

# **SECTION ONE**

# **APPENDIX A.I: METHODOLOGY AND SEARCH STRATEGY – SYSTEMATIC REVIEWS ON OPIOIDS AND CHRONIC LOW BACK PAIN**

## **Inclusion criteria**

### **Types of studies**

Only systematic reviews on a single intervention were included for analysis. Reviews that assessed a broad treatment category comprising multiple interventions, such as pharmacotherapy or conservative treatment, or conditions (treatment of patients with chronic low back pain and pain in other regions of the body) were excluded. An article was deemed to be a systematic review if it met all of the following criteria as defined by Cook et al.:<sup>1</sup>

- 1) focused clinical question;
- 2) explicit search strategy;
- 3) use of explicit, reproducible, and uniformly applied criteria for article selection;
- 4) critical appraisal of the included studies encompassing the use of a quality tool or checklist;
- 5) qualitative or quantitative data synthesis.

### **Participants**

Data were collected on patients with non-malignant chronic pain that had persisted for at least three months. Patients with acute pain or pain secondary to a defined systemic disease, such as cancer, AIDS, diabetes, or sickle cell anemia were excluded. However, patients with disorders of the skeletal system, such as osteoarthritis, were included.

### **Index intervention**

For opioids, any review assessing an opioid analgesic, administered by any route, which was used either alone or in combination with another drug or treatment was included. Reviews of combination drugs that have an opioid component, such as mersyndol, were excluded because of the difficulty in determining the contribution of the opioid compound to the overall treatment effect.

For low back pain, any medical, mechanical, or non-surgical intervention designed to treat patients with chronic low back pain was considered.

### **Comparative intervention**

Any medical, mechanical, or non-surgical intervention designed to treat patients with non-malignant chronic pain. Placebo and no treatment comparisons were also included. For opioids, reviews comparing different treatment regimens or types of opioid therapy were also included.

### **Literature search strategy**

The medical literature was searched to identify relevant reviews published in English from 2000 to May, 2004. The date restriction was applied to ensure that the research collected was current and clinically relevant. Fourteen update searches were conducted for SRs on non-malignant

chronic low back pain, between November 2004 and August 2009\*. Two update searches for SRs on opioids were conducted in June 2006 and September 2007.

SRs detailed in the *Evidence in Brief* summaries were replaced if the update searches identified a more recently published SR of the same or better quality that used identical comparators. In cases where a SR described a particular subgroup of chronic pain patients (e.g. low back pain, osteoarthritis) or used different or additional comparators to those of the original SR, both the original and the newer SR were included in the *Evidence in Brief* summary.

## Search summary for systematic reviews on opioids for non-malignant chronic pain

The literature search was conducted by the Research Librarian between May 18, 2004 and May 28, 2004. The search was updated in June 2006 and September 2007 because two comprehensive meta-analysis on the use of opioids for treating non-malignant chronic pain and non-malignant chronic low back pain were published in May 2006 and July 2007 respectively.

Medical Subject Headings (MeSH) relevant to this topic are: Analgesics, Opioid; Narcotics.

Database	Search Date/Edition	Search Terms
Cochrane Database of Systematic Reviews (Licensed resource - Wiley)	Issue 3, 2007	MeSH descriptor <b>ANALGESICS, OPIOID</b> explode all trees OR MeSH descriptor <b>NARCOTICS</b> , this term only OR (opiates or opiate or opioid or opioids or narcotics or opium or morphine)
NHS Centre for Reviews and Dissemination (CRD) Databases: HTA, DARE, NHS EED ( <a href="http://www.york.ac.uk/inst/crd/crddatabases.htm">http://www.york.ac.uk/inst/crd/crddatabases.htm</a> )	HTA September 14, 2007 DARE September 14, 2007 NHS EED September 14, 2007	#1 MeSH Analgesics, Opioid #2 opiate OR opioid OR Narcotics OR opium OR morphine OR Codeine OR Fentanyl OR duragesic OR hydrocodone OR hydromorphone OR dilaudid OR levorphanol OR Meperidine OR demerol OR pethidine OR Methadone OR oxycodone OR oxycontin OR oxymorphone OR numorphan OR propoxyphene OR darvon #3 (meta-analysis OR meta-anal OR metaanal OR quantitativ review OR quantitative overview OR systematic review OR systematic overview OR methodologic review OR methodologic overview) OR (review AND (medline OR pubmed OR embase OR cinahl)) For HTA and Dare: #1 AND #2 For NHS EED: #1 AND #2 AND #3
ECRI's HTAIS resources (Licensed Resource)	September 14, 2007	opioid* OR opiate* OR narcotic* OR opium OR morphine OR codeine OR fentanyl

\* Updates were conducted in November 2004, March 2005, July 2005, December 2005, May 2006, November 2006, March 2007, August 2007, December 2007, April 2008, August 2008, December 2008, April 2009, and August 2009.

Database	Search Date/Edition	Search Terms
PubMed: National Library of Medicine (www.pubmed.gov)	September 14, 2007	<p>#1 (opiates OR opiate OR opioid OR opioids OR Analgesics, Opioid OR Narcotics OR opium OR morphine OR Codeine OR Fentanyl OR duragesic OR hydrocodone OR hydromorphone OR dilaudid OR levorphanol OR Meperidine OR demerol OR pethidine OR Methadone OR oxycodone OR oxycontin OR oxymorphone OR numorphan OR propoxyphene OR darvon) AND systematic[sb]</p> <p>#2 (opiates OR opiate OR opioid OR opioids OR Analgesics, Opioid OR Narcotics OR opium OR morphine OR Codeine OR Fentanyl OR duragesic OR hydrocodone OR hydromorphone OR dilaudid OR levorphanol OR Meperidine OR demerol OR pethidine OR Methadone OR oxycodone OR oxycontin OR oxymorphone OR numorphan OR propoxyphene OR darvon) AND ((meta-analysis OR meta-anal* OR metaanal* OR quantitativ* review* OR quantitative* overview* OR systematic* review* OR systematic* overview* OR methodologic* review* OR methodologic* overview*) OR (review* AND (medline OR pubmed OR embase OR cinahl)))</p> <p>#3 (opiates OR opiate OR opioid OR opioids OR Analgesics, Opioid OR Narcotics OR opium OR morphine OR Codeine OR Fentanyl OR duragesic OR hydrocodone OR hydromorphone OR dilaudid OR levorphanol OR Meperidine OR demerol OR pethidine OR Methadone OR oxycodone OR oxycontin OR oxymorphone OR numorphan OR propoxyphene OR darvon), Limits: Meta-Analysis</p> <p>#1 OR #2 OR #3</p>

