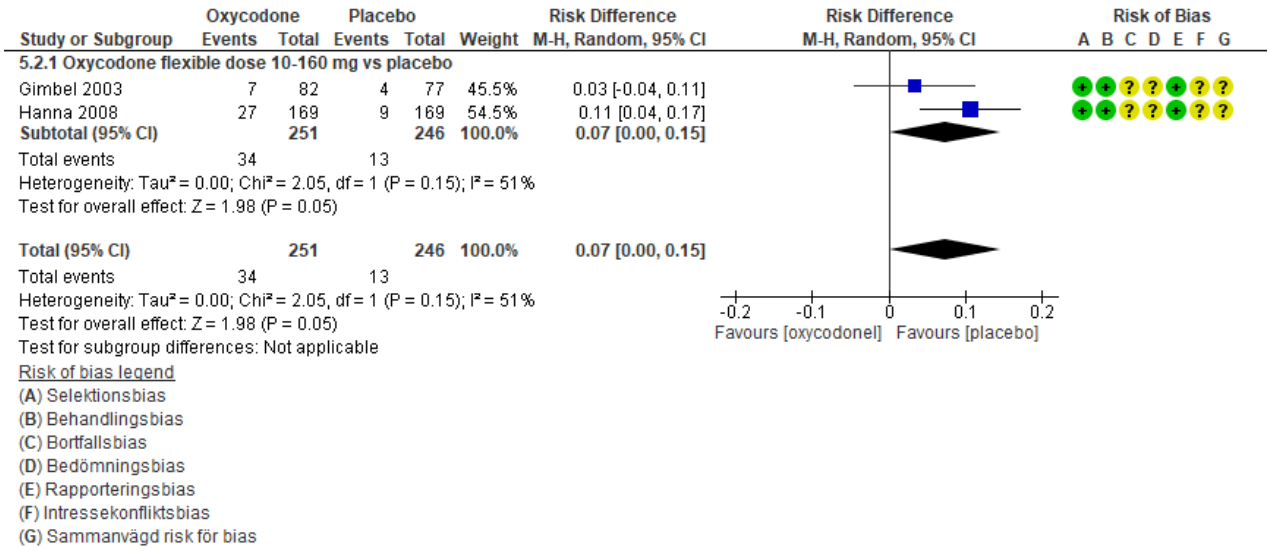


Tabell 2.16 Oxikodon jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Oxikodon 10–160 mg jämfört med placebo				
Andel patienter som avbryter behandling på grund av biverkningar	n=497 2 RCT	Placebo 5,3 %, oxikodon 13,5 %. Absolut riskökning 8,3 %[1] (95 % KI, 0 % till 15 %). NNH=12.	⨁⨁ Låg tillförlitlighet för en *måttlig*[2] riskökning för behandlingsavbrott p.g.a. biverkningar	Överförbarhet[3]: –1 Precision[4]: –1

1) Data för absolut riskökning och NNH gäller behandling under studietidens längd. Genomsnittlig uppföljningstid i de ingående studierna var nio veckor.
2) En absolut riskökning på 8 procent med nio veckors behandling bedömer vi som en *måttlig* riskökning.
3) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
4) Bristande precision: konfidensintervallet angränsar 0.

Figur 2.15 Metaanalys oxikodon jämfört med placebo (behandlingsavbrott p.g.a. biverkningar).



Tabell 2.17 Tramadol respektive buprenorfi jämfört med placebo.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Tramadol 100–400 mg jämfört med placebo				
Förändring i smärta på en Likertskala (0–4)	n=131 1 RCT [33]	Tramadol minskar smärta med i genomsnitt 0,7 skalsteg mer än placebo, p<0,001 Spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=131 1 RCT [33]	Placebo 1,5 %, tramadol 13,8 %. Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2
Buprenorfin 5–40 µg/h jämfört med placebo				
Andel patienter där smärtan minskar 30 % eller mer under studiens gång på en numerisk skala (0–10)	n=186 1 RCT [45]	Buprenorfin 51,7 %, placebo 41,3%, p=0,175. Spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2

Andel patienter som avbryter behandling på grund av biverkningar	n=186 1 RCT [45]	Placebo 6,5 %, buprenorfin 30,1%. Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Risk för bias: stora bortfall i studierna av Harati et al [33] samt Simpson et al [45] innebär hög risk för bortfallsbias.
3) Bristande precision: Spridningsdata och/eller statistisk analys saknas.

Topikalt lokalbedövande

Tabell 2.18 Capsaicin.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Capsaicinkräm 0,075 % jämfört med vehikel				
Förändring i smärta mätt med VAS-skala (0–100 mm)	n=277 1 RCT [22]	Cirkapsaicinkräm jämfört med vehikel –9,4 mm. Spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=277 1 RCT [22]	Vehikel 3,6 %, cirkapsaicin 13,0 %. Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2
Cirkapsaicinplåster 8 % jämfört med placebo				
Förändring i smärta på numerisk skala (0–10)	n=369 1 RCT [44]	Cirkapsaicin minskar smärta med i genomsnitt 0,47 (95 % KI, 0,26 till 0,88) skalsteg mer än placebo	⊕⊕ Låg tillförlitlighet för en *mycket liten*[4] effekt av cirkapsaicinplåster vad gäller smärta	Överförbarhet[1]: –1 Risk för bias[2]: –1
Cirkapsaicinplåster 8 % jämfört med konventionell vård				
Procentuell förändring i livskvalitet mätt med skalan Norfolk QoL.	n=468 1 RCT [49]	*30 min applicering*: Förbättring med 20,9 procent–enheter (95 % KI, 10,1 till 31,7) . *60 min applicering*: Förbättring med 26,1 procent–enheter (95 % KI, 15,4 till 36,8)	⊕⊕ Låg tillförlitlighet för en *mycket liten*[5] effekt av cirkapsaicinplåster vad gäller livakvalitet	Överförbarhet[1]: –1 Risk för bias[2]: –1
Andel patienter som avbryter behandling på grund av biverkningar	n=468 1 RCT [49]	Cirkapsaicinplåster 4,8 %, konventionell vård 1,9 %. Statistsik analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Risk för bias[2]: –1 Precision[3]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Risk för bias: Hög risk för behandlingsbias. En av studierna var oblindad och de övriga två studierna bedömdes ha hög risk för att patient och/eller prövare får reda på patientens allokering p.g.a. den aktiva substansens egenskaper.
3) Bristande precision: Spridningsdata och/eller statistisk analys saknas.
4) En effektskillnad vad gäller smärta med cirka 0,5 skalsteg på en skala 0–10 bedömer vi som en mycket liten effekt.
5) En effektskillnad vad gäller lijämfört medkvalitet med cirka 25 procentenheter bedömer vi som en mycket liten effekt.

Direkta jämförelser mellan två eller flera olika läkemedel

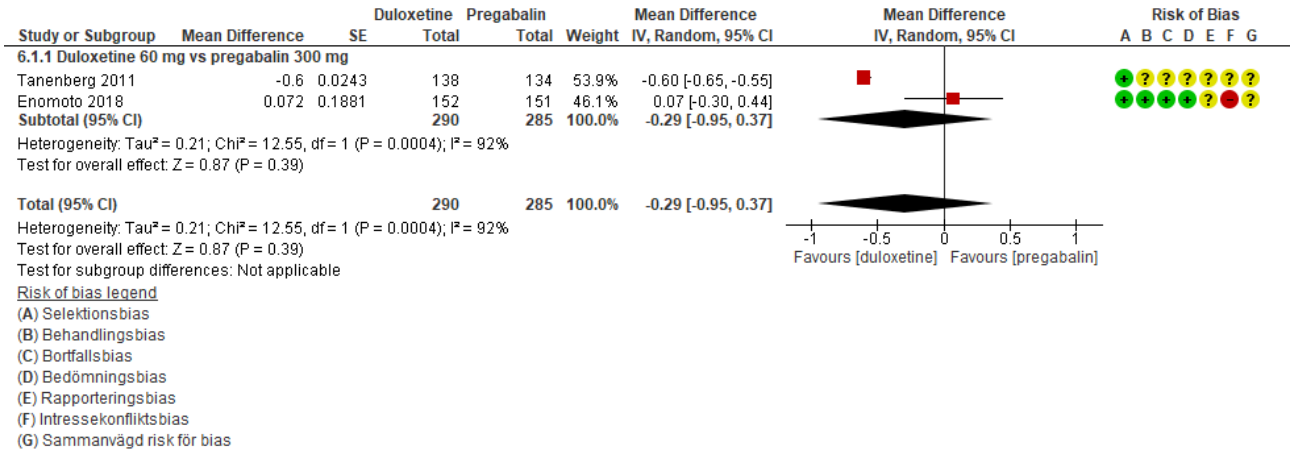
Tabell 2.19 Direkta jämförelser mellan två eller flera olika läkemedel.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 300–600 mg jämfört med duloxetin 60–120 mg jämfört med amitryptilin 25–50 mg jämfört med placebo				
Förändring i smärta mätt med en numerisk smärtskala (0–10)	n=83 1 RCT [20]	Skillnad i antal skalsteg baslinje–studieslut: Pregabalin –0,7 Duloxetin: –1,2 Amitryptilin: –1,1. Spridningsdata saknas. Inga statistiskt signifikanta skillnader mellan några av behandlingsarmarna.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Förändring i livskvalitet mätt med SF-36	n=83 1 RCT [20]	Skillnad i antal skalsteg baslinje–studieslut: Pregabalin –0,4 Duloxetin: +0,8 Amitryptilin: +0,6. Spridningsdata saknas. Inga statistiskt signifikanta skillnader mellan behandlingsarmarna.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=83 1 RCT [20]	Pregabalin 22 %, duloxetin 11 %, amitryptilin 4 %. Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Gabapentin jämfört med nortriptylin jämfört med gabapentin + nortriptylin. Doser titrerade till maximalt tolererbara.				
Förändring i smärta mätt med en numerisk smärtskala (0–10)	n=56 1 RCT [27]	Kombination jämfört med gabapentin –0,9 skalsteg (spridningsdata saknas) Kombination jämfört med nortriptylin –0,6 skalsteg (spridningsdata saknas).	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

Förändring i livskvalitet mätt med SF-36	n=56 1 RCT [27]	Förändring baslinje till studieslut: gabapentin +8,6, nortriptylin +6,3, kombination +9,5. Spridningsdata saknas. Inga statistiskt signifikanta skillnader mellan behandlingsarmarna.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=56 1 RCT [27]	Gabapentin 0 %, nortriptylin 11 %, kombination 16 %. Statistisk analys saknas.	Mycket låg tillförlitlighet ⊕	Överförbarhet[1]: –1 Precision[2]: –2
Pregabalin 300 mg jämfört med duloxetin 60 mg jämfört med kombination av de båda				
Andel patienter som avbryter behandling på grund av biverkningar	n=407 1 RCT [46]	Duloxetin 19,6 %, pregabalin 10,4 % (p=0.04 jämfört med duloxetin), combination 13,3 %, (n.s jämfört med duloxetin)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Pregabalin 300 mg jämfört med duloxetin 60 mg				
Förändring i smärta mätt med en numerisk smärtskala (0–10)	n=575 2 RCT	Duloxetin jämfört med pregabalin –0,29 skalsteg (95 % KI, –0,95 till 0,37)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[3]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Spridningsdata och/eller statistisk analys saknas
3) Bristande precision: Konfidensintervallet överlappar 0.

Figur 2.16 Metaanalys duloxetin jämfört med pregabalin (medelvärdesskillnad smärta).

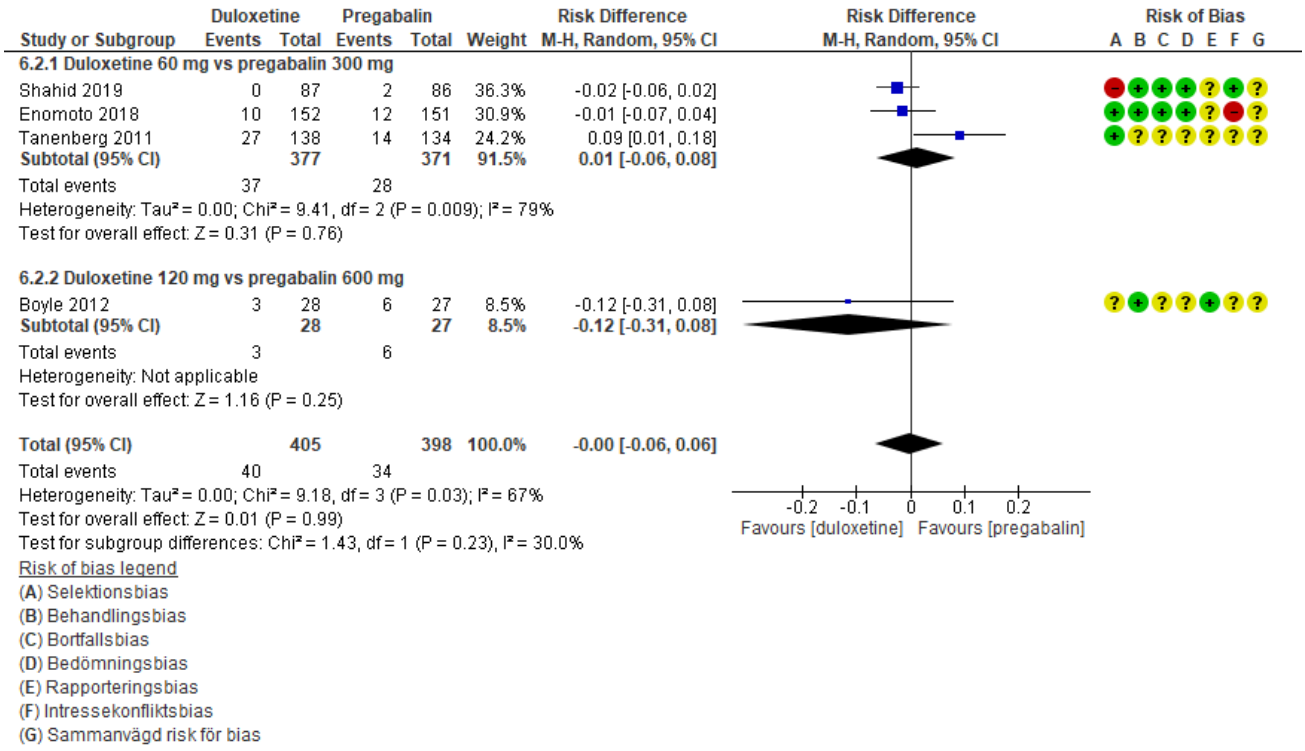


Tabell 2.20 Direkta jämförelser mellan pregabalin och duloxetin (behandlingsavbrott p.g.a. biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 300 mg jämfört med duloxetin 60 mg				
Andel patienter som avbryter behandling på grund av biverkningar	n=803 4 RCT	Duloxetin 9,9 %, pregabalin 8,5 %. Skillnad 1,4 % (95 % KI, –6 till 6 %)	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet överlappar 0.