Database	Search Date/Edition	Search Terms
Cinahl (Licensed Resource – EBSCOHOST)	September 19, 2007	<ol style="list-style-type: none"> <li>1. opiates or opiate or opioid or opioids or Analgesics, Opioid or Narcotics or opium or morphine or Codeine or Fentanyl or duragesic or hydrocodone or hydromorphone or dilaudid or levorphanol or Meperidine or demerol or pethidine or Methadone or oxycodone or oxycontin or oxymorphone or numorphan or propoxyphene or darvon</li> <li>2. PT systematic review</li> <li>3. meta-anal* or metaanal*</li> <li>4. (systematic* OR quantitativ* OR methodologic) AND (review* OR overview*)</li> <li>5. integrat* AND research</li> <li>6. quantitative* AND synthes*</li> <li>7. S2 OR S3 OR S4 OR S5 OR S6</li> <li>8. PT review or (review* or overview*)</li> <li>9. medline or medlars or pubmed or index medicus or embase or cochrane</li> <li>10. scisearch or web of science or psycinfo or psychinfo or cinahl or cinhal</li> <li>11. excerpta medica or psychlit or psychlit or current contents or science citation index or sciences citation index</li> <li>12. hand search* or manual search*</li> <li>13. ((electronic or bibliographic) AND database*) or periodical index*</li> <li>14. pooling or pooled or mantel haenszel</li> <li>15. peto or der simonian or dersimonian or fixed effect*</li> <li>16. (combine* or combining) AND (data or trial or trials or studies or study or result or results)</li> <li>17. S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16</li> <li>18. 8 and 17</li> <li>19. 7 or 18</li> <li>20. hta* or "health technology assessment*" or "biomedical technology assessment*"</li> <li>21. 1 and (19 or 20)</li> </ol>

Database	Search Date/Edition	Search Terms
<p>AMED (Allied and Complementary Medicine)</p> <p>EMBASE</p> <p>International Pharmaceutical Abstracts</p> <p>PsycINFO</p>	<p>AMED September 2007</p> <p>EMBASE 2007, Week 37</p> <p>International Pharmaceutical Abstracts September 19, 2007</p> <p>PsycINFO September 19, 2007</p>	<ol style="list-style-type: none"> <li>1. (opiates or opiate or opioid or opioids or Analgesics, Opioid or Narcotics or opium or morphine or Codeine or Fentanyl or duragesic or hydrocodone or hydromorphone or dilaudid or levorphanol or Meperidine or demerol or pethidine or Methadone or oxycodone or oxycontin or oxymorphone or numorphan or propoxyphene or darvon).mp. [mp=ab, hw, ti, sh, tn, ot, dm, mf, rw]</li> <li>2. meta-analysis.pt</li> <li>3. (meta-anal\$ or metaanal\$).mp</li> <li>4. (((quantitativ\$ adj3 review\$1) or quantitativ\$) adj3 overview\$).mp</li> <li>5. (((systematic adj3 review\$1) or systematic) adj3 overview\$1).mp</li> <li>6. (((methodologic adj3 review\$1) or methodologic) adj3 overview\$).mp</li> <li>7. (integrat\$ adj5 research).mp</li> <li>8. (quantitativ\$ adj3 synthes\$).mp</li> <li>9. or/2-8</li> <li>10. review.pt. or (review\$ or overview\$).mp</li> <li>11. (medline or medlars or pubmed or index medicus or embase or cochrane).mp</li> <li>12. (scisearch or web of science or psycinfo or psychinfo or cinahl or cinhal).mp</li> <li>13. (excerpta medica or psychlit or psyclit or current contents or science citation index or sciences citation index).mp</li> <li>14. (hand search\$ or manual search\$).mp</li> <li>15. (((electronic adj3 database\$) or bibliographic) adj3 database\$) or periodical index\$).mp</li> <li>16. (pooling or pooled or mantel haenszel).mp</li> <li>17. (peto or der simonian or dersimonian or fixed effect\$).mp</li> <li>18. ((combine\$ or combining) adj5 (data or trial or trials or studies or study or result or results)).mp</li> <li>19. or/11-18</li> <li>20. 10 and 19</li> <li>21. 9 or 20</li> <li>22. (hta\$ or health technology assessment\$ or biomedical technology assessment\$).mp</li> <li>23. technology assessment, biomedical/ or biomedical technology assessment</li> <li>24. 22 or 23</li> <li>25. 21 or 24</li> <li>26. 1 and 25</li> <li>27. remove duplicates from 26</li> </ol>

Database	Search Date/Edition	Search Terms
AETMIS ( <a href="http://www.aetmis.gouv.qc.ca">http://www.aetmis.gouv.qc.ca</a> )	September 19, 2007	Narcotic; opioid; opioids; morphine
CADTH ( <a href="http://www.cadth.ca">www.cadth.ca</a> )	September 19, 2007	Opioid OR opioids OR opiate OR narcotics or morphine
Institute for Clinical and Evaluative Sciences (ICES) ( <a href="http://www.ices.on.ca/">http://www.ices.on.ca/</a> )	September 19, 2007	Narcotic, opioid, opioids, opiate; morphine
NZHTA ( <a href="http://nzhta.chmeds.ac.nz">http://nzhta.chmeds.ac.nz</a> )	September 19, 2007	Opioid OR opioids OR opiate OR narcotics or morphine
Web of Science (Licensed Resource -ISI)		TS=(opiates OR opiate OR opioid OR opioids OR Analgesics, Opioid OR Narcotics OR opium OR morphine OR Codeine OR Fentanyl OR duragesic OR hydrocodone OR hydromorphone OR dilaudid OR levorphanol OR Meperidine OR demerol OR pethidine OR Methadone OR oxycodone OR oxycontin OR oxymorphone OR numorphan OR propoxyphene OR darvon) AND TS=((meta-analysis OR meta-anal* OR metaanal* OR quantitativ* review* OR quantitative* overview* OR systematic* review* OR systematic* overview* OR methodologic* review* OR methodologic* overview*) OR (review* AND (medline OR pubmed OR embase OR cinahl)))

Notes: “\*”, “\$ “, and “?” are truncation characters that retrieve all possible suffix variations of the root word e.g. surg\* retrieves surgery, surgical, surgeon, etc.

Semicolons are used to separate search terms that were searched separately

### Search summary for systematic reviews on non-malignant chronic low back pain

The literature search was conducted by the Research Librarian between May 03, 2004 and May 21, 2004. Fourteen updated searches were conducted between November 2004 and August 2009\*. SRs detailed in the *Evidence in Brief* summaries were replaced if the update searches identified a more recently published SR of the same or better quality that used identical comparators. In cases where a SR used different or additional comparators to those of the original SR, both the original and the newer SR were included in the *Evidence in Brief* summary.

Medical Subject Headings (MeSH) relevant to this topic are: low back pain, back pain, pain, Sacrococcygeal Region, sciatica.

\* Updates were conducted in November 2004, March 2005, July 2005, December 2005, May 2006, November 2006, March 2007, August 2007, December 2007, April 2008, August 2008, December 2008, April 2009, and August 2009.

Database	Search Date/ Edition	Search Terms
Cochrane Database of Systematic Reviews (Wiley Interface)	2009, Issue 3 Aug 26, 2009, 2009	((sacral region OR lumbago) AND pain) OR low* back pain* OR LBP OR sciatica in Title, Abstract or Keywords (2 new results)
PubMed <a href="http://www.pubmed.gov">http://www.pubmed.gov</a>	Aug 26, 2009	#1: ((sacral region OR sacrococcygeal region OR lumbago) AND pain) OR ((low OR lower) AND back pain*) OR LBP OR sciatica  #2: meta-analysis OR meta-anal* OR metaanal* OR quantitativ* review* OR quantitative* overview* OR systematic* review* OR systematic* overview* OR methodologic* review* OR methodologic* overview* OR (review* AND (medline OR pubmed OR embase OR cinahl))  #3: #1 AND #2 OR (#1 AND (systematic[ <i>sb</i> ] OR meta-analysis[ <i>pt</i> ])) (61 results before dup removal)
CRD Databases <a href="http://www.crd.york.ac.uk/crdweb/">http://www.crd.york.ac.uk/crdweb/</a> (HTA and DARE only)	Aug 26, 2009	((sacral region OR lumbago) AND pain) OR low* back pain OR LBP OR sciatica  (33 results before removing duplicates)
ECRI HTAIS Database <a href="http://www.ta.ecri.org/Topics/prod/home/current.aspx">http://www.ta.ecri.org/Topics/prod/home/current.aspx</a>	Aug 26, 2009	Browse Evidence Reports section (0 new results)
AMED (Allied and Complementary Medicine) Ovid Licensed Resource	Aug 26, 2009	((sacral region OR sacrococcygeal region OR lumbago) AND pain) OR low\$ back pain\$ OR LBP OR sciatica) AND (Systematic review OR meta analysis OR technology assessment) (6 results before removing duplicates)
CINAHL EBSCO Licensed Resource	Aug 26, 2009	S1: meta analy* OR review S2: ((sacral region OR sacrococcygeal region OR lumbago) AND pain) OR low* back pain* OR LBP OR sciatica S3 S1 AND S2 (55 results before removing duplicates)
EMBASE Ovid Licensed Resource	Aug 26, 2009 [2009 Week 34]	1: Ovid Systematic Review Search*** 2: ((sacral region OR sacrococcygeal region OR lumbago) AND pain) OR low\$ back pain\$ OR LBP OR sciatica 3 1 AND 2 (55 results before duplicate removal)
Web of Science Licensed Resource	Aug 26, 2009	TS=(((sacral region OR lumbago) AND pain) OR low* back pain* OR LBP OR sciatica) AND TS=(meta-analysis OR meta-anal* OR metaanal* OR quantitativ* review* OR quantitative* overview* OR systematic* review* OR systematic* overview* OR methodologic* review* OR methodologic* overview*) (140 before duplicate removal)
PsycINFO	Aug 26,2009	#1: Ovid Systematic Review Search***

Ovid Licensed Resource	[August Week 4 2009]	#2: ((sacral region OR sacrococcygeal region OR lumbago) AND pain) OR low\$ back pain\$ OR LBP OR sciatica #3 #1 AND #2 (6 results before duplicate removal)
AETMIS <a href="http://www.aetmis.gouv.qc.ca">http://www.aetmis.gouv.qc.ca</a>	Aug 26,2009	Browsed list of publications (no new results)
CADTH <a href="http://www.cadth.ca/index.php/en/hta/reports-publications/search">http://www.cadth.ca/index.php/en/hta/reports-publications/search</a>	Aug 26,2009	pain ; LBP ; sciatica (no new results)
ICES <a href="http://www.ices.on.ca/">http://www.ices.on.ca/</a>	Aug 26,2009	sacral; lumbago; "low back pain" ; "lower back pain"; LBP; sciatica (no new relevant results)
NZHTA <a href="http://nzhta.chmeds.ac.nz">http://nzhta.chmeds.ac.nz</a>	June 2007	Stopped producing June 2007 Browsed publications list
<b>Rehabilitation Databases</b>		
RehabData <a href="http://www.naric.com/research/rehab/default.cfm">http://www.naric.com/research/rehab/default.cfm</a>	Aug 26,2009 (newest results 2007)	With all the words: low back pain With at least one of the words: review meta-analysis search medline (no new results)
Cirrie Database of International Rehabilitation Research <a href="http://cirrie.buffalo.edu/search/index.php">http://cirrie.buffalo.edu/search/index.php</a>	Aug 26,2009	Subject Heading: "back pain" AND review (no results)
PEDro: The Physiotherapy Evidence Database <a href="http://www.pedro.org.au/">http://www.pedro.org.au/</a>	Aug 26,2009	Problem: pain Body Part: lumbar spine, sacro-iliac joint or pelvis Method: systematic review (5 results before duplicate removal)
OTSeeker <a href="http://www.otseeker.com/">http://www.otseeker.com/</a>	Aug 26,2009	Keywords: (low OR lower) AND back pain Method: Systematic Reviews (4 results before duplicate removal (2008-09))
SPORT Discus Ebsco Licensed Resource	Aug 26, 2009	(Low* back pain OR backache) AND (review OR medline OR search OR meta analysis) (28 results before duplicate removal)

**Notes:**

*Truncation:* The \* and \$ symbol are truncation character that retrieves possible suffix variations of the root word e.g. surg\* retrieves surgery, surgical, surgeon, etc. In databases accessed via the OVID platform the truncation character is \$;

Semicolons are used to indicate terms that were searched separately.

**\*\*\* OVID Methodology Search Filter for Systematic Reviews Only (Used for EMBASE and PsycInfo):**

- 1 meta-analysis.pt.
- 2 (meta-anal\$ or metaanal\$).mp.
- 3 (((quantitativ\$ adj3 review\$1) or quantitativ\$) adj3 overview\$).mp.
- 4 (((systematic adj3 review\$1) or systematic) adj3 overview\$1).mp.
- 5 (((methodologic adj3 review\$1) or methodologic) adj3 overview\$).mp.
- 6 (integrat\$ adj5 research).mp.
- 7 (quantitativ\$ adj3 synthes\$).mp.
- 8 or/1-7
- 9 review.pt. or (review\$ or overview\$).mp.
- 10 (medline or medlars or pubmed or index medicus or embase or cochrane).mp.

- 11 (scisearch or web of science or psycinfo or psychinfo or cinahl or cinhal).mp.
- 12 (excerpta medica or psychlit or psychlit or current contents or science citation index or sciences citation index).mp.
- 13 (hand search\$ or manual search\$).mp.
- 14 (((electronic adj3 database\$) or bibliographic) adj3 database\$) or periodical index\$).mp.
- 15 (pooling or pooled or mantel haenszel).mp.
- 16 (peto or der simonian or dersimonian or fixed effect\$).mp.
- 17 ((combine\$ or combining) adj5 (data or trial or trials or studies or study or result or results)).mp.
- 18 or/10-17
- 19 9 and 18
- 20 8 or 19
- 21 (hta\$ or health technology assessment\$ or biomedical technology assessment\$).mp.
- 22 technology assessment, biomedical/ or biomedical technology assessment/
- 23 21 or 22
- 24 20 or 23

## **Literature selection process**

Study selection was conducted by one reviewer for the opioid studies and another reviewer for the chronic low back pain studies. Articles were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of potentially eligible studies were retrieved. In some cases, when the full text of the article was retrieved, closer examination revealed that it did not meet the inclusion criteria specified by the protocol. Consequently these papers were excluded (Appendix B.I.). When the same studies were reported in more than one systematic review, only the review quoting the most complete data set was used to avoid data duplication.