Figur 2.17 Metaanalys pregabalin jämfört med duloxetin (behandlingsavbrott p.g.a. biverkningar).

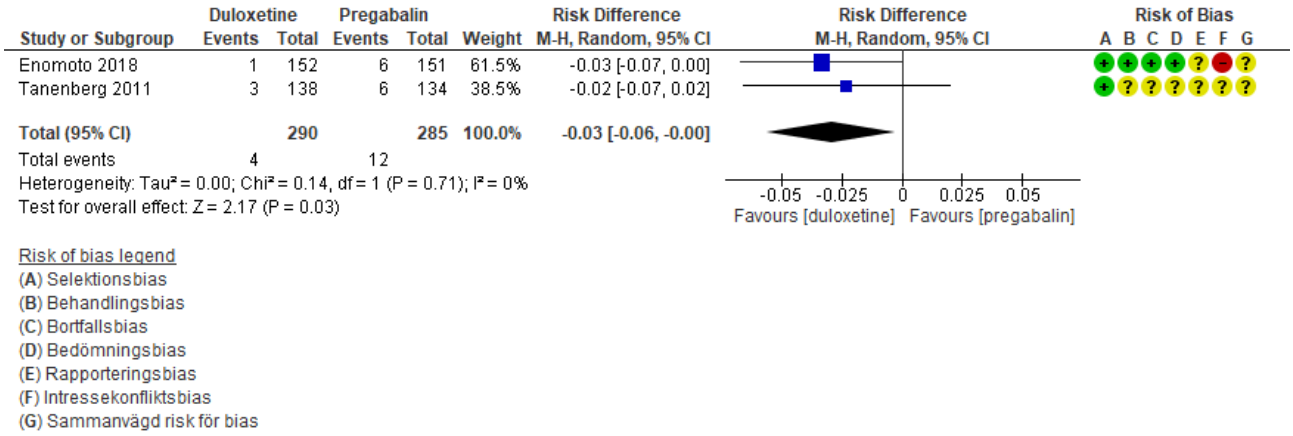


Tabell 2.21 Direkta jämförelser mellan pregabalin och duloxetin (allvarliga biverkningar).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Pregabalin 300 mg jämfört med duloxetin 60 mg				
Frekvens av allvarliga biverkningar	n=575 2 RCT	Duloxetin 1,4 %, pregabalin 4,2 %. Skillnad 2,8 % (95 % KI, –6 till 0 %)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Konfidensintervallet angränsar 0.

Figur 2.18 Metaanalys pregabalin jämfört med duloxetin (allvarliga biverkningar).



Tabell 2.22 Direkta jämförelser mellan två eller flera olika läkemedel (fortsättning).

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i veten skapligt underlag	Kommentarer
Pregabalin 300 mg jämfört med duloxetin 60 mg				
Förändring i smärta mätt med en numerisk smärtskala (0–10)	n=173 1 RCT [42]	Duloxetin jämfört med pregabalin –0,72 skalsteg (spridningsdata saknas, n.s.)	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=173 1 RCT [42]	Duloxetin 0 %, pregabalin 2,3 % (statistisk analys saknas)	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Duloxetin 60 mg x 2 jämfört med Duloxetin 120 mg x 1				
Förändring i smärta mätt med en numerisk smärtskala (0–10)	n=449 1 RCT [38]	Duloxetin 60 mg x 2 jämfört med duloxetin 120 mg x 1 –0,0 skalsteg (spridningsdata saknas)	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=449 1 RCT [38]	Duloxetin 60 mg x 2 20,1 %, duloxetin 120 mg x 1 27,0 %. (statistisk analys saknas)	⨁ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

Frekvens av allvarliga biverkningar	n=449 1 RCT [38]	Duloxetin 60 mg x 2 7,5 %, duloxetin 120 mg x 1 8,7 %. (statistisk analys saknas)	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Lidokainplåster 5 % jämfört med Pregabalin titrering till max 600 mg				
Andel responders enligt en definierad förändring på en numerisk smärtskala (0–3)	n=311 1 RCT [17]	Lidokainplåster 68 %, pregabalin 68,3% (n.s.) Spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Förändring i smärta mätt med en numerisk smärtskala (0–3)	n=311 1 RCT [17])	Förändring från baslinje till studieslut (SD): Lidokainplåster –2,4 (2,07), pregabalin –2,0 (2,24). Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Andel patienter som avbryter behandling på grund av biverkningar	n=311 1 RCT [17]	Lidokainplåster 5,8 %, pregabalin 25,5 %. (Statistisk analys saknas).	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Påverkan på livskvalitet mätt med EQ-5D (0–1)	n=311 1 RCT [17]	Förändring från baslinje till studieslut (SD): Lidokainplåster +0,13 (0,245), pregabalin +0,06 (0,211). Statistisk analys saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2
Cirkapsaicinkräm 0,075 % jämfört med amitryptilin 25–125 mg				
Andel patienter som rapporterade åtminstone ”bättre” i prövarvärderad smärta mätt med numerisk skala i sex steg	n=235 1 RCT [19]	Cirkapsaicinkräm 73 %, amitriptylin 73 %. Statistisk analys samt spridningsdata saknas.	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –
Förändring i patientvärderad smärta mätt med VAS-skala (0–100 mm)	n=235 1 RCT [19]	Förändring från baslinje till studieslut (SD): Cirkapsaicinkräm – 26,1 (2,9),	⊕ Mycket låg tillförlitlighet	Överförbarhet[1]: –1 Precision[2]: –2

		amitriptylin –29,1 (3,0). Spridningsdata vad gäller skillnad i förändring mellan grupperna saknas.		

1) Bristande överförbarhet: Studiedeltagarna var i genomsnitt cirka 60 år. Vår frågeställning berör individer 65 år och äldre.
2) Bristande precision: Spridningsdata och/eller statistisk analys saknas

Del III: Läkemedelsbehandling vid kotkompression hos äldre

Resultat identifierade i systematiska översikter

En systematisk översikt identifierades [52] som inte fann några studier relevanta för vårt PICO.

Resultat identifierade i primärstudier

Inga primärstudier hittades.

Del IV: Risk för akut njurpåverkan vid NSAID–behandling av individer 65 år eller äldre

Resultat identifierade i systematiska översikter

En systematisk översikt identifierades [53]. Denna fann fyra studier [54-57] som studerade individer 65 år eller äldre. En av dessa [56] exkluderades på grund av fel intervention.

Resultat identifierade i primärstudier

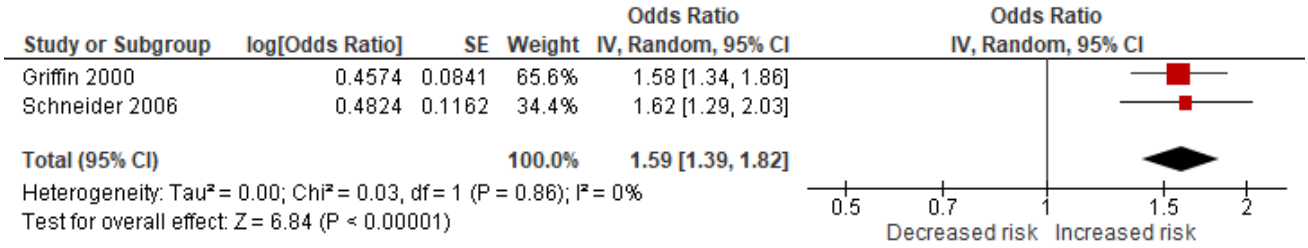
Ytterligare en primärstudie [58] inkluderades, vilken publicerades efter Zhang och medarbetare utförde sin sökning.

Tabell 4.1 Risk för sjukhusinläggning p.g.a. akut njurpåverkan med NSAID–användning hos äldre.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
NSAID–användning jämfört med ingen NSAID–användning				
Risk för sjukhusinläggning p.g.a. akut njurpåverkan	n=100 466 2 NRSI	Justerad oddskvot 1,59 (95 % KI, 1,39 till 1,82).	⨁⨁ Låg tillförlitlighet för en *måttlig*[1] riskökning med NSAID–användning hos äldre	Risk för bias[2]: –2

1) En oddskvot på 1,6 bedömer vi som en *måttlig* riskökning.
2) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.

Figur 4.1 Metaanalys risk för sjukhusinläggning p.g.a. akut njurpåverkan med NSAID–användning hos äldre.



Tabell 4.2 Risk för akut njurpåverkan med NSAID–behandling hos kvinnor respektive män.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
NSAID–användning jämfört med ingen NSAID–användning				
Risk för sjukhusinläggning p.g.a. akut njurpåverkan	n=1 445 1 NRSI [54]	Män: Justerad oddskvot 1,48 (95 % KI, 1,08 till 2,11). Kvinnor: Justerad oddskvot 1,59 (95 % KI, 1,32 till 1,91).	⊕ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: –2

1) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.
2) Precision: Konfidensintervallen för oddskvoten hos kvinnor respektive män överlappar varandra.

Tabell 4.3 Risk för serumkreatinistegring med NSAID–användning hos äldre.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Risk för serumkreatininstegring ≥150 µmol/L jämfört med inte kreatininstegring <120 µmol/L				
NSAID–användning den senaste månaden	n=299 1 NRSI [55]	Oddskvot i NSAID användning mellan patienter med respektive utan serumkreatininstegring (95 % KI): 1,8 (0,97 till 3,4)	⊕ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: –2

1) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.
2) Bristande precision: Oddskvotens konfidensintervall överlappar 1.

Tabell 4.4 Risk för akut njurskada med NSAID–användning hos äldre.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
NSAID–användning jämfört med ingen NSAID–användning				
Risk för akut njurskada	n=92 214 1 NRSI [58]	Oddskvot 1,41 (95 % KI, 1,20 till 1,65).	⨁⨁ Låg tillförlitlighet för ökad risk med NSAID–användning	Risk för bias[1]: –2

1) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.

Del V: Risk för PUB (perforationer, ulcus eller blödning) vid NSAID–behandling av individer 65 år eller äldre

Resultat identifierade i systematiska översikter

En relevant systematisk översikt [59] med analys av individuella patientdata från 274 primärstudier inkluderades.

Tabell 5.1 Risk för PUB hos individer över 60 år. Data i tabellen kommer från den systematiska översikten av CNT Collaboration [59].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
tNSAID[1] jämfört med placebo				
Absolut risk för PUB hos individer 60 år och äldre	43 261 individer 158 RCT	tNSAID[1] 1,24 %, placebo 0,37 %. Absolut riskökning 0,87 %[2]. NNH=115. Rate ratio 3,12 (95 % KI, 1,98 till 4,91).	⨁⨁⨁ Måttlig tillförlitlighet för en *måttlig*[3] riskökning för PUB hos äldre med tNSAID jämfört med placebo	Risk för bias[4]: –1
Coxiber jämfört med placebo				
Absolut risk för PUB hos individer 60 år och äldre	29 099 individer 184 RCT	Coxiber 0,74 %, placebo 0,37 %. Absolut riskökning 0,37 %[2]. NNH=270. Rate ratio 1,77 (95 % KI, 1,14 till 2,74).	⨁⨁⨁⨁ Hög tillförlitlighet för en *liten*[5] riskökning för PUB hos äldre med coxiber jämfört med placebo	
tNSAID[1] jämfört med coxiber				

Absolut risk för PUB hos individer 60 år och äldre	61 248 individer 103 RCT	tNSAID[1] 1,24 %, coxiber 0,78 %. Absolut riskökning 0,46 %[2]. Rate ratio 0,58 (95 % KI, 0,47 till 0,72).	⨁⨁⨁⨁ Hög tillförlitlighet för en *liten*[5] riskökning för PUB hos äldre med coxiber jämfört med tNSAIDs	

1) tNSAID: Traditionella NSAID eg. ibuprofen och diklofenak.
2) Data på absolut riskförändring samt Numbers needed to harm (NNH) ajämfört meder behandling under ett år.
3) En årlig absolut riskökning på 0,9 procent bedömer vi som en *måttlig* riskökning.
4) Risk för bias: Indirekt jämförelse med coxiber som gemensam direkt jämförelse.
5) En årlig absolut riskökning på 0,4 procent bedömer vi som en *liten* riskökning.