## **Assessment methods**

### **Study methodology appraisal**

The included trials were assessed with respect to various aspects of methodology and reporting using a checklist adapted from a number of sources (Appendix C.I.).<sup>2-5</sup> The study quality assessments were undertaken by two independent reviewers and any disagreements that could not be resolved by discussion were referred to a third reviewer for mediation until consensus was reached. The checklist was operationalised by constructing a dictionary that explained each criterion. The two reviewers discussed the dictionary with respect to the interpretation of questions prior to assessing the reviews. The systematic reviews were rated according to six essential quality criteria as good, average or poor. Critical appraisal results for all included reviews are tabulated in Appendix D.I.

### **Outcome measures and data extraction**

Study profile information as well as safety and efficacy data were extracted by one reviewer for the opioid studies and another reviewer for the chronic low back pain studies using standardised data extraction forms developed *a priori* (Appendix E.I.).

## References

1. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: Synthesis of best evidence for clinical decisions. *Annals of Internal Medicine* 1997;126:376-80.
2. Fishbain D, Cutler RB, Rosomoff HL, Rosomoff RS. What is the quality of the implemented meta-analytic procedures in chronic pain treatment meta-analyses? *Clinical Journal of Pain* 2000;16(1):73-85.
3. Aggressive Research Intelligence Facility - University of Birmingham. ARIF Critical Appraisal Checklist. Available at: <http://www.bham.ac.uk/arif/caprocess.htm> (accessed 2002 Feb 19).
4. University of Alberta. Evidence Based Medicine Tool Kit. University of Alberta. Available at: <http://www.med.ualberta.ca/ebm/main.htm> (accessed: 2000 Nov 1).
5. Greenhalgh T. How to read a paper. Papers that summarise other papers (systematic reviews and meta-analysis). *BMJ* 1997;315:672-5.

## APPENDIX B.I: EXCLUDED STUDIES

Table 1: Summary of excluded reviews on opioids for non-malignant chronic pain (listed in alphabetical order of first author)

Study	Study Type	Reason for Exclusion
State Medical Society of Wisconsin statement on the use of opioids for the treatment of chronic pain. <i>WMJ</i> 2001;100:22-5	Clinical practice guidelines	Not a systematic review
Agency for Healthcare Research and Quality. <i>Management of chronic central neuropathic pain following traumatic spinal cord injury</i> . 2001. Rockville: Agency for Healthcare Research and Quality (AHRQ)	Systematic review	No definition of chronic pain provided in the study selection criteria. The review pooled results from studies of patients with chronic and acute/subacute (<3 months duration) pain. It was impossible to separate the results for the chronic pain patients from those with acute pain.
Alper BS, Lewis PR. Treatment of postherpetic neuralgia: a systematic review of the literature. <i>J Fam Pract</i> 2002;51:121-8	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Amabile CM, Bowman BJ. Overview of oral modified-release opioid products for the management of chronic pain. <i>Ann Pharmacother</i> 2006;40(7-8):1327-35	Review	The quality of the included studies was not formally assessed with a quality tool.
Anseau M, Reggers J, Somers L, Richy F, Van Deun P, Sabbe B. Meta-analyses of opiate maintenance therapies. <i>European Neuropsychopharmacology</i> 2006;16:S503	Conference abstract	Abstract based on a study referred as: Cucherat M. Meta-analysis des essais therapeutiques, Paris, Masson 1997.
Avouac J, Gossec L, Dougados M. Opioids in osteoarthritis are efficacious but with side effects: A systematic literature review. <i>Arthritis and Rheumatism</i> 2006;54(9):S672	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Bartleson JD. Evidence for and against the use of opioid analgesics for chronic nonmalignant low back pain: a review. <i>Pain Med</i> 2002;3:260-71	Review	The quality of the included studies was not formally assessed with a quality tool.
Bennett G, Serafini M, Burchiel K, Buchser E, Classen A, Deer T et al. Evidence-based review of the literature on intrathecal delivery of pain medication. <i>J Pain Symptom Manage</i> 2000;20:S12-S36	Review	The quality of the included studies was not formally assessed with a quality tool. The review pooled results from patients with non-malignant chronic pain and cancer pain.
Bjordal JM, Klovning A, Ljunggren AE, Slordal L. Short-term efficacy of pharmacotherapeutic interventions in osteoarthritic knee pain: A meta-analysis of randomised placebo-controlled trials. <i>Eur J Pain</i> 2006;May 6	Systematic review	Included different interventions.

Study	Study Type	Reason for Exclusion
Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. <i>Cochrane Database Syst Rev</i> 2006(3):CD005522	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Chamberlin KW, Cottle M, Neville R, Tan J. Oral oxycodone for pain management. <i>Ann Pharmacother</i> 2007;41(7):1144-52	Review	The quality of the included studies was not formally assessed with a quality tool.
Chan PSL, Clark AJ. Postherpetic neuralgia: Review of treatment modalities. <i>Pain Research &amp; Management</i> 2000;5(1):69-74	Narrative review	Not a systematic review
Clark AJ, Ahmedzai SH, Allan LG, Camacho F, Horbay GL, Richarz U et al. Efficacy and safety of transdermal fentanyl and sustained-release oral morphine in patients with cancer and chronic non-cancer pain. <i>Curr Med Res Opin</i> 2004;20(9):1419-28	Review	The quality of the included studies was not formally assessed with a quality tool.
Curatolo M, Bogduk N. Pharmacologic pain treatment of musculoskeletal disorders: current perspectives and future prospects. <i>Clin J Pain</i> 2001;17:25-32	Review	The quality of the included studies was not formally assessed with a quality tool.
Dale O, Hjortkjaer R, Kharasch ED. Nasal administration of opioids for pain management in adults. <i>Acta Anaesthesiol Scand</i> 2002;46:759-70	Review	No results for chronic non-malignant pain.
Deer TR, Serafini M, Buchser E, Ferrante FM, Hassenbusch SJ. Intrathecal bupivacaine for chronic pain: A review of current knowledge. <i>Neuromodulation</i> 2002;5:196-20	Review	The quality of the included studies was not formally assessed with a quality tool.
Devulder J, Richarz U, Nataraja SH. Impact of long-term use of opioids on quality of life in patients with chronic, non-malignant pain. <i>Curr Med Res Opin</i> 2005;21(10):1555-68	Systematic review	The review pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Dickinson BD, Altman RD, Nielsen NH, Williams MA, for the Council on Scientific Affairs. Use of opioids to treat chronic, noncancer pain. <i>West J Med</i> 2000;172:107-15	Review	The quality of the included studies was not formally assessed with a quality tool.
Dühmke RM, Cornblath DD, Hollingshead JRF. Tramadol for neuropathic pain. <i>Cochrane Database Syst Rev</i> . 2004;(2):CD003726	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.

Study	Study Type	Reason for Exclusion
Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennett GJ et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. <i>Arch Neurol</i> 2003;60:1524-34	Narrative review	Not a systematic review.
Eisenberg E, McNicol ED, Carr DB. Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: systematic review and meta-analysis of randomized controlled trials. <i>JAMA</i> 2005;293(24):3043-52	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Eisenberg E, McNicol ED, Carr DB. Efficacy of mu-opioid agonists in the treatment of evoked neuropathic pain: Systematic review of randomized controlled trials. <i>Euro J Pain</i> 2006;10(8):667-76	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. <i>Cochrane Database Syst Rev</i> 2006(3):CD006146	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Finnerup NB, Otto M, McQuay HJ, Jensen TS, Sindrup SH. Algorithm for neuropathic pain treatment: an evidence based proposal. <i>Pain</i> 2005;118(3):289-305	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Gates BJ. Update on migraines, neuropathy, and opioids. <i>Advances in Pharmacy</i> 2005;3(3):264-81	Review	The quality of the included studies was not formally assessed with a quality tool.
Gladstone JP, Dodick DW. Current and emerging treatment options for migraine and other primary headache disorders. <i>Expert Review of Neurotherapeutics</i> 2003;3(6):845-72	Narrative review	Not a systematic review.
Guay DR. Use of oral oxymorphone in the elderly. <i>Consult Pharm</i> 2007;22(5):417-30	Review	The quality of the included studies was not formally assessed with a quality tool.
Hempnall K, Nurmiikko TJ, Johnson RW, A'Hern RP, Rice AS. Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. <i>PLoS Med</i> 2005;2(7):e164	Systematic review	Included different interventions.
Hollingshead JRF, Dühmke RM, Cornblath DD. Tramadol for neuropathic pain. <i>Cochrane Database Syst Rev</i> 2004;(2)	Systematic review	No results for chronic non-malignant pain.
Jarrell JF, Vilos GA, Allaire C, Burgess S, Fortin C, Gerwin R et al. Consensus guidelines for the management of chronic pelvic pain. <i>J Obstet Gynaecol Can</i> 2005;27(8):781-826	Clinical practice guidelines	Not a systematic review.

Study	Study Type	Reason for Exclusion
Jovey RD, Ennis J, Gardner-Nix J, Goldman B, Hays H, Lynch M et al. Use of opioid analgesics for the treatment of chronic noncancer pain - a consensus statement and guidelines from the Canadian Pain Society, 2002. <i>Pain Res Manag</i> 2003;8 Suppl A:3A-28A	Narrative review	Not a systematic review.
Kahan, M, Srivastava, A, Wilson, L, Mailis-Gagnon, A, Midmer D. Opioids for managing chronic non-malignant pain: safe and effective prescribing. <i>Can Fam Physician</i> 2006;52(9):1091-96	Narrative review	Not a systematic review.
Kalso E, Allan L, DelleMijn PL, Faura CC, Ilias WK, Jensen TS et al. Recommendations for using opioids in chronic non-cancer pain. <i>Eur J Pain</i> 2003;7:381-6	Narrative review	Not a systematic review.
Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. <i>Pain</i> 2004;112(3):372-80	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Knight KH, Brand FM, Mchaourab AS, Veneziano G. Implantable intrathecal pumps for chronic pain: highlights and updates. <i>Croat Med J</i> 2007;48(1):22-34	Narrative review	Not a systematic review.
Kvien TK, Viktil K. Pharmacotherapy for regional musculoskeletal pain. <i>Best Practice &amp; Research in Clinical Rheumatology</i> 2003;17:137-50	Narrative review	Not a systematic review.
Latta KS, Ginsberg B, Barkin RL. Meperidine: a critical review. <i>Am J Ther</i> 2002;9:53-68	Narrative review	Not a systematic review.
Layson-Wolf C, Goode JV, Small RE. Clinical use of methadone. <i>J Pain Palliat Care Pharmacother</i> 2002;16:29-59	Review	No results for chronic non-malignant pain.
List T, Axelsson S, Leijon G. Pharmacologic interventions in the treatment of temporomandibular disorders, atypical facial pain, and burning mouth syndrome. A qualitative systematic review. <i>J Orofac Pain</i> 2003;17:301-10	Systematic review	No results for an opioid drug alone, only for a drug (mersyndol) with an opioid component.
Lynch ME. A review of the use of methadone for the treatment of chronic noncancer pain. <i>Pain Res Manage</i> 2005;10(3):133-44	Narrative review	Not a systematic review.
Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA. Systematic review: Opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. <i>Ann Internal Med</i> 2007;146:116-27	Review	The type of studies included in the review were not mentioned in the background or method section of the study.

Study	Study Type	Reason for Exclusion
Moore RA, McQuay HJ. Prevalence of opioid adverse events in chronic non-malignant pain: systematic review of randomised trials of oral opioids. <i>Arthritis Res Ther</i> 2005;7(5):R1046-R1051	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Moulin DE. Systemic drug treatment for chronic musculoskeletal pain. <i>Clin J Pain</i> 2001;17:S86-S93	Review	The quality of the included studies was not formally assessed with a quality tool.
Naliboff D, Wu SM, Pham Q. Clinical considerations in the treatment of chronic pain with opiates. <i>J Clin Psychol</i> 2006;62(11):1397-1408	Case study and narrative review	Not a systematic review.
Nedeljkovic SS, Wasan A, Jamison RN. Assessment of efficacy of long-term opioid therapy in pain patients with substance abuse potential. <i>Clin J Pain</i> 2002;18:S39-S51	Narrative review	Not a systematic review.
Neighbors DM, Bell TJ, Wilson J, Dodd SL. Economic evaluation of the fentanyl transdermal system for the treatment of chronic moderate to severe pain. <i>J Pain Symptom Manage</i> 2001;21(2):129-43	Cost utility analysis with a review component	The quality of the included studies was not formally assessed with a quality tool. The review section pooled results from patients with non-malignant chronic pain and cancer pain.
Nicholas MK, Molloy AR, Brooker C. Using opioids with persisting noncancer pain: a biopsychosocial perspective. <i>Clin J Pain</i> 2006;22(2):137-46	Narrative review	Not a systematic review.
Nicholson B. Responsible prescribing of opioids for the management of chronic pain. <i>Drugs</i> 2003;63:17-32	Narrative review	Not a systematic review.
Nicholson BD. Diagnosis and management of neuropathic pain: a balanced approach to treatment. <i>JAANP Supplement</i> 2003;15(12):3-9	Review	The quality of the included studies was not formally assessed with a quality tool.
Podichetty VK, Mazanec DJ, Biscup RS. Chronic non-malignant musculoskeletal pain in older adults: clinical issues and opioid intervention. <i>Postgrad Med J</i> 2003;79:627-33	Narrative review	Not a systematic review.
Polatin PB, Dersh J. Psychotropic medication in chronic spinal disorders. <i>Spine J</i> 2004;4(4):436-50	Systematic review	Included different intervention drugs.
Quigley C. Hydromorphone for acute and chronic pain. <i>Cochrane Database Syst Rev</i> 2002;(1):CD003447	Systematic review	No results for chronic non-malignant pain.
Quigley, C. Opioid switching to improve pain relief and drug tolerability. <i>Cochrane Database of Systematic Reviews</i> 2004(3):CD004847	Systematic review	Included only two studies (non-randomized control studies) out of 52 on non-cancer pain.