Tabell 5.2 Risk för PUB hos kvinnor respektive män. Data i tabellen kommer från den systematiska översikten av CNT Collaboration [59].

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
tNSAIDs[1] jämfört med placebo				
Absolut risk för symtomatisk övre gastrointestinal händelse (perforation, ulcus, obstruktion eller blödning) hos kvinnor respektive män	43 261 individer, 158 RCT	Män: Rate ratio 3,70 (95 % KI, 2,08 till 6,60) Kvinnor: Rate ratio 3,19 (95 % KI, 1,77 till 5,75)	⨁ Mycket låg tillförlitlighet	Precision[2]: –2 Risk för bias[3,4]: –2
Coxiber jämfört med placebo				
Absolut risk för symtomatisk övre gastrointestinal händelse (perforation, ulcus, obstruktion eller blödning) hos kvinnor respektive män	29 099 individer, 184 RCT	Män: Rate ratio 2,19 (95 % KI, 1,35 till 3,55) Kvinnor: Rate ratio 1,63 (95 % KI, 0,86 till 3,08)	⨁ Mycket låg tillförlitlighet	Precision[2]: –2 Risk för bias[4]: –1
Coxiber jämfört med tNSAIDs				
Absolut risk för symtomatisk övre gastrointestinal händelse (perforation, ulcus, obstruktion eller blödning) hos	61 248 individer, 103 RCT	Män: Rate ratio 0,57 (95 % KI, 0,39 till 0,82) Kvinnor: Rate ratio 0,56 (95 % KI, 0,45 till 0,69)	⨁ Mycket låg tillförlitlighet	Precision[2]: –2 Risk för bias[4]: –1

kvinnor respektive män				

1) tNSAIDs: Traditionella NSAIDs eg. ibuprofen och diklofenak.
2) Precision: Konfidensintervallen för rate ratio hos kvinnor respektive män överlappar varandra.
3) Risk för bias: Indirekt jämförelse med coxiber som gemensam direkt jämförelse.
4) Risk för bias: Skillnad i baslinjerisk för kvinnor respektive män med ajämfört medeende på gastrointestinala PUB kan snedvrida resultatet i post–hoc analys på eventuella riskskillander med ajämfört medeende på kön.

Resultat identifierade i primärstudier

Tre relevanta primärstudier [60-62] med låg risk för bias inkluderades.

Tabell 5.3 Fynd från primärstudier på risken för PUB med NSAID–användning hos äldre.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
tNSAID med PPI jämfört med tNSAID utan PPI				
Risk för sjukhusinläggning p.g.a. PUB	n=7 708 1 NRSI [60]	Oddskvot 0,69 (95 % KI, 0,47 till 1,03).	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: –2
Coxib jämfört med tNSAID				
Risk för sjukhusinläggning p.g.a. PUB	n=7 708 1 NRSI [60]	Ingen statistiskt signifikant skillnad i risk, OR 0,88 (95 % KI, 0,64 till 1,22).	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: –2
tNSAID med PPI, individer ≥75 år jämfört med individer <75 år				
Risk för sjukhusinläggning p.g.a. PUB	n=7 708 1 NRSI [60]	Oddskvot 0,79 (95 % KI, 0,6 till –0,99).	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[3]: –1
Coxib med PPI, individer ≥75 år jämfört med individer <75 år				
Risk för sjukhusinläggning p.g.a. PUB	n=7 708 1 NRSI [60]	Oddskvot 0,84 (95 % KI, 0,7 till 1,00).	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: –2
Coxib utan PPI, individer ≥75 år jämfört med individer <75 år				
Risk för sjukhusinläggning p.g.a. PUB	n=7 708 1 NRSI [60]	Oddskvot 1,22 (95 % KI, 1,01 till 1,47).	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[3]: –1

Coxibanvändning hos patienter som läggs in på sjukhus p.g.a. PUB				
Coxibanvändning en månad före sjukhusinläggning jämfört med användning i månaden innan dess	n=40 635 1 NRSI [61]	Oddskvot 65–79 år, 1,97 (95 % KI, 1,53 till 2,54). Oddskvot ≥80 år, 1,63 (1,18 till 2,24).	⊕ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[3]: –1
tNSAID–användning hos patienter som läggs in på sjukhus p.g.a. PUB				
tNSAID–användning en månad före sjukhusinläggning jämfört med användning i månaden innan dess	n=40 635 1 NRSI [61]	Oddskvot 65–79 år, 3,42 (95 % KI, 3,14 till 3,72). Oddskvot ≥80 år, 4,35 (3,85 till 4,93).	⊕ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[3]: –1
Celecoxib 200 mg jämfört med diklofenak 100 mg				
Andel patienter som avbryter behandling p.g.a. biverkan	n=925, 1 RCT [62]	Celecoxib jämfört med diklofenak – 3.9 % (95 % KI, –9.8 till 1.9).	⊕ Mycket låg tillförlitlighet	Precision[2]: –2 Risk för bias[4]: –1

1) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.
2) Bristande precision: Avdrag med två steg p.g.a. att oddskvotens konfidensintervall överlappar 1.
3) Bristande precision: Avdrag med ett steg p.g.a. att oddskvotens konfidensintervall angränsar till 1 och/eller få händelser.
4) Risk för bias: Bortfallen var cirka 40 procent i båda grupperna i studien.

Del VI: Risk för fall vid opioid–behandling av individer 65 år eller äldre

Resultat identifierade i systematiska översikter

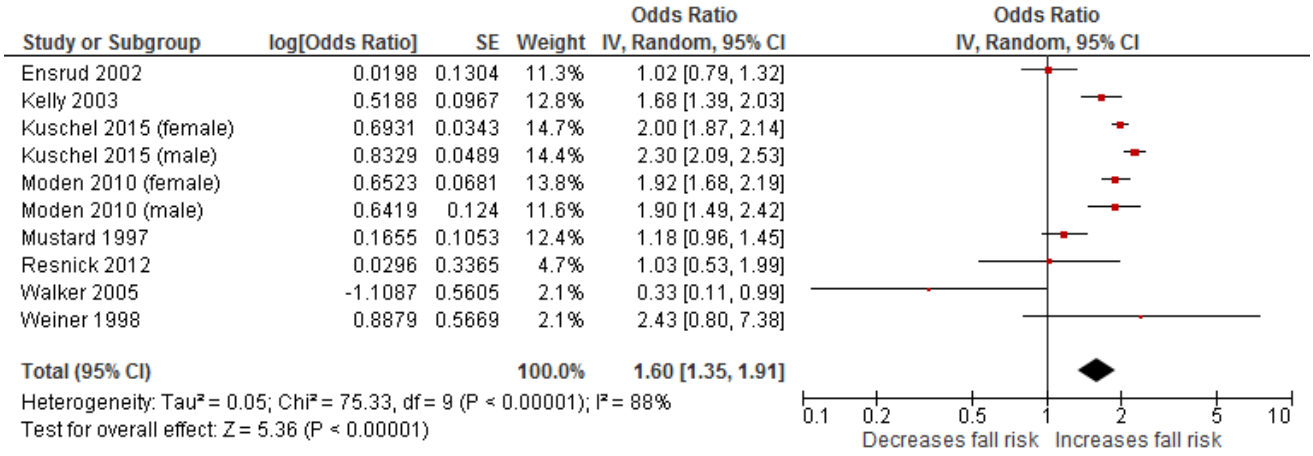
En systematisk översikt inkluderades [63].

Tabell 6.1 Risk för fall hos äldre med opioid–användning. Data i tabellen kommer från den systematiska översikten av Seppälä och medarbetare [63].

Effektmått	Antal patienter (studier)	Sammanvägd effekt	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Opioidanvändning jämfört med ingen opioidanvändning				
Risk för fall	n=366 036, 8 NRSI	Ökad risk med opioidanvändning, OR 1,60 (95 % KI, 1,35 till 1,91).	⊕⊕ Låg tillförlitlighet för en *måttlig*[1] riskökning för fall vid opioidanvändning hos äldre	Risk för bias[2]: –2

1) En oddskvot på 1,6 bedömer vi som en *måttlig* riskökning.
2) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.

Figur 6.1 Metaanalys risk för fall hos äldre med opioid–användning. Data i analysen kommer från den systematiska översikten av Seppälä och medarbetare [63].



Resultat identifierade i primärstudier

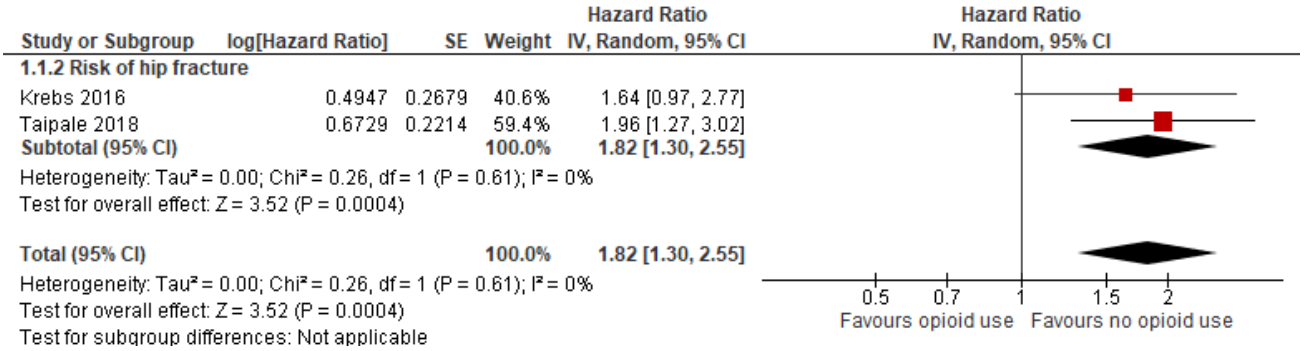
5 relevanta primärstudier [64-68] med låg risk för bias inkluderades.

Tabell 6.2 Risk för fall som resulterar i höftfraktur hos äldre med opioid–användning.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Opioidanvändning jämfört med ingen opioidanvändning				
Risk för fall som resulterar i höftfraktur	12 232 individer, 2 NRSI	Ökad risk med opioidanvändning, HR 1,82 (95 % KI, 1,30 till 2,55).	⨁⨁ Låg tillförlitlighet för en *måttlig*[1] riskökning för fall som resulterar i höftfraktur vid opioidanvändning hos äldre	Risk för bias[2]: –2

1) En hazardkvot på 1,8 bedömer vi som en *måttlig* riskökning.
2) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.

Figur 6.2 Metaanalys risk för fall som resulterar i höftfraktur hos äldre med opioid–användning.



Tabell 6.3 Övriga fynd från primärstudier på risken för fall hos äldre med opioidanvändning.

Utfallsmått	Antal individer respektive studier	Sammanvägt resultat	Tillförlitlighet i vetenskapligt underlag	Kommentarer
Opioidanvändning				
Risk för fall	67 929 individer, 1 NRSI [64]	2,4 gånger vanligare (95 % KI, 1,9 till 3,0) med opioidanvändning hos de som har fallit jämfört med de som har skadat sig på annat sätt	⨁⨁ Låg tillförlitlighet för ökad risk för fall vid opioidanvändning hos äldre	Risk för bias[1]: –2
Tramadol jämfört med oxikodon				
Risk för fall som resulterar i sjukhusinläggning p.g.a. fraktur	65 250 individer, 1 NRSI [66]	Antal sjukhusinläggningar p.g.a. fraktur per 100 personår: Tramadol 5,0 (95 % KI, 4,3 till 5,7), oxikodon 9,4 (95 % KI, 7,5 till 11,7). Statistisk analys saknas.	⨁ Mycket låg tillförlitlighet	Risk för bias[1]: –2 Precision[2]: – 2
Opioid–användning jämfört med ingen opioid–användning				
Risk för fall som resulterar i fraktur hos patienter med yrsel	20 645 individer, 1 NRSI [65]	HR 3,59 (95 % KI, 1,97 till 6,13)	⨁⨁ Låg tillförlitlighet för en *stor*[3] riskökning för fall med opioidanvändning hos äldre patienter med yrsel	Risk för bias[1]: –2

1) Risk för bias: Bias från confounding p.g.a. icke–randomiserad studiedesign.
2) Bristande precision: Statistisk analys saknas.
3) En hazardkvot på 3,6 bedömer vi som en *stor* riskökning.

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Bilaga 5
Läkemedelsbehandling av vanliga smärttillstånd hos äldre personer/ Pharmacological treatment of common pain conditions in the elderly, rapport 315 (2020)

Bilaga 5 - Tabeller över risk för bias i studier med kvantitativ metodik

Innehållsförteckning

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Tabell 1. Bedömning av risk för bias (enligt SBU:s granskningsmall för systematiska översikter) i relevanta systematiska översikter för artros.