Study	Study Type	Reason for Exclusion
Risचितelli DG, Karbowicz SH. Safety and efficacy of controlled-release oxycodone: a systematic literature review. <i>Pharmacotherapy</i> 2002;22:898-904	Review	The quality of the included studies was not formally assessed with a quality tool.
Sandoval JA, Furlan AD, Mailis-Gagnon A. Oral methadone for chronic noncancer pain: a systematic literature review of reasons for administration, prescription patterns, effectiveness, and side effects. <i>Clin J Pain</i> 2005;21(6):503-12	Systematic review	No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Schnitzer T. The new analgesic combination tramadol/acetaminophen. <i>Eur J Anaesthesiol – Supplement</i> 2003;20(28):13-7	Narrative review	Not a systematic review.
Schnitzer TJ. Update of ACR guidelines for osteoarthritis: Role of the coxibs. <i>J Pain &amp; Symptom Manage</i> 2002;23(4 Suppl 1):S24-S30	Narrative review	Not a systematic review.
Simpson KH. Individual choice of opioids and formulations: strategies to achieve the optimum for the patient. <i>Clin Rheumatol</i> 2002;21(Suppl 1):S5-S8	Narrative review	Not a systematic review.
Sindrup SH, Jensen TS. Pharmacologic treatment of pain in polyneuropathy. <i>Neurology</i> 2000;55(7):915-20	Review	The quality of the included studies was not formally assessed with a quality tool.
Todd C. Meeting the therapeutic challenge of the patient with osteoarthritis. <i>J Am Pharm Assoc (Wash)</i> 2002;42:74-82	Review	The quality of the included studies was not formally assessed with a quality tool.
Trescot AM, Boswell MV, Atluri SL, Hansen HC, Deer TR, Abdi S, et al. Opioid guidelines in the management of chronic non-cancer pain. <i>Pain Physician</i> 2006;9(1):1-39	Narrative review	Not a systematic review.
Turner JA, Sears JM, Loeser JD. Programmable intrathecal opioid delivery systems for chronic noncancer pain: a systematic review of effectiveness and complications. <i>Clin J Pain</i> 2007;23(2):180-95	Systematic review	Included different intervention drugs.
Watson CP. The treatment of neuropathic pain: antidepressants and opioids. <i>Clin J Pain</i> 2000;16:S49-S55	Review	The quality of the included studies was not formally assessed with a quality tool.
Weinbroum AA, Rudick V, Paret G, Ben Abraham R. The role of dextromethorphan in pain control. <i>Can J Anaesth</i> 2000;47:585-96	Review	The quality of the included studies was not formally assessed with a quality tool.

Study	Study Type	Reason for Exclusion
Williams JE, Louw G, Towler G. Intrathecal pumps for giving opioids in chronic pain: a systematic review. <i>Health Technol Assess</i> 2000;4(32):1-65	Review	The quality of the included studies was not formally assessed with a quality tool. No definition of chronic pain provided in the study selection criteria – the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
Zernikow B, Michel E, Anderson B. Transdermal fentanyl in childhood and adolescence: a comprehensive literature review. <i>J Pain</i> 2007;8(3):187-207	Review	The quality of the included studies was not formally assessed with a quality tool. The review pooled results from patients with non-malignant chronic pain and cancer pain. No study selection criteria provided.

**Table 2: Summary of excluded reviews on treatments for chronic low back pain (LBP) (listed in alphabetical order of first author)**

Study	Study Type	Reason for Exclusion
Acupuncture for chronic osteoarthritis pain, headache and low back pain, <i>Bloomington</i> . MN: Institute for Clinical Systems Improvement, 2000	Health technology assessment report	Presented combined results obtained with acupuncture in studies of patients with acute, sub-acute and chronic LBP.
Allen R, Williams ACD. Review: behavioural treatment has a small to moderate beneficial effect on chronic low back pain. <i>Evidence-Based Mental Health</i> , 2001;4(2):55	Brief review of a Cochrane publication	Not a systematic review.
Assendelft WJ, Morton SC, Yu EI et al. Spinal manipulative therapy for low back pain. A meta-analysis of effectiveness relative to other therapies. <i>Ann Intern Med</i> 2003;138(11):871-81	Systematic review	Pooled the results from studies of patients with sub-acute (semi-acute) and chronic pain. A systematic review: Assendelft WJJ, Morton SC, Yu Emily I, Suttorp MJ, Shekelle PG. Spinal manipulative therapy for low-back pain. <i>Cochrane Database Syst Rev</i> . 2004;(1):CD000447 was excluded for the same reason.
Argueta-Bernal G. Behavioral approaches for chronic low back pain. <i>Seminars in Pain Medicine</i> 2004;2(3):197-202	Review	Not a systematic review.
Bartleson JD. Evidence for and against the use of opioid analgesics for chronic nonmalignant low back pain: a review. <i>Pain Med</i> 2002;3(3):260-71	Review	No definition of chronic pain specified for the selection of studies; the quality of the studies included was not assessed with a quality tool.
Bell JA, Burnett A. Exercise for the primary, secondary and tertiary prevention of low back pain in the workplace: a systematic review. <i>J Occup Rehabil</i> 2009;19(1):8-24	Systematic review	Did not focus on chronic low back pain.
Boswell MV, Hansen HC, Trescot AM, Hirsch JA. Epidural steroids in the management of chronic spinal pain and radiculopathy. <i>Pain Physician</i> , 2003;6(3):319-34	Systematic review	Pooled the results from studies of patients with duration of pain less than 3 months.
Bronfort G, Haas M, Evans RL, Bouter LM. Efficacy of spinal manipulation and mobilization for low back pain and neck pain: a systematic review and best evidence synthesis. <i>Spine J</i> 2003;4(3):335-56	Systematic review	Defined chronic pain as pain $\geq 6$ weeks. Included two conditions (low back pain and neck pain).
Bronfort G, Haas M, Evans R, Kawchuk G, Dagenais S. Evidence-informed management of chronic low back pain with spinal manipulation and mobilization. <i>Spine J</i> 2008;8(1):213-25	Systematic review	Updates the systematic review by Branfort et al. <i>Spine J</i> 2003;4(3):335-56 (see reason for exclusion). The review published in 2008 includes two interventions.

Study	Study Type	Reason for Exclusion
Brosseau L, Milne S, Robinson V, et al. Efficacy of the transcutaneous electrical nerve stimulation for the treatment of chronic low back pain: a meta-analysis. <i>Spine</i> 2002;27(6):596-603	Systematic review (Meta-analysis)	Another systematic review published in 2005 was included: Khadilkar A, Milne S, Brosseau L, Robinson V, Saginur M, Shea B, Tugwell P, Wells G. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. <i>Cochrane Database Syst Rev</i> , 2005;(3):CD003008.
Browning R, Jackson JLO, apos, Malley PG. Cyclobenzaprine and back pain: a meta-analysis. <i>Arch Intern Med</i> 2001;161(13):1613-20	Systematic review (Meta-analysis)	Pooled the results from studies of patients with acute and chronic pain; included different conditions (neck pain).
Canadian Coordinating Office for Health Technology Assessment. <i>Spinal manipulation for lower back pain</i> . Canadian Coordinating Office for Health Technology Assessment, 2002	Health technology pre-assessment review	Not focused on chronic LBP.
Canadian Coordinating Office for Health Technology Assessment. <i>Intradiscal electrothermal therapy (IDET) for the treatment of chronic, discogenic low back pain</i> . Canadian Coordinating Office for Health Technology Assessment, 2003	Health technology pre-assessment review	Not focused on chronic LBP.
Canadian Coordinating Office for Health Technology Assesment, Cassidy D, Laupacis A, Maheu E, Saunders D. <i>Chiropractic treatment of neck and back disorders: a review of selected studies</i> , 2002	Health technology assessment review	Old report (published in 1992).
Canter PH and Ernst E. Sources of bias in reviews of spinal manipulation for back pain. <i>Wien Klin Wochenschr</i> 2005;117 (9-10):333-41	Review	Did not specify in the inclusion criteria the duration of pain (>3 months); included reviews on spinal manipulation.
Cleland J, Schulte C, Durall C. The role of therapeutic exercise in treating instability-related lumbar spine pain: a systematic review. <i>J Back Musculoskel Rehabil</i> 2002;16(2-3):105-15	Review	Did not include patients with chronic LBP.
Cooperstein R, Perle SM, Gatterman MI et al. Chiropractic technique procedures for specific low back conditions: characterizing the literature. <i>J Manipulative Physiol Ther</i> 2001;24(6):407-24	Systematic review	Did not specify in the inclusion criteria the duration of pain (>3 months).
Cook C, Hegedus EJ, Ramey K. Physical therapy exercise intervention based on classification using the patient response method: a systematic review of the literature. <i>J Manual &amp; Manipulative Ther</i> 2005;13(3):152-162	Systematic review	Did not focus on chronic LBP (>3 months).

Study	Study Type	Reason for Exclusion
Dagenais S, Mayer J, Haldeman S, Borg-Stein J. Evidence-informed management of chronic low back pain with prolotherapy. <i>Spine J</i> 2008;8(1):203-12	Review	The review updates the systematic review by Dagenais et al. <i>Cochrane Database Syst Rev.</i> 2007;(2):CD004059. (See Evidence in Brief.). Did not include new studies. The quality of the included studies is not provided.
Dagenais S, Mayer J, Wooley JR, Haldeman S. Evidence-informed management of chronic low back pain with medicine-assisted manipulation. <i>Spine J</i> 2008;8(1):142-49	Review	Focuses on manipulation under anesthesia (epidural steroid injection and joint anesthesia). The quality of the included studies was not formally assessed with a quality tool.
Derry CJ, Derry S, McQuay H, Moore RA. Systematic review of systematic reviews of acupuncture published 1996-2005. <i>Clin Med</i> 2006;6(4):381-86	Systematic review	Did not focus on chronic low back pain.
DeSantana JM. Effectiveness of transcutaneous electrical nerve stimulation for treatment of hyperalgesia and pain. <i>Current Rheumatology Reports</i> 2008;10(6):492-99	Narrative review	Not a systematic review. Did not focus on chronic low back pain.
Dryden T, Baskwill A, Preyde M. Massage therapy for the orthopaedic patient: a review. <i>Orthopaedic Nursing</i> 2004;23(5):327-334	Qualitative review	Included studies of patients with sub-acute and chronic pain.
Ernst E, Furlan A. A systematic review of massage for low back pain. <i>Focus on Alternative &amp; Complementary Therapies</i> 2003;8(1):58-59	Abstract	Abstract of a Cochrane review: Furlan AD, Brosseau L, Imamura M, Irvin E. Massage for low-back pain. <i>Cochrane Database Syst Rev.</i> 2002;(2):CD001929. (see Appendix E: Data extraction)
Ernst E. The definitive meta-analysis of spinal manipulation for back pain. <i>Focus on Alternative &amp; Complementary Therapies</i> 2003;8(4):436-37	Abstract	Abstract of a Cochrane review: Assendelft WJJ, Morton SC, Yu Emily I, Suttorp MJ, Shekelle PG. Spinal manipulative therapy for low-back pain. <i>Cochrane Database Syst Rev.</i> 2004;(1):CD000447. This review was excluded because it pooled results from studies of patients with sub-acute (semi-acute) and chronic pain.
Ferreira PH, Ferreira ML, Maher CG, Herbert RD, Refshauge K. Specific stabilisation exercise for spinal and pelvic pain: a systematic review. <i>Aust J Physiother</i> 2006;52(2):79-88	Systematic review	Pooled results from studies of patients with different conditions and durations of low back pain.
Furlan AD, Lui PW, Mailis A. Chemical sympathectomy for neuropathic pain: does it work? Case report and systematic literature review. <i>Clin J Pain</i> 2001;17(4):327-36	Review	Other conditions investigated.

Study	Study Type	Reason for Exclusion
Furlan AD, Imamura M, Dryden T, Irvin E. Massage for Low Back Pain: An Updated Systematic Review Within the Framework of the Cochrane Back Review Group. <i>Spine (Phila Pa 1976)</i> 2009;34(16):1669	Systematic review	Same as: Furlan AD, Imamura M, Dryden T, Irvin E. Massage for low-back pain. <i>Cochrane Database Syst Rev</i> (4):CD001929, 2008. (see Appendix E: Data extraction)
Gadsby JG, Flowerdew MW. Transcutaneous electrical nerve stimulation and acupuncture-like transcutaneous electrical nerve stimulation for chronic low back pain. <i>Cochrane Database Syst Rev</i> . 2000;(2):CD000210	Systematic review	Another systematic review published in 2005 was included: Khadilkar A, Milne S, Brosseau L, Robinson V, Saginur M, Shea B, Tugwell P, Wells G. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. <i>Cochrane Database Syst Rev</i> , 2005;(3):CD003008.
Gaid M, Cozens A. The role of transcutaneous electric nerve stimulation (TENS) for the management of chronic low back pain. <i>International Musculoskeletal Medicine</i> 2009;31(1):19-23	Review	Did not formally assessed studies with a quality tool. Did not specify the duration of chronic low back pain (>3 months).
Gatchel RJ and Rollings KH. Evidence-informed management of chronic low back pain with cognitive behavioral therapy. <i>Spine J</i> 2008;8(1):40-4	Narrative review	Not a systematic review.
Gay RE, Bronfort G, Evans RL. Distraction manipulation of the lumbar spine: A review of the literature. <i>J Manipulative Physiological Ther</i> 2005;28(4):266-73	Review	Did not focus on chronic LBP (>3 months).
Geurts JW, van Wijk RM, Stolker RJ, Groen GJ. Efficacy of radiofrequency procedures for the treatment of spinal pain: a systematic review of randomized clinical trials. <i>Reg Anesth Pain Med</i> 2001;26(5):394-400	Systematic review	Pooled the results from studies of patients with different conditions (LBP, neck-shoulder, whiplash).
Geytenbeek J. Evidence for effective hydrotherapy. <i>Physiotherapy</i> 2002;88(9):514-29	Review	Included and pooled the results of patients with different conditions.
Guzmán J, Esmail R, Karjalainen K, Malmivaara A, Irvin E, Bombardier C. Multidisciplinary bio-psycho-social rehabilitation for chronic low-back pain. <i>Cochrane Database Syst Rev</i> . 2002;(1):CD000963.	Systematic review	A report generated by the HTA Unit at the AHFMR Ospina M, Harstall C. Multidisciplinary pain programs for chronic pain - evidence from systematic reviews was included.
Harte AA, Baxter GD, Gracey JH. The efficacy of traction for back pain: a systematic review of randomized controlled trials. <i>Arch Phys Med Rehabil</i> . 2003;84(10):1542-53	Systematic review	Included studies of patients with acute, sub-acute and chronic LBP.
Hauggaard, A. and Persson, A. L. Specific spinal stabilisation exercises in patients with low back pain -- a systematic review. <i>Physical Therapy Reviews</i> 2007;12(3):233-48	Systematic review	No definition of chronic pain provided in the study selection criteria. The review pooled the results from studies of patients with acute, subacute, and chronic pain.