Författare, år, ref	Syfte och kriterier för urval av studier	Identifikation och val av studier	Bedömning av studier och dataextraktion	Analys och syntes	Sammantagen bedömning
Leopoldini et al, 2019, [1]	Låg	Låg	Låg	Oklar	Låg
Osani et al, 2019, [2]	Låg	Oklar	Låg	Oklar	Låg
Derry et al, 2016, [3]	Låg	Oklar	Låg	Oklar	Låg
da Costa et al, 2014, [4]	Låg	Oklar	Låg	Låg	Låg
Toupin April et al, 2019, [5]	Låg	Oklar	Låg	Låg	Låg
Megale et al, 2018, [6]	Låg	Låg	Låg	Hög	Hög
Smith et al, 2016, [7]	Oklar	Låg	Låg	Hög	Hög
da Costa et al, 2017, [8]	Låg	Oklar	Låg	Hög	Hög
Gunter et al, 2017, [9]	Låg	Oklar	Hög	Hög	Hög
O´Neil et al, 2012, [10]	Oklar	Oklar	Hög	Hög	Hög
Stewart et al, 2018, [11]	Låg	Hög	Låg	Låg	Hög
Jevsevar et al, 2018, [12]	Låg	Oklar	Låg	Hög	Hög
Jung et al, 2018, [13]	Låg	Oklar	Låg	Hög	Hög

Tabell 2. Bedömning av risk för bias (enligt SBU:s granskningsmall för randomiserade studier) i relevanta primärstudier för artros.

Författare, år, ref	Jämförelse	Selektion	Behandling	Bortfall	Bedömning	Rapportering	Intressekonflikt	Sammanvägd risk
Verkleij et al, 2015, [14]	Diklofenak jämfört med paracetamol	Måttlig	Måttlig	Låg	Låg	Måttlig	Måttlig	Måttlig
Serrie et al, 2017, [15]	Tapentadol jämfört med oxikodon	Måttlig	Måttlig	Måttlig	Låg	Låg	Måttlig	Måttlig
Moss et al, 2017, [15]	Celecoxib jämfört med placebo	Måttlig	Hög	Hög	Hög	Låg	Måttlig	Hög

Tabell 3. Bedömning av risk för bias (enligt SBU:s granskningsmall för systematiska översikter) i relevanta systematiska översikter för diabetesneuropati.

Författare, år, ref	Syfte och kriterier för urval av studier	Identifikation och val av studier	Bedömning av studier och dataextraktion	Analys och syntes	Sammantagen bedömning
Griebeler et al, 2014, [16]	Låg	Hög	Låg	Oklar	Hög
Snedecor et al, 2014, [17]	Låg	Hög	Låg	Låg	Hög
Waldfogel et al, 2017, [18]	Oklar	Hög	Låg	Låg	Hög
Vilar et al, 2018, [19]	Oklar	Hög	Oklar	Oklar	Hög

Tabell 4. Bedömning av risk för bias (enligt SBU:s granskningsmall för randomiserade studier) i relevanta primärstudier för diabetesneuropati.

Författare, år, ref	Jämförelse	Selektion	Behandling	Bortfall	Bedömning	Rapportering	Intressekonflikt	Sammanvägd risk
Freynhagen et al, 2005, [20]	Pregabalin jämfört med placebo	Låg	Måttlig	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Guan et al, 2011, [21]	Pregabalin jämfört med placebo	Måttlig	Låg	Låg	Måttlig	Låg	Måttlig	Måttlig
Huffman et al, 2015, [22]	Pregabalin jämfört med placebo	Låg	Låg	Låg	Låg	Låg	Måttlig	Måttlig
Lesser et al, 2004, [23]	Pregabalin jämfört med placebo	Låg	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig
Mu et al, 2018, [24]	Pregabalin jämfört med placebo	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig	Måttlig
Rosenstock et al, 2004, [25]	Pregabalin jämfört med placebo	Måttlig	Låg	Låg	Låg	Låg	Måttlig	Måttlig
Satoh et al, 2011, [26]	Pregabalin jämfört med placebo	Måttlig	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig
Tölle et al, 2008, [27]	Pregabalin jämfört med placebo	Måttlig	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig
Beydoun et al, 2006, [28]	Oxkarbazepin jämfört med placebo	Låg	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Dogra et al, 2005, [29]	Oxkarbazepin jämfört med placebo	Låg	Måttlig	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Grosskopf et al, 2006, [30]	Oxkarbazepin jämfört med placebo	Måttlig	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig

Shaibani et al, 2009, [31]	Lakosamid jämfört med placebo	Låg	Låg	Hög	Måttlig	Låg	Måttlig	Måttlig
Thienel et al, 2004, [32]	Topiramat jämfört med placebo	Låg	Låg	Hög	Måttlig	Måttlig	Låg	Måttlig
Gao et al, 2015, [33]	Duloxetin jämfört med placebo	Måttlig	Låg	Måttlig	Låg	Låg	Måttlig	Måttlig
Gao et al, 2010, [34]	Duloxetin jämfört med placebo	Låg	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Goldstein et al, 2005, [35]	Duloxetin jämfört med placebo	Låg	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Raskin et al, 2005, [36]	Duloxetin jämfört med placebo	Låg	Låg	Låg	Låg	Låg	Måttlig	Måttlig
Wernicke et al, 2006, [37]	Duloxetin jämfört med placebo	Låg	Låg	Måttlig	Låg	Låg	Måttlig	Måttlig
Yasuda et al, 2011, [38]	Duloxetin jämfört med placebo	Låg	Måttlig	Låg	Låg	Låg	Måttlig	Måttlig
Rowbotham et al, 2004, [39]	Venlafaxin jämfört med placebo	Låg	Låg	Låg	Måttlig	Hög	Måttlig	Måttlig
Donofrio et al, 1991, [40]	Capsaicinkräm jämfört med vehikel	Låg	Hög	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Simpson et al, 2017, [41]	Capsaicinplåstrer jämfört med placebo	Låg	Hög	Låg	Låg	Låg	Måttlig	Måttlig
Vinik et al, 2016, [42]	Capsaicinplåster jämfört med ingen behandling	Måttlig	Hög	Måttlig	Låg	Låg	Måttlig	Måttlig
Harati et al, 1998, [43]	Tramadol jämfört med placebo	Måttlig	Låg	Hög	Låg	Låg	Måttlig	Måttlig
Gimbel et al, 2003, [44]	Oxykodon jämfört med placebo	Låg	Låg	Måttlig	Låg	Låg	Måttlig	Måttlig
Hanna et al, 2008, [45]	Oxykodon jämfört med placebo	Låg	Låg	Måttlig	Låg	Måttlig	Måttlig	Måttlig
Simpson et al, 2016, [46]	Buprenorfin-plåster jämfört med placebo	Låg	Låg	Hög	Låg	Måttlig	Måttlig	Måttlig
Boyle et al, 2012, [47]	Amitryptilin jämfört med duloxetin jämfört med pregabalin	Måttlig	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig

Gilron et al, 2009, [48]	Nortryptilin jämfört med gabapentin jämfört med kombination	Låg	Låg	Måttlig	Måttlig	Måttlig	Låg	Måttlig
Tanenberg et al, 2011, [49]	Duloxetin jämfört med pregabalin jämfört med kombination	Låg	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Shahid et al, 2019, [50]	Duloxetin jämfört med pregabalin	Måttlig	Låg	Låg	Låg	Måttlig	Låg	Måttlig
Raskin et al, 2006, [51]	Duloxetin x1 jämfört med x2	Låg	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Enomoto et al, 2018, [52]	Duloxetin jämfört med pregabalin	Låg	Låg	Låg	Låg	Måttlig	Hög	Måttlig
Baron et al, 2009, [53]	Lidokainplåster jämfört med pregabalin	Måttlig	Måttlig	Låg	Måttlig	Låg	Måttlig	Måttlig
Biesbroeck et al, 1995, [54]	Capsaicinkräm jämfört med amitryptilin	Låg	Måttlig	Låg	Måttlig	Låg	Måttlig	Måttlig
Gorson et al, 1999, [55]	Gabapentin jämfört med placebo	Måttlig	Måttlig	Hög	Måttlig	Måttlig	Måttlig	Hög
Scheffler et al, 1991, [56]	Capsaicinkräm jämfört med vehikel	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Hög
Schwartz et al, 2011, [57]	Tapentadol jämfört med placebo	Hög	Låg	Hög	Låg	Låg	Måttlig	Hög
Shamsinejad et al, 2018, [58]	Topiramat jämfört med gabapentin	Hög	Hög	Hög	Hög	Oklar	Låg	Hög
Vinik et al, 2014, [59]	Tapentadol jämfört med placebo	Hög	Låg	Hög	Måttlig	Låg	Måttlig	Hög

Tabell 5. Bedömning av risk för bias (enligt SBU:s granskningsmall för systematiska översikter) i relevanta systematiska översikter för kotkompression.

Författare, år, ref	Syfte och kriterier för urval av studier	Identifikation och val av studier	Bedömning av studier och dataextraktion	Analys och syntes	Sammantagen bedömning
Rzewuska et al, 2015, [60]	Låg	Låg	Låg	Oklar	Låg

Tabell 6. Bedömning av risk för bias (enligt SBU:s granskningsmall för systematiska översikter) i relevanta systematiska översikter för NSAID och risken för akut njurpåverkan, NSAID och risken för PUB samt opioider och risken för fall.

Författare, år, ref	Syfte och kriterier för urval av studier	Identifikation och val av studier	Bedömning av studier och dataextraktion	Analys och syntes	Sammantagen bedömning
Bhala et al, 2013*, [61]	Låg	Låg	Oklar	Låg	Låg
Zhang et al, 2017, [62]	Låg	Låg	Oklar	Låg	Låg
Seppälä et al, 2018, [63]	Låg	Låg	Låg	Oklar	Låg
Hernandez-Diaz et al, 2000, [64]	Låg	Hög	Oklar	Låg	Hög
Loke et al, 2008, [65]	Oklar	Hög	Hög	Oklar	Hög
Loza, 2008, [66]	Låg	Oklar	Oklar	Hög	Hög
Hegeman et al, 2009, [67]	Oklar	Oklar	Låg	Hög	Hög
Makris et al, 2010, [68]	Låg	Oklar	Hög	Oklar	Hög
Papaleontiou et al, 2010, [69]	Låg	Hög	Oklar	Oklar	Hög
O´Neil et al, 2012, [10]	Oklar	Oklar	Hög	Oklar	Hög
Chen et al, 2014, [70]	Oklar	Oklar	Hög	Oklar	Hög
Oka et al, 2014, [71]	Låg	Hög	Oklar	Oklar	Hög
Park et al, 2015, [72]	Låg	Oklar	Hög	Hög	Hög

*)Bhala et al inkluderade totalt 754 primärstudier och en stor del av materialet är en analys av individuella patientdata (IPD-analys) från de ingående studierna. Författarna har inte gjort en formell bedömning av risken för bias i de ingående studierna men de har inte heller använt resultatet på gruppnivå från flertalet av studierna. På grund av tillvägagångssättet och de objektiva utfallsmåtten bedömer vi den sammantagna risken för bias i översikten som låg.

Tabell 7. Bedömning av risk för bias (enligt SBU:s granskningsmall för icke-randomiserade studier) i relevanta primärstudier för NSAID och risken för akut njurpåverkan.

Författare, år, ref	Confounding	Selektion	Klassificering	Avvikelser	Bortfall	Mätning	Rapportering	Intressekonflikt	Övergripande risk
Henry et al, 1997, [73]	Hög	Låg	Måttlig	Måttlig	Måttlig	Låg	Måttlig	Måttlig	Måttlig
Griffin et al, 2000, [74]	Hög	Låg	Låg	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Schneider et al, 2006, [75]	Hög	Låg	Måttlig	Låg	Måttlig	Måttlig	Låg	Måttlig	Måttlig
Nash et al, 2019, [76]	Hög	Låg	Måttlig	Låg	Måttlig	Låg	Låg	Måttlig	Måttlig
Turgutalp et al, 2017, [77]	Oacceptabelt Hög	Måttlig	Oacceptabelt Hög	Måttlig	Hög	Hög	Hög	Måttlig	Hög

Tabell 8. Bedömning av risk för bias (enligt SBU:s granskningsmall för randomiserade studier) i relevanta randomiserade primärstudier för NSAID och risken för PUB.

Författare, år, ref	Jämförelse	Selektion	Behandling	Bortfall	Bedömning	Rapportering	Intressekonflikt	Sammanvägd risk
Dahlberg et al, 2009, [78]	Celecoxib jämfört med diklofenak	Låg	Måttlig	Måttlig	Måttlig	Låg	Måttlig	Måttlig

Tabell 9. Bedömning av risk för bias (enligt SBU:S granskningsmall för icke-randomiserade studier) i relevanta icke-randomiserade primärstudier för NSAID och risken för PUB.

Författare, år, ref	Confounding	Selektion	Klassificering	Avvikelser	Bortfall	Mätning	Rapportering	Intressekonflikt	Övergripande risk
Bakhriansyah et al, 2017, [79]	Hög	Måttlig	Låg	Låg	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Chang et al, 2011, [80]	Hög	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig

Tabell 10. Bedömning av risk för bias (enligt SBU:s granskningsmall för icke-randomiserade studier) i relevanta icke-randomiserade primärstudier för opioider och risken för fall.

Författare, år, ref	Confounding	Selektion	Klassificering	Avvikelser	Bortfall	Mätning	Rapportering	Intressekonflikt	Övergripande risk
Daoust et al, 2018, [81]	Hög	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Grewal et al, 2018, [82]	Hög	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Hunnicutt et al, 2018, [83]	Hög	Måttlig	Låg	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig	Måttlig
Krebs et al, 2016, [84]	Hög	Måttlig	Låg	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig
Taipale et al, 2018, [85]	Hög	Måttlig	Låg	Låg	Låg	Låg	Måttlig	Måttlig	Måttlig

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Bilaga 6

Läkemedelsbehandling av vanliga smärttillstånd hos äldre personer/ Pharmacological treatment of common pain conditions in the elderly, rapport 315 (2020)

Bilaga 6 Kodning metasynteser

Innehållsförteckning

Kodning metasyntes 1

Författare År Ref	Meningsenhet	Nivå 1 tema
Informanter: Patienter med osteoarthritis		
Baumann et al 2007 [1]	The main issues patients required more information about in order to cope better with daily life related to their disease, its origins, the outlook, and the role and possible side effects of treatment. Information about recent developments was seen as inadequate. Without information, there was a tendency to think of the disease as a consequence of lifestyle - leading to guilt - or as bad luck.	Patienterna behövde mer information för att kunna hantera dagligt liv med sin sjukdom och biverkningar av behandling. Information om den senaste utvecklingen uppfattades som otillräcklig. Utan information fanns en tendens att tänka på sjukdomen som en konsekvens av livsstil – något som leder till skuldkänslor eller som otur.
	OA patients surveyed appeared to feel that they had too little opportunity to express themselves.	Patienter med OA menade att de hade för lite möjlighet att uttrycka sig.
	Patients also wanted to be able to ask questions of their practitioners and to see them, above all, as genuine partners.	Patienter ville också kunna ställa frågor till sin läkare och se läkaren som en äkta partner.
	Patients said they were surprised when their GPs did not have specific information on new treatments or means of pre-venting OA in their children and grandchildren.	Patienterna var förvånad när deras läkare inte kunde ge specifik information om nya behandlingsmetoder eller möjligheter att förebygga sjukdomen hos barn och barnbarn.
	The ability of patients to communicate their daily experience to the practitioners is a priority if they are to build genuine agreement and if the best treatment strategy for each individual patient is to be identified.	Patienterna behöver ha förmåga att kommunicera med läkaren för att komma överens om en äkta överenskommelse.
	Patients wanted practitioners to participate in an authentic teaching process. The majority of the problems highlighted relate to vocabulary and teaching tools (lack of diagrams). There is a need for more clarity, accessibility, and simplicity.	Patienterna önskade att läkaren informerade på ett tydligt och lättfattligt sätt.
	Computers may facilitate information management, but do nothing to improve communication because they ‘steal’ time from relationships, and may upset the patient by ‘hiding’ the practitioner’s face. Facial expression and body language enhance communication.	Datorer kan förenkla information men också bygga upp en barriär mellan läkare och patient.
	Patients said practitioners were often not explicit enough when discussing the seriousness of the diagnosis or the value of certain drugs compared with others.	Läkarna var inte tillräckligt tydliga när de diskuterade hur allvarlig diagnosen var.

Författare År Ref	Meningsenhet	Nivå 1 tema
	They (doctor) were frequently seen as being distant, with little time to listen, understand or explain, and were often perceived as tactless.	Läkarna var distanserade och hade för lite tid, och uppfattades som taktlösa.
	Inappropriate gestures generate anxiety; for example, a shrug is no substitute for a clear answer.	Olämpligt kroppsspråk kan leda till oro.
	Some lack of dialogue seems linked with avoidance strategies, such as minimizing suffering, using fatalisic wordings, and being difficult to approach.	Brister i dialogen verkar vara kopplat till undvikande strategier som minimering (läkare) av lidande och att vara svåra att nå.
	Lack of communication skills is crucial in some exchanges, notably regarding pain. Silence from the practitioner was interpreted as powerlessness, and patients stopped asking questions. Yet they would be prepared to hear the practitioner say 'I don't know', and to be sent for a second opinion.	Brist på kommunikationsförmåga är avgörande särskilt när det gäller smärta. Tystnad hos läkaren tolkades som maktlöshet. Patienterna slutade att ställa frågor.
	Advice and response to questions, in particular about topics highlighted in the media, were seen as generally good, but patients often felt that they had to seek information rather than being given it spontaneously.	Läkarna gav inte information spontant men kunde svara på frågor. Patienterna var tvungen att söka information själva istället för att få den.
	Dissatisfied patients complained about poor quality treatment and late diagnosis and described practitioners as fatalistic and poorly informed about the disease.	Missnöjda patienter uppfattade att läkarna var fatalistiska och hade låg kunskap om sjukdomen.
	Satisfied patients appreciated their practitioners because they gave them time and support,	Nöjda patienter uppskattade läkarna p.g.a. att de fick tid och stöd.
	'Take this and that, with no explanations.'	Acceptera utan att ifrågasätta.
	'They have no cure.'; 'They are helpless'; 'You just have to put up with it and that's that.'	
	'You dare not ask (for information).'; 'They don't really like people asking questions.'; 'He made me feel I was being a nuisance.'; 'I told him about newspaper articles about a new treat- ment, and he just waved it away.'	Vill inte ha frågor. Att känna att man är till besvär. Problemen viftas bort.
	'You always have to take the initiative.'; '(I have to say) I am suffering terribly, please give me something.'; 'You always have to ask.'	Patienten måste själv ta initiativ.

Författare År Ref	Meningsenhet	Nivå 1 tema
	'A doctor can't know everything.'; 'I feel that (the doctor) was right and courageous when he said that he couldn't give me clear information, and he sent me to someone who could.'	Min läkare kunde inte tillräckligt men skickade mig vidare.
	'You are just an object, a ping-pong ball going to and fro.'; 'They pass on x-rays and little notes to colleague that are sealed and you aren't shown what is in them.'; 'They should leave the letters unsealed.'; 'I feel I can open the notes.'; 'I try to understand what they are telling each other, it concerns me and I feel I have the right to know.'	Läkarna pratade över patientens huvud.
	Patients did not see much sign of interest in their disorder among practitioners, whereas they experienced its growing impact day-to-day (having to give up what they used to enjoy, having to stop caring about appearance, feeling that people are looking at them).	Läkarna var inte intresserade av deras sjukdom.
	Nevertheless, patients said they trusted their GPs and did not plan to change (as they may under the French system).	Patienterna litade på sin läkare och ville inte byta läkare.
Informanter: Äldre personer som har hemsjukvård		
Blomqvist et al 2002 [2]	Being dependent on home care staff due to pain brought a longing for an independent life: 'That's what I miss, though, you don't have the freedom. I do not have the freedom to lie as long as I want. That's what I miss.'	Smärtan skapar ett beroende av vårdpersonal men man längtar efter oberoende.
	They expressed confidence in family and staff. Observations that staff came without always being asked made them feel cared for. They were sure that in times of need they would get the help they required.	De litar på personalen ska hjälpa dem. De kände sig omhändertagen när personalen kom utan att vara efterfrågad.
	People felt that their families or care staff did not pay enough attention to their pain problems and Wished that staff would ask about their pain.	Personalen uppmärksammade inte deras smärtproblem. Önskar att personalen ska fråga om deras smärta.
	People felt that others did not understand how bad the pain was. Although they tried not to bother care staff or their families, they believed they were viewed as an encumbrance.	Känslan av att personalen inte förstår inte hur svår smärtan är. De försöker att inte störa men har känslan av att vara en börda.
Informanter: Äldre personer med osteoartrit		
Bower et al 2006 [3]	Asked about discussing this information with the doctor, a participant said, "Yeah,	Läkare och patient diskuterar på ett respektfullt sätt.

Författare År Ref	Meningsenhet	Nivå 1 tema
	we talk a lot, yeah. We respect each other.”	
	Another said, “No, no. I went to one doctor, I won’t mention his name, but I did read an article one time and I went to him and he said ‘I don’t want to listen to that BS and all that.	Läkaren avfärdade en artikel som patienten tagit med sig som strunt.
Informanter: Patienter med knä osteoarthritis		
Carmona-Terés et al 2017 [4]	A participant told that sometimes she did not understand the information provided. Others were not satisfied with the information received, in particular by specialists; they considered that it amounted practically to nothing and That the interaction was limited to prescribing painkillers and to referring them for diagnostic tests.	Att inte förstå informationen som hon hade fått. Andra var inte nöjda med den information som de fått - Meningslös information. Interaktionen begränsades till recept och remisser för diagnostiska test.
	None of the participants received materials on these issues, and some said it would be useful for them to have this information although they did not specify which type of materials they expected. The patients’ expectations aimed to obtain more information on their condition, prognosis and treatment”.	Ingen har fått material om artrit men några ansåg att det skulle ha varit användbart med information. Förväntningar på mer information om tillstånd, prognos och behandlingar.
Informanter: Äldre kvinnor och män med musculoskeletal kronisk smärta		
Clarke et al 2014 [5]	A variety of reasons were offered for participants’ reluctance to see their GP, although the concern not ‘‘to bother’’ physicians, or ‘‘waste’’ their time appeared paramount.	Deltagarna var motvilliga att söka hjälp hos allmänläkare för de ville inte slösa på deras tid eller störa dem.
	This appeared to add to their reticence to seek professional support since they were concerned not to be seen as ‘‘complainers’’ by visiting GPs ‘‘too often.’’ Most participants discussed the importance of having a diagnosis and the frustration when none was apparent: ‘‘When I think about it, I think there must be some reason for this, why… you know?’’	De ville inte bli sedda som “complainers” genom att besöka läkarna för ofta. Deltagarna ansåg att det var viktigt med en diagnos och blev frustrerade när det inte fanns någon.
	One woman was unimpressed by the consultant’s diagnosis of sciatica since she felt she had not had the tests to support the claim: [He] breezed into the room like a gale of wind and said ‘‘what are you doing back here? There’s nothing we can do for you!’’ …	En deltagare hade erfarenhet av att läkaren hade ställt diagnos utan ordentlig undersökning.

Författare År Ref	Meningsenhet	Nivå 1 tema
	But I stuck to my guns and managed to extract an MRI scan for my knee.	Genom envishet fick personen en MRI undersökningen av knäet.
	HPs had been disparaging and dismissive rather than supplying the information and support anticipated. This, it was felt, led to treatment that was based on assumptions, (''professionals tend to want to make up their own minds'') rather than their own experiences and knowledge of their own bodies. Again, the importance of presentation – this time the participant's history – was emphasised.	Vårdpersonalen var nedsättande och avfärdande istället för att ge information och stöd. Läkarna fattade beslut på egna antaganden istället för att lyssna på patienten.
	You've to have your story very short and succinct, present it well. You've to get through to him [GP]. If he short-circuits you, because he's a habit of putting his hand out to try and stop you speaking, you've got to shut up [laughs]! He does it all the time! You can never get your story out. …I've had physio three times, but it doesn't help… nobody seems to listen to me.	
	GPs who took time to listen were perceived as ''traditional'' or ''family practitioners'' who participants felt ''fortunate'' to have. One woman said, ''I've a holistic GP practice,' elucidating ''they really get to know the person''. She also said she was ''lucky'' with her orthopaedic surgeons, ''they were very approachable and tened.''	Deltagarna som hade en läkare som tog sig tid att lyssna upplevde att de hade haft tur.
	One woman felt aggrieved by hospital doctors talking to her daughter ''over my head,'' which she attributed to her age. The perceived reluctance of HPs to manage pain in all but a ''conservative way'' was felt also by some to be influenced by age: Is it because I'm over 65, they're not doing anything about it?	Läkaren talade över patientens huvud vilket hon tillskrev sin ålder. Smärtbehandlingen sköttes konservativt baserat på personernas ålder.
	Who's asked me? The GP, her attitude is ''nothing very much you can do about it''	
	I think the attitude to people over 70 is wrong, just tablets, treat them conservatively…a lot of people have got a lot of life in them still …	
	I get tablets, but [GP] wasn't willing to give me an operation. She didn't come out and say ''your heart is maybe not very good'' but I'd the feeling maybe that was	

Författare År Ref	Meningsenhet	Nivå 1 tema
	my age, but a lot of people older than me get hips and knees and things.	
	One woman went further in suggesting that HPs sometimes made too many assumptions and should be more prepared to listen to older adults about their pain precisely because of their advanced age. She considered that older individuals are more conscious of their bodies and sensitive to when something is wrong such as pain.	En deltagare gick längre och menade att vårdpersonal hade föreställningar om äldre och skulle lyssna mer till den smärta som den äldre uttryckte.
	Sometimes, doctors don't give people credit for knowing their bodies. We've lived in our bodies and as we get older, we've lived in them for a long time; we're aware of when things are not working as well as they should and it's sometimes difficult to convince them	Läkare ger inte personer kredit för att de kände sin kropp.
Informanter: Äldre personer med artrit		
Davis et al 2002 [6]	Some participants voiced concerns that their care might be compromised by providers' beliefs about aging. One participant said, "I think after you get a certain age the doctors don't care. They give you this or that, and if it doesn't work, try something else. They don't believe what you say a lot of times or pay attention to what you say, because you are getting old." "They don't fool with us long," and "They don't ask questions." Low expectations of either patients or providers for managing chronic pain might negatively contribute to decisions about pain management methods.	Deltagare uttryckte att vården kunde påverkas av vårdarnas tankar om åldrande. Efter en viss ålder så bryr sig inte läkarna. Läkarna tror inte på patient som börjar bli gammal. Låga förväntningar – relaterat till ålder
	One participant said, "I'm convinced in my heart and mind that if I had a good line of communication with my medical doctor, then I wouldn't have to go and see him as frequently as I do. I certainly would be taking less medication, because he could come up with an alternative to medicines. "Unmet care expectations were also an issue. The failure of providers to suggest management techniques other than medicine was stated again, "I think my physician is too ready to write a	En bättre kommunikation skulle innebära färre återbesök. Behov som inte blev bemötta var också en sak. Läkarna förskrev bara läkemedel.

Författare År Ref	Meningsenhet	Nivå 1 tema
	prescription for me ... and so I think that it's kind of the wrong thing for me to say that I have another pain. I don't want another prescription.	
	Participants described mistrust related to the assessment, advice, and care received from providers. One participant said, "Sometimes I don't think they [physicians] understand what you tell them. They don't understand what kind of pain you are in." Several references were made to the actual pain experienced during an examination, when the provider was perceived as not understanding or acknowledging the pain. In another instance, mistrust was related to differing kinds of exercise recommendations received from the physician and the physical therapist.	Patienterna beskrev misstroende relaterat till bedömning, rådgivning och vård. Läkarna förstår inte vilken sorts smärta man har. Läkarna förstod inte att undersökningen gjorde ont. Läkarens och fysioterapeutens olika råd angående träning gjorde att deltagarna kände misstro.
	Participants reflected lack of knowledge about their own medical diagnosis, as well as about pain management strategies. These knowledge deficits were influenced by poor communication between clients and providers. One woman, who did not understand the purpose of the medicine she was taking, talked about taking Celebrex but questioned why she would take it because she had arthritis rather than osteoporosis.	Deltagare kände sig okunnig om sin diagnos och hur de ska hantera sin smärta. Denna okunnighet påverkades av bristande kommunikation mellan deltagaren och vårdaren.
Informanter: Äldre patienter med artrit		
Erwin et al 2017 [7]	It was felt that some professionals still thought of arthritis as "an old persons' disease" and were not sufficiently aware that inflammatory arthritis can present differently and can affect all ages.	Artrit sågs av en del av personalen som en äldre persons sjukdom.
	The need for a holistic approach was strongly emphasized by all participants. Those with osteoarthritis felt that often health professionals dealing with their condition were reductionist and did not look at the impact on the whole person.	Patienterna betonar att de behöver en helhetssyn men läkarna tar en sak i taget. Detta leder till att patienterna upplever att de viftas bort.
	It was strongly felt by participants with OA that their condition was not taken sufficiently seriously by health professionals, including nurses and AHPs	Deltagarna kände starkt att deras tillstånd inte togs på allvar av läkare och sjuksköterskor och att de inte förstod konsekvenserna av det.

Författare År Ref	Meningsenhet	Nivå 1 tema
	working in the community, and that they did not understand its impact.	
	Participants felt that community-based health professionals did not sufficiently understand flares, the unpredictability of the condition and the impact of this.	Deltagare kände att vårdpersonalen inte tillräckligt förstod att RA går i skov och dess påverkan.
	Participants expressed the need for health professionals to be able to adjust normal practice for people with arthritis – for example, how to hold and manoeuvre limbs comfortably. This was raised particularly in relation to how health professionals in the community handle patients with sore joints and mobility problems which may not be evident.	Personalen hanterar ömma leder och rörlighetsproblem utan att förstå att det är smärtsamt
	Pacing was recognized by participants as an important tool to manage their arthritis but many felt that nurses and AHPs did not have a good understanding of this and did not give sufficient advice. This was par- ticularly true for patients with OA.	Personalen kände inte till pacing som ett viktigt verktyg för att klara artriten.
	Participants felt that the mental health impacts of having a long-term condition such as arthritis was not understood or fully addressed either in the community or in secondary care.	Personal förstår inte hur tillståndet påverkar den psykiska hälsan
	Several of the participants with OA felt that they had not been made fully aware of the different management options for their condition and had not been given adequate information to make an informed decision about how to manage their condition. They felt that this should be an important aspect of training for community-based health professionals.	Patienterna fick inte tillräcklig information för att fatta informerade beslut
	A number of people with OA felt that they hadn't received suitable information about their condition. The following comment is typical.	Patienter med OA får inte passande information om sin sjukdom.
	Participants highlighted the importance of good communication skills for community-based nurses and AHPs. They drew attention to the quality of communication available with AHPs, such as physiothera- pists and OTs, who have longer appointments over a period of time. They also highlighted the need for better communication between health professionals.	Deltagarna ansåg att personalen måste bli bättre på att kommunicera med patienten och med varandra. Det kan behövas längre konsultationstider för att få bättre kommunikation.
Informanter: Personer med kronisk smärta på ett äldreboende		

Författare År Ref	Meningsenhet	Nivå 1 tema
Gudmannsdottir et al 2009 [8]	Many of the residents had a sense of abandonment, both regarding relatives and health professionals.	Många av de boende kände sig övergiven av vårdpersonal.
	Maria connected old age with the disinterest of doctors. She was very sick and asked for a doctor who never came. She explained: 'I once asked him [the doctor] to come to me, but he did not come. We are old people'.	Att inte vara intressant för doktorn p.g.a .ålder.
	Matthew, for example, was very reluctant to express his pain to doctors or nurses. He did not receive any medication for his growing pain in both knees. His perception was that the doctor was against him talking about the pain. He stated: 'I was going to talk to him when he came. I felt he was somehow a little against it [laughs with embarrassment] or something. I don't know, I don't know'.	Personen med smärta var motvillig att uttrycka sin smärta och upplevde att doktorn var emot honom.
	The doctors were connected with pain management in their minds. A few doctors had disappointed them but their role was clear. The Registered Nurses seemed strangely distant in the residents' narratives. They were connected with bringing the pills, but not much with pain management.	Några läkare hade gjort dem besvikna. Personerna beskrev starkt distanserade sjuksköterskor. Ssk distribuerade piller med deltog ej i behandlingen.
	Some of the residents seemed to lack information. Jacob has pain in different joints and sometimes in the abdomen. He was also blind. When asked if he has thought of seeking help from doctors when he has the worst pain, he answered: No, no, no, ... there are no doctors around here. Researcher: do you think you can be helped concerning your health? Jacob: No, no. My dear, let me tell you, I am so old. I can't have more than 2 or 3 years to live, then I am 100 years old.	Boende saknade information och det saknades även läkare på boendet.
Informanter: Äldre personer med kronisk smärta på ett äldreboende		
Higgins 2005 [9]	There was a chap next to me .../... and he used to be calling out and he used to be in pain. He was calling out to the sisters and they wouldn't come and I pressed the buzzer. And they used to book it down against me. I get bad circulation and when they touched the sheet, any part where they touched the sheet it used to burn like it had a candle underneath it, and I couldn't move my foot and I used to hold on to the buzzer for a long time	Personalen på boendet uppmärksammar inte när någon har ont.

Författare År Ref	Meningsenhet	Nivå 1 tema
	sometimes until they come and moved me foot.	
	The nurses who walked away 'as if' they did not hear Tony sadly reflect the poor quality of care provided. Tony knew the nurses had heard him but chose not to respond, reinforcing how complaints of pain can alienate its sufferers. 'Isolation' as a form of punishment for complaints reinforces the power and control that health carers have over those with pain. These actions alone reinforce the imperative to 'unvoice' pain for fear of reprisal.	Att bli nonchalerad av personalen när personen reflekterade över vårdkvalitén. Personalen utövar makt mot dem som har smärta. Smärtan blir tyst p.g.a. rädsla för repressalier.
	Pain and pain relief were rendered unimportant by caregivers; nurses and physicians alike. Responses to pain and the need for pain relief were often overlooked, subsumed to routines, other priorities and the expectation that pain was an integral part of growing old.	Sjuksköterskor och läkare bedömer smärta och smärtlindring som ointressant. Personalen struntade i behovet av smärtlindring. Smärta ansågs av personal som en naturlig del av åldrandet.
	Not wanting to worry or bother nurses was also a frequent comment. Participants simply 'put up with pain' as an attempt to dismiss its significance because past experience suggested that help would not be forthcoming.	Att inte vilja störa ssk vara vanligt. Att stå ut med smärtan pga att de inte tidigare har fått hjälp.
	Ellen, being 'full' of pain, reflects the extent and significance that pain had for her. It could not be ignored. She had no expectation for relief.	Personen hade inga förväntningar på att få lindring.
	Pain and pain relief were rendered unimportant by caregivers; nurses and physicians alike. Responses to pain and the need for pain relief were often overlooked, subsumed to routines, other priorities and the expectation that pain was an integral part of growing old.	Smärta och smärtlindring var oviktigt för vårdpersonalen. Svar på smärta och behovet av smärtlindring var ofta förbisett. Det var inordnat i rutiner och smärta var en del av att bli gammal.
	When pain became overwhelming, when it became too much for the participants to bear, only then did many of the participants request pain relief. The other night I asked for a pain killer and I think he [the nurse] must have	När smärta blev outhärdlig så bad personerna om smärtlindring, endast då. Bad om smärtlindring men fick det aldrig.

Författare År Ref	Meningsenhet	Nivå 1 tema
	forgot about it. I was cranky about that. Did you eventually get it? No I didn't.	
	Requests for pain relief that are forgotten, or when the elderly people themselves are placed in situations that may aggravate their pain and then forgotten, reinforces the view that pain is to be expected. It also shows that pain is not seen as a need that requires urgent attention and conveys the idea that they are unworthy of the care and attention that others receive.	När begäran om smärtlindring glömdes bort förstärktes synen att smärta är något att förvänta. Det visar också att smärta är inte ett behov som kräver omedelbar uppmärksamhet och förmedlar en känsla att personerna är ovärdig att få vård och uppmärksamhet som andra får.
Informanter: Äldre personer med hand osteoartrit		
Hill et al 2011 [10]	The groups talked about dissatisfaction with the perceived lack of understanding, help and type of information received from some health care practitioners, and the uncertainty this caused in their own management of their hand problem	Missnöjd med bristande förståelse, hjälp och information från hälso- och sjukvårdspersonal. Brister skapar osäkerhet hur de ska hantera sina probem.
	'Nothing we can do about it' he said and at the time I'd got really bad pain, which was why I went down the thumb. So oh well live with it, so no, no help at all. From what they said to me I honestly wouldn't ever go back and waste their time, wouldn't go back and tell them my hand, my hands are playing up, 'cause he said there was nothing they could do'.	Resignation när läkare säger att inget kan göras. Att inte slösa på deras (personal) tid för det finns ändå inget att göra.
	They have been giving me exercises for my neck [physiotherapists] but they have never mentioned about my hands at all and I have said I've got arthritis in them but they've never offered any help for them. Health care practitioners are unaware of the specific importance that patients place on the recognition of their hand OA problems, participants experienced a possible lack of understanding by some health care practitioners of the impact of hand symptoms on the individual.	Fick inte hjälp med min hand artrit trots att jag påtalade det. Bristande medvetenhet hos vårdpersonalen om hur viktigt det är att deras handproblem erkänns. Deltagarna upplevde en möjlig brist på förståelse för hur symtomen från händerna påverkar dem.
	There also appeared to be contradiction in the advice and information given to some of the participants by various health care practitioners.	Somliga deltagare hade fått motstridig information från olika vårdgivare vilket gjorde dem osäkra hur de ska hantera sina handproblem.

Författare År Ref	Meningsenhet	Nivå 1 tema
	'But you don't know what to do for the best because she said rest them when they're like that and then they tell you to exercise [several respondents nod in agreement] in case they go stiff, so you don't know what you're supposed to be doing'. I don't think the doctors know enough about it.	Upplevde att läkare har otillräcklig kunskap om handartrit.
Informanter: Äldre personer med osteoartrit		
McHugh et al 2006 [11]	The use of services and treatments was very dependent on participants' previous experiences and attitude. Participants reported little active management by health professionals in both primary and secondary care while on the waiting list and there was no re-assessment of their symptoms. There was a perception that care had been transferred from primary care to secondary care and that they just had to wait for their joint replacement.	Deltagarnas erfarenheter och attityder påverkade deras användning av service och behandling. Deltagarna saknade vårdkontakt i väntan på specialistvård.
	They (the GPs) just really treat what I go to see them about. They have said you are under treatment at the specialist hospital so they don't get involved, other than this blood pressure check.	Allmänläkare undviker att engagera sig i problem efter remiss.
	Last time I went to the hospital, the consultant was more or less saying to me – go home and keep taking painkillers, we can't do an operation till you've turned 70.	Att bli avfärdad med uppmaningen att gå hem och vänta till 70årsdagen.
	Study participants spoke of 'not letting on to health professionals' regarding the pain they were in. Individuals reported that they 'masked the pain' and did not discuss their OA with their GP.	Dölja smärta för vårdpersonal.
Informanter: Äldre personer med osteoartrit		
Paskins et al 2015 [12]	Dissonance, misalignment of patient and physician expectations or agendas, was both observed during consultation analysis and reported by participants in postconsultation interviews. Patient expectations of the consultation varied significantly, with some wanting information, some being exclusively focused on symptom relief, and others	Oenighet mellan patienten och läkarens förväntningar och agenda fanns under konsultationen. Patientens förväntningar av konsultationen varierade, en del önskade information, några hade fokus

Författare År Ref	Meningsenhet	Nivå 1 tema
	desiring a combination of information and active management.	på symtom andra ha önskemål och både information och aktiv behandling.
	Patients who were seeking clear diagnostic information, not reassurance, described feeling that their concerns were not validated when the GP downplayed or normalized symptoms or otherwise provided reassurance.	Patienter som sökte tydlig information kände att deras farhågor ej validerades när vårdgivaren normaliserade symtomen.
	Many patients, however, wanted a clearer and more meaningful diagnosis (Q7).	Patient ville ha en klar och meningsfull diagnos.
	The patient could then interpret the lack of diagnostic specificity as “nothing showing” and “noth- ing being done” (Q11). Patients also talked about joint pain being “normal”; however, dissonance in the consultation resulted when patients felt the messages about OA being nor- mal or early onset failed to validate the importance and impact of their symptoms (Q6).	Patienterna tolkade den bristande diagnostiken som att det inte visade något och ingenting kan göras. Patienterna talade om ledsmärta som något som är normalt. Otydligheten i konsultationen resulterade i att patienterna uppfattade att OA är normalt.
	Patients commonly felt the need for information about diagnosis, self-management, employment, and prognosis; dissonance resulted when these needs were not met (Q12).	Patienterna hade behov av information om diagnos, egenvård, sysselsättning och prognos. Utebliven information om detta skapade oenighet i dialogen.
Informanter: Äldre personer med knä osteoartrit		
Spitaels et al 2016 [13]	Poor communication with the patient was the most described barrier. Patients experienced they did not receive sufficient medical information about their disease process. The term OA was often not even mentioned by doctors or in medical reports. Patients were disappointed to learn that their doctors presented knee OA as a normal aging phenomenon with limited treatment options. Patients concluded that health care professionals underestimated the physical complaints and were not supportive enough. The limited consultation time was a major concern because it interfered with good communication and providing patient tailored treatments.	Bristande kommunikation med patienten var det mest beskrivna hindret. Patienterna upplevde bristande information om sin sjukdomsprocess. Patienterna var besvikna att få lära sig att deras OA var normalt för åldern med begränsade behandlingsmetoder. Patienterna ansåg att vårdpersonalen underskattade deras fysiska begränsningar och var ej stödjande. Tiden för vårdmötet var begränsad så god kommunikation fick ej plats.

Författare År Ref	Meningsenhet	Nivå 1 tema
	Older adults in particular complained that the limited time was often spent on “more important” comorbidities. Finally, patients mentioned they were referred to a physiotherapist to improve their general condition, but they received no specific training, like strengthening exercises, for their knee OA.	Äldre patienter klagade på att tiden lades på mer viktig samsjuklighet. Patienterna nämnde att de var remitterade till sjukgymnaster för att förbättras deras grund kondition men fick inte någon träning för deras knä OA.
	Lack of support by health care professionals to keep them motivated was repeatedly mentioned as a reason to discontinue physical activities.	Brist på stöd från vårdpersonal gjorde att de inte fortsätt med fysisk aktivitet.
	Lack of communication between health care professionals could delay the treatment process and confused patients in choosing their follow-up.	Den bristande kommunikationen mellan vårdpersonal försenade behandlingen och gjorde patient förvirrad.
	Hence, only the most striking facilitators were reported: good communication and a confident relationship with the health care professional were imperative for sustainable follow-up.	Bra kommunikation och bra förhållande med vårdpersonal var avgörande för en hållbar uppföljning.
Informanter: Äldre kvinnor med kotkompression		
Svensson et al 2015 [14]	In order to find a way to improve their health and to avoid developing dependency, they tried to understand why and what had caused their condition. They often felt that they were not being taken seriously by health-care providers, who saw them as untrustworthy and constantly referred them elsewhere. Despite increasing pain and discomfort, they felt they never got a thorough examination and ultimately, they ended up being sent home with pain medication and advice to rest; in effect, no specific treatment at all.	Deltagarna med kotkompression söker förståelse till vad som orsakat deras tillstånd. Att inte bli tagen på allvar av vårdpersonal. Att bli sedd som opålitlig och hela tiden bli remitterad vidare. Deltagarna med kotkompression upplevde att de aldrig undersöktes ordentligt utan skickades hem med smärtläkemedel.
	They felt distrusted and met with reluctance by health-care providers and were always given low priority. All the women had continually been asking for radiographic examination and referral to the orthopedic department for a correct diagnosis.	Bemötas med misstro och motvillighet av vårdpersonal. Kvinnor med kotkompression kände sig alltid lågprioriterad. Alla kvinnor hade varit tvungna att tjata för att få röntgenundersökning och remiss till ortopeden för att få en korrekt diagnos.

Författare År Ref	Meningsenhet	Nivå 1 tema
	This was perceived as unsatisfying and frustrating; they describe feelings of being belittled.	Personer med kotkompression kände otillfredsställelse, frustration och att bli förringad.
	They felt that the care professionals saw them as unnecessary care seekers, and they felt ashamed when they were told that other patients where in greater need of care. An uninterested and indifferent attitude from health-care providers created a sense in the patient of no longer being significant and of being seen as a liability to society; in other words, they were no longer worth investing in but instead they had become a burden to society.	Att bli sedd som en onödig vårdsökare. Att de kände skam när de fick veta att personalen ansåg att andra behövde vården bättre. Att mötas av ointresse och likgiltighet från vårdpersonalens sida gav en känsla av att inte ha något värde. De kände att de inte vara värda att satsa på och blev en börda för samhället.
Informanter: Äldre personer på ett vård- och omsorgs boende		
Yates et al 1995 [15]	The respondents frequently reported a reluctance to discuss their pain with significant others or with other residents for fear of 'worrying them' or being perceived as a 'complainer'.	Deltagarna beskrev en motvilja till att diskutera deras smärta med andra personer eller andra boende för inte oroa eller att bli upplevd som en som klagar.
	While the respondents appeared to be less reluctant to talk with nursing staff' about pain, their perception of nurses' attitude and their beliefs about nurses' ability to help them have some important implications for education and practice.	Deltagarna var mindre motvilliga att tala med sjuksköterskorna om sin smärta.
	Two particular issues relating to staff emerged. First, there was concern that staff were simply 'too busy' to help them.	Vårdpersonalen var för upptagna för att hjälpa dem.
	They're always short of time. Yes, all I can say is it would be nice if they had a little more patience. Not that they haven't, but a little more, that's all, to listen to you.	De (personalen) har alltid brist på tid. Önskar att de hade lite mer tålamod. Att personalen lyssnade.

Kodning metasyntes 2

Författare År Ref	Nivå 1	Utdrag
Baumann et al 2007 [1]	Knowing about treatment and its effects as a way to better understanding	Treatment and its effects: I would like to explain to med why and how the does should be increased when there is a flare-up and why it is decreased afterwards Are there side-effects? Why is it important to avoid getting too used to these drugs?
	Expectations in terms of communication skills: improving dialogue	Patients said that practitioners were often not explicit enough when discussing the seriousness of the diagnosis or the value of certain drugs compared with others.
Bower et al 2006 [1]	The recommendations from the physician influenced senior's medication choices	Recommendations from the GP (and free samples) were influential in trying a new medication. Patients shared a spectrum of views ranging from accepting their (GPs) recommendations to questioning the physician's judgement.
	Switched out fear for side-effects Fear of deteroriation led to resistance to change the drug regimen.	Some switched out of a fear of developing side-effects Patients' fear of a deterioration in health led to "pharmaceutical inertia", i.e. resistance to making any changes to their drug regimen. It also emerged as an unwillingness to change drugs without any guarantee of improvement.
	Discontinuation because of side effects and finding the coxibs ineffective	Coxibs had been discontinued mostly because of side effects but also finding them ineffective.
	Pharmacists, social networks and the media were used as sources of information along with GPs	Some found social networks credible sources of information, others were sceptical about their reliability. Participants also varied in how they used information gleaned from social networks. Articles in magazines and the press were also mentioned as sources of information but they had not much effect on drug use.
Carmona-Teres et al 2017 [4]	Anxious about side effects from painkillers and NSAID and they avoid taking them except when it hurt too much and otherwise bear the pain.	Informants mentioned painkillers and NSAIDs, usually prescribed by health professionals. They are anxious about the side effects of these medications. "I avoid taking pills…I have some in case one day it hurts too much". Depending on the situation they choose to take paracetamol, NSAIDs, sometimes with a

Författare År Ref	Nivå 1	Utdrag
		gastric protection agent or bear the pain without taking any tablets
Davis et al 2002 [6]	Decision-making about use of pain management was influenced by comorbidity, hesitancy to take medication and reluctance to try nonpharmacological methods. Hesitancy could result from wanting to use medication only when the pain was at its worst, fear of addiction, side-effects and perceived allergic reactions and dissatisfaction with the effectiveness	The properties of comorbidity, hesitancy to take medication and reluctance to try nonpharmacological methods indicated the major factors, perceptions and beliefs that influenced the participants' decision-making about their use of pain management methods The hesitancy might have resulted from a wanting to take medication only when the pain was at its worst, fear of addiction, side effects and perceived allergic reactions, dissatisfaction with the effectiveness.
Gudmundsdottir et al 2009 [8]	Residents sometimes had too much faith in the original numbers, colors and shapes of pills	Interestingly, on a few occasions residents had too much faith in the original number of pills. The residents counted them every time, knew their sizes, colours and shapes by heart. It was as if everything was in order as long as the original number was given
Hill et al 2011 [10]	Made their own reasoned decision about treatment, based on their own beliefs and the information given to them.	Participants were not passive or powerless and made their own reasoned decisions about treatment, based on their own beliefs and the information given to them. One of the main reasons for not taking medication as prescribed was the perceived or actual side-effects of medication. In addition.. a further reason was fear of tolerance to medication
Mc Hugh et al 2007 [11]	Fear of side effects and addiction	Only two of the 21 participants were not taking analgesics. The perception among participants concerning the fear of side-effects and addiction was evidenced by participants not taking or reducing their medication
Spitaels et al 2017 [13]	Fear was an important reason to discontinue medication. Some were afraid of addiction, side effects or interactions with other medications. Some did not have faith in EBM, they wanted to experience themselves if medication worked or not.	Negative experience with drugs was an important reason for patients to discontinue their medications. All patients mentioned fear as an important reason for patients to discontinue their medication…. Some patients were reluctant to use analgesics. They were afraid of addiction, side effect or interaction with other medication. Patients sometimes did not have enough faith in EBM: proven or not proven by science, they wanted to experience themselves if medication worked or not.

Författare År Ref	Nivå 1	Utdrag
Yates et al 1995 [15]	Ambivalence about the benefits of pain relivers and how effective they were.	An apparent ambivalence on the part of many residents about the benefits of taking any action to relieve their pain emerged as another category of beliefs/attitudes. For many residents, this attitude was one which reflected little hope or optimism. … A number of respondents commented that they would take medication when they had pain. However, there were clearly some differences of opinion about how effective pain-relieving medications actually were

Kodning metasyntes 3

Författare År Ref	Meningsenhet	Tema nivå 1
Informanter: Läkare i primärvård		
Paskins et al 2015 [12]	GPs described a strong reassurance agenda, which underpinned their explanations for their using the term osteoarthritis infrequently. They felt the term to be alarmist	För att inte oroa patienterna undvek läkarna ofta benämningen OA
	GPs described the need to play down OA to avoid encouraging the patient to adopt the “sick role”.	Det var viktigt att tona ner OA för att inte uppmuntra patienterna att anta en sjukroll
	Some GPs did not recognize patient education as a priority and others reflected that they might not have the knowledge to provide the necessary education	Utbildning av patienter var inte prioriterat. Kunskapen var inte tillräcklig för att ge nödvändig utbildning av patienterna
	Some participants felt that patients assigned joint pain a low priority, assuming it to be a normal consequence of aging.	Upplevelse att patienterna ser OA som en normal konsekvens av åldrande och ger ledsmärtor låg prioritet
	GPs described influences on prioritization such as patient safety and conditions for which management is financially incentivized. Prioritization was also influenced by availability of resources such as physical therapy.	Prioritering (av behandling) påverkades av patientsäkerhet, hur behandlingen finansierades och tillgänglighet till t ex fysioterapi.
	When symptoms of joint pain were brought up after discussion of other topics some GPs described frustration with patients’ “late-arising concerns”. Others assumed that joint pain mentioned late in the consultation was unlikely to be troublesome and was a result of the patient making conversation.	När patienter tog upp symtom på ledsmärtor i slutet av konsultationen kunde läkarna bli frustrerade eller så antog de att patienterna ville ha ett samtal och att problemen sannolikt inte var besvärande.

Författare År Ref	Meningsenhet	Tema nivå 1
Informanter: Sjuksköterskor och några läkare inom långvården (HCPs)		
Kaasalainen et al 2007 [16]	Residents' lack of ability to report pain created many obstacles for HCPs. It was often difficult to discriminate pain from other common conditions such as delirium or depression. Consequently, they stated that pain for those residents was not typically managed well.	De boendes oförmåga att rapportera smärta skapade problem. Det blev svårt att skilja smärta från andra vanliga tillstånd som delirium eller depression.
	Often, family members would be used as a proxy for assessing pain in residents who were unable to provide their own pain reports. In relying on family members, HCPs gained insight into a resident's typical behavioural response to pain, and found this information was most helpful at the time of admission.	Familjemedlemmar kunde vara ett stöd för att förstå hur de boende visade tecken på smärta.
	At times, family input, however, presented dilemmas for staff, including some family members' concerns about increased confusion, falls and opioid dependency associated with resident use of pain medication.	Familjers oro för ökad förvirring, fall och beroende av läkemedel som följd av medicinering kunde ge upphov till dilemma.
	For HCPs, the importance of individualizing pain interventions was paramount so that the desired balance of pain relief and the side effects of pain medications could be achieved.	För läkarna var det viktigt att medicineringen för smärta blev individanpassad för att få en balans mellan grad av smärtlindring och biverkningar.
	Many staff members commented that they did not always believe residents' verbal reports of paint or they felt that residents were overstating their pain.	Personalen litade inte alltid på de boendes beskrivning av smärta. Personalen kunde känna att de boende överdrev smärtan.
	Most participants commented on the widespread need for education across. HCP groups and their lack of specialized skills in pain management.	Personalen upplevde behov av utbildning och att deras förmåga var bristande.
	They identified a need for knowledge related to using non-pharmacological interventions for pain relief and felt that they should be using these modalities more in their practice.	Personalen upplevde att de behövde mer kunskap om icke-farmakologiska alternativ och kände att sådana borde användas mer.
	For the licenced nurses, lack of continuity and communication, particularly from one shift to another regarding pain management was troublesome.	Bristande kontinuitet och kommunikation om handläggning av smärta mellan skift var ett hinder för sjuksköterskorna.
	The most common barrier described at the system level was related to time constraints.	Det största hindret på systemnivå var tidsbrist.
	Participants highlighted the lack of attention given to pain management during orientation sessions for newly hired staff.	Handläggning av smärta fick litet uppmärksamhet vid utbildning av nyanställda.
Informanter: Sköterskor i kommunal sjukvård		

Författare År Ref	Meningsenhet	Tema nivå 1
Park et al 2015 [17]	Participants stated that older patients often applied pain relief self-management based on inaccurate knowledge. /…/. Furthermore, patients' perceived limited understanding about drug reactions and side effects contributed to taking their medications differently than prescribed.	Äldre patienter självmedicinerade baserat på otillräcklig kunskap. Äldre patienters begränsade förståelse för effekter och biverkningar bidrog till att de tog läkemedlen på annat sätt än förskrivet.
	The participants reported that /…/ age-related physical or cognitive changes led to limited desire for active pain management participation	Åldersrelaterade kognitiva eller fysiska förändringar ledde till att de äldre inte var intresserade av aktiv behandling
	Older patients trusted and followed unverified experiences from acquaintances rather than utilizing education or advice from HCPs.	Äldre patienter litade mer på råd och erfarenheter från vänner och bekanta än från sjukvården
	Some patients with limited incomes could not receive sufficient pain management due to the high care costs of medical institutions.	En del äldre fick inte tillgång till tillräcklig behandling beroende på höga vårdkostnader
	Faced with prolonged patient pain complaints during home visits, they felt ineffective and found pain management difficult. They were likely to passively manage chronic pain because it "cannot be fully cured" or "cannot be resolved".	Känslan av att inte kunna erbjuda en effektiv smärtlindring ledde till passiv handläggning
	They often put more value on non-pharmacological interventions such as exercise. Their own interpretations of their patients' pain led to reluctance to administer medications, thus undermanaging the pain	Egen tolkning av patienternas smärta ledde till motvilja mot att ge läkemedel, icke-farmakologiska insatser som träning föredrogs
	They had difficulty understanding patients' pain objectively and professionally due to the subjective nature of pain and individual differences in patients' expressions. Some patients exaggerated and some underreported the amount of pain they were feeling.	Svårt att tolka grad av smärta objektivt beroende på patienternas subjektiva bedömning, där några överdrev och andra underrapporterade smärtor.
	Inadequate knowledge about chronic pain management made it difficult to perform individualized interventions.	Upplevd brist på kunskap om kronisk smärta försvårade individanpassad behandling.
	Uncertainty about chronic pain resolution led participants to passive management by referral to hospitals for help or letting their patients select therapeutic options.	Osäkerhet om smärtbehandling ledde till att patienterna remitterades till sjukhus eller att patienterna fick välja behandling själva.
	Because of their own skill and knowledge deficits, they lacked the capacity to make decisions on types of pain management.	Brister I förmåga och kunskap ledde till att de saknade kapacitet att besluta om handläggning av smärta.
	Inadequate levels of staffing and time necessary for home-visiting care were significant organizational barriers.	Tid- och personalbrist var barriärer för god smärtlindring.
Informanter: Sjuksköterskor, arbetsterapeuter och fysioterapeuter, vård för smärta i hemmet		

Författare År Ref	Meningsenhet	Tema nivå 1
Berglund et al 2015 [18]	Vårdpersonalen upplever en känsla av maktlöshet som uttrycker sig som känslor av frustration, otillräcklighet och hopplöshet. De får insikt i att smärta inte alltid kan botas.	Upplevde maktlöshet som ledde till känslor av frustration, otillräcklighet och hopplöshet. De fick insikten att smärta inte alltid kan botas
	Vårdpersonalen ”acknowledges” att många av de äldre har haft sin smärta länge och att den har inkorporerats som en naturlig del av livet. Tillståndet ”being in pain” har enligt vårdpersonalen blivit ett tillstånd som uthärdas i tysthet vilket ibland komplicerar personalens möjlighet att finna sätt att närma sig de äldres smärta	Upplevde att många äldre haft smärta länge och att den inkorporerats som naturlig del av livet. Upplevde att tillståndet att leva med smärta uthärdas i tysthet, vilket komplicerade möjligheten att hitta sätt att närma sig de äldres smärta
	Känslan av maktlöshet manifesteras i situationer där personalen upplever att det är svårt att få den uppmärksamhet som behövs från andra vårdgivare som läkare och undersköterskor för att möta de äldres behov. /../ de känner att de andra inte lyssnar på eller tror på den äldre./../ Flera beskriver situationer där läkare inte identifierar äldres behov av smärtlindring.	Svårt att uppmärksamma andra vårdgivare på behov av smärtlindring.
	Personalen är medvetna om att smärta inte behöver vara en naturlig del av åldrandet (här finns citat).	Medvetenhet att smärta inte behöver vara en naturlig del av åldrandet.
	Känslan av maktlöshet relateras också till de äldres villighet eller motvillighet till att vara följsam med den föreslagna interventionen.	Upplevd maktlöshet relaterade till de äldres grad av följsamhet med föreslagen intervention.
	Personalen upplever att det är svårt att besluta om de ska rekommendera och motivera äldre att ta smärtlindring eller avråda dem. Svårigheten beror på överväganden om förutsedda bieffekter och risker förenade med läkemedlet som t. ex. slöhet, yrsel, fallrisk…	Överväganden om biverkningar och andra risker med läkemedel leder till osäkerhet om huruvida patienten ska övertygas att ta smärtlindring.
	Känslan av maktlöshet ökar om det finns förväntningar på att smärtan ska elimineras. Personalen möter desperationen hos anhöriga och deras eget team. En komplicerad situation uppstår är när de försöker ge information men inser att de äldre, deras anhöriga och annan vårdpersonal har andra perspektiv och finner det svårt att förstå de begränsade möjligheterna att helt eliminera smärtan.	Bristande förståelse hos anhöriga och kollegor för att smärta inte alltid kan elimineras helt ökar känslan av maktlöshet.
	De prövar andra metoder som TENS som komplement till förskrivna läkemedel. De	Frustration och resignation när de försöker alla tillgängliga metoder som

Författare År Ref	Meningsenhet	Tema nivå 1
	känner sig frustrerade och ibland resignerade när de känner att de försöker allting men ingenting hjälper.	komplement till läkemedel men det inte heller hjälper.
	De försöker uppmuntra till så mycket fysisk aktivitet som möjligt. /../ Ibland upplever de ett motstånd mot aktiviteter och att få råd.	Tro på fysisk aktivitet. Ibland motstånd mot aktiviteter och rådgivning från patienter.
Informanter: Multidisciplinärt, i hemmet eller på särskilda boenden, äldre med långvarig smärta		
Blomquist 2003 [19]	För äldre med smärta som personalen uppfattade som ”verklig”: fastän de äldre ofta klagade på smärta betraktades inte klagomålen som problematiska. Det som försvårade vård och orsakade frustration var när de kände att de hade begränsade möjligheter att hjälpa, när biverkningar begränsade valet av smärtlindring eller när de kände att sjuksköterskor eller läkare inte var tillräckligt uppmärksamma.	Frustration när behandlingsalternativen var begränsade för äldre med ”verklig smärta”. Frustration när kollegor inte var tillräckligt uppmärksamma på smärtor.
	En del äldre som hade oklar medicinsk diagnos och som klagade överdrivet mycket ledde till frustration och fick personalen att tvivla på smärtorna (citat finns).	Äldre med oklar diagnos och som klagade mycket ledde till frustration. Tvivel på smärtor när de uttrycktes av äldre med oklar medicinsk diagnos och som klagade överdrivet.
	Vissa äldre döljer sin smärta och personalen var inte säker på om de hade smärta eller inte. De försökte förstå beteendet. I situationer när personalen kände sig rädd för att såra personens integritet eller när personen vägrade ta emot hjälp ledde till känslor av ”distress” eller förolämpade.	Svårt att bedöma smärta hos de som döljer smärtan. Känslor av distress eller att bli förolämpade när sådana personer vägrade ta emot hjälp.
	Oftast upplevde personalen att de inte gjort något speciellt för att lindra smärta under den senaste veckan. Det förklarade med att de litade på medicineringen, tidsbrist, känslor av resignation eller attityder att åldrande oundvikligen medför smärta.	Speciella insatser för smärtlindring gjordes inte p.g.a. tilltro till medicinering, tidsbrist, attityd att åldrande medför smärta eller känsla av resignation.
	Ett sätt att lindra smärta var att hjälpa personen att få kontakt med en läkare eller annan vårdpersonal. Kontakten kunde innebära att överlämna problemet till någon annan eller att aktivt föreslå eller övertyga en läkare om att förskriva smärtstillande.	Smärtlindring genom att överlämna patienten till annan för att bli av med problemet eller för att övertyga läkare om behov av smärtstillande.
Informanter: Läkare i primärvården		
Rosemann et al 2006 [20]	It sometimes represents a challenge for GPs to distinguish between complaints resulting from the joint affection and complaints that are mainly related to depressed mood.	Upplevelse av utmaning att skilja mellan klagomål på ledproblem och klagomål relaterade till förstämning.

Författare År Ref	Meningsenhet	Tema nivå 1
	Some GPs stated that they try to assess the patients need for information and their capacity to understand, but also what they assume that the patient can handle. Overall, patients were considered to be well informed due to their utilisation of countless other sources of information such as print media and TV.	Upplevelse att patienterna var välinformerade via andra informationskällor som tidningar och TV. Några försökte bedöma patienternas behov och kapacitet att förstå information.
	GP hade en ambivalent inställning till remittering till ortopedkirurg. Å ena sidan kände de inte att kirurgen hade bättre kunskap och behandlingsalternativ. Å andra sidan kunde de ibland använda kirurgen för att undfly den psykologiska bördan som patienten och frånvaron av behandlingsalternativ innebar.	Beskrev ambivalent inställning till vidareremittering till kirurg, å ena sidan upplevdes inte kirurgen ha bättre kunskap och behandlingsalternativ. Å andra sidan ett sätt att slippa den psykologiska bördan av en patient utan behandlingsalternativ.
	GP kände ett tryck från patienterna att remittera till specialist. Några sade att de ibland kände sig ”abused” av såväl patienter som specialist eftersom patienten krävde remittering medan kirurgen inte tog sig tid att förklara resultaten av undersökningarna. Därför ignorerade GP ofta krav på remittering.	Upplevde tryck från patienterna att remittera till specialist, vilket ofta ignorerades. Orsaken var att kirurgen inte tog sig tid att förklara resultaten av undersökningarna.
	GPs sade att paracetamol som är förstahandsval inte accepterades som en äkta smärtlindrare eftersom de flesta patienterna kände till det som ett läkemedel mot huvudvärk som finns tillgängligt utan recept. Patienterna hade därför oftast redan provat paracetamol. För GPs var därför NSAIDs huvudpelaren i behandlingen. Sedan COX-2 hämmarna hade dragits in kände läkarna sig osäkra på vad som kunde ses som en ”appropriate” behandling.	Upplevelse att paracetamol på recept inte accepterades som äkta smärtlindrare av patienterna, eftersom det finns receptfritt mot huvudvärk och de redan hade provat det. NSAID huvudpelare men osäkerhet om val av substans.
	GPs kände att, tack vare bipacksedlarna, fokuserade patienterna i huvudsak på biverkningar och broschyrerna betraktades som ett hinder för optimal behandling. GPs huvudsyfte var att tillförsäkra att patienterna faktiskt tog sitt läkemedel. Därför hade de oftast utvecklat individuella strategier som bestod av en balansakt mellan förklaringar för förväntade invändningar mot behandlingen, legala krav och förminskning (belittlement).	Bipacksedlarna leder till att patienterna fokuserar på biverkningar och de betraktades som ett hinder för optimal behandling. Huvudsyftet var att tillförsäkra att patienterna tog sitt läkemedel och läkarna hade individuella strategier för att nå patienten.
	Beträffande opiater sa GPs att många patienter skulle vägra ta dessa ”heavy	Upplevde att många patienter vägrade att ta ett tungt läkemedel som opiater

Författare År Ref	Meningsenhet	Tema nivå 1
	drugs" och det verkade som om även GPs såg dem som överbehandling vid OA. Dessutom sade de att de inte förskrev opiater pga att de är illa tolererade och orsakar illamående.	och läkare såg dem som överbehandling med toleransproblem och biverkningar.
	Nästan samtliga GPs underströk att de adresserade beteendeförändringar som kan försena progression av OA, inklusive viktnedgång och stärkande av muskler. Emellertid medgav de flesta att de inte fokuserade på att öka patienternas motivation till beteendeförändringar utan endast gav allmänna rekommendationer.	Inget fokus på att motivera patienterna att ändra levnadsvanor även om de tog upp det som allmänna rekommendationer

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