Study	Study Type	Reason for Exclusion
Hayden JA, van Tulder MW, Tomlinson G. Systematic review: strategies for using exercise therapy to improve outcomes in chronic low back pain. <i>Ann Intern Med.</i> 2005;142(9):776-85	Meta-regression	Used meta-regression analysis to synthesize data. The systematic review (meta-analysis) of the same studies was included: Hayden JA, van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: exercise therapy for nonspecific low back pain. <i>Ann Intern Med.</i> 2005;142(9):765-75.
Health Technology Advisory Committee. <i>Intradiscal electrothermal therapy (IDET) for lower back pain.</i> Minnesota: Health Technology Advisory Committee, 2001	Narrative paper	Not a systematic review.
Henchoz Y, Kai-Lik So A. Exercise and nonspecific low back pain: A literature review. <i>Joint Bone Spine</i> 2009;75(5):533-39	Review	The quality of the included studies was not formally assessed with a quality tool.
Henderson H. Acupuncture: evidence for its use in chronic low back pain. <i>Br J Nurs</i> 2002;11(21):1395-403	Review	Not a systematic review, included studies of patients with LBP with pain >6 weeks.
Hoffman BM, Papas RK, Chatkoff D, Kerns RD. Meta-Analysis of Psychological Interventions for Chronic Low Back Pain. <i>Health Psychology</i> 2007;26(1):1-9	Systematic review	Included psychological interventions broadly defined and delivered either alone or as a component of a multidisciplinary intervention for chronic LBP of known and unknown etiology.
Hubley-Kozey CL, McCulloch TA, McFarland DH. Chronic low back pain: a critical review of specific therapeutic exercise protocols on musculoskeletal and neuromuscular parameters. <i>J Manual &amp; Manipulative Ther</i> 2003;11(2):78-87	Systematic review	Included in the analysis studies of patients with LBP, with pain for more than 3 or 6 weeks.
Imamura M, Furlan AD, Dryden T, Irvin E. Evidence-informed management of chronic low back pain with massage. <i>Spine J</i> 2008;8(1):121-33	Systematic review	Same as Furlan AD et al. <i>Cochrane Database Syst Rev</i> 2008;(4):CD001929. See the updated Cochrane review (Evidence in Brief summary): Furlan AD et al. Massage for low-back pain. <i>Cochrane Database Syst Rev</i> 2008;(4):CD001929.
Khadiilkar A, Milne S, Brosseau L, Wells G, Tugwell P, Robinson V et al. Transcutaneous electrical nerve stimulation for the treatment of chronic low back pain: a systematic review. <i>Spine J</i> 2005;30(23):2657-66	Systematic review	Same as Khadiilkar A et al. <i>Cochrane Database Syst Rev.</i> 2005;(3):CD003008. See the updated Cochrane review (Evidence in Brief summary): Khadiilkar A et al. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. <i>Cochrane Database Syst Rev</i> 2008;(4): CD003008.
Karjalainen K, Malmivaara A, van Tulder M, Roine R, Jauhiainen M, Hurri H, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low-back pain among working age adults. <i>Cochrane Database Sys Rev.</i> 2001;(3):CD002193	Systematic review	Included studies of patients with sub-acute LBP (pain <12 weeks).

Study	Study Type	Reason for Exclusion
Keller K. Exercise therapy for low back pain: a narrative review of the literature. <i>J Chiropract Med</i> 2006;5(1):38-42	Narrative review	Not a systematic review.
Kofotolis N, Sambanis M. The influence of exercise on musculoskeletal disorders of the lumbar spine. <i>J Sports Medicine and Physical Fitness</i> 2005;45 (1):84-92	Review	The quality of the included studies was not formally assessed with a quality tool.
Kool J, de Bie R, Oesch P, Knusel O, vanden Brandt P, Bachmann S. Exercise reduces sick leave in patients with non-acute non-specific low back pain: A meta-analysis. <i>J Rehab Med</i> 2004;36(2):49-62	Systematic review (Meta-analysis)	Included studies of patients with non-acute LBP with a duration of pain at least 4 weeks.
La Touche R, Escalante K, Linares MT. Treating non-specific chronic low back pain through the Pilates Method. <i>Journal of Bodywork &amp; Movement Therapies</i> 2008;12(4):364-70	Systematic review	Did not specify in the inclusion criteria the duration of pain (>3 months).
Lawrence DJ, Meeker W, Branson R, Bronfort, G, Cates JR, Haas M, et al. Chiropractic management of low back pain and low back-related leg complaints: a literature synthesis. <i>J Manipulative Physiol Ther</i> 2008;31(9):659-74	Review	The quality of the included studies was not formally assessed with a quality tool. Included multiple interventions.
Lee TL. Acupuncture and chronic pain management. <i>Ann Acad Med Singapore</i> 2000;29(1):17-21	Narrative paper	Not a systematic review.
Lewis M, Johnson MI. The clinical effectiveness of therapeutic massage for musculoskeletal pain: a systematic review. <i>Physiotherapy (London)</i> (3), 2006.	Systematic review	Pooled results from patients with different conditions (LBP, neck and shoulder pain, and diffuse muscular pain) and also from healthy participants).
Licciardone JC, Brimhall AK, King LN. Osteopathic manipulative treatment for low back pain: a systematic review and meta-analysis of randomized controlled trials. <i>BMC Musculoskeletal Disord</i> 2005;6:43	Systematic review (Meta-analysis)	Did not specified in the inclusion criteria the duration of pain (>3 months). No results for chronic non-malignant pain.
Liddle SD, Baxter GD, Gracey JH. Exercise and chronic low back pain: what works? <i>Pain</i> 2004;107(1-2):176-90	Systematic review	This systematic review was replaced with another systematic review by Hayden et al. Meta-analysis: Exercise therapy for nonspecific low back pain. <i>Ann Intern Med</i> 2005;142 (9):765-75.
Macedo LG, Maher CG, Latimer J, McAuley JH. Motor control exercise for persistent, nonspecific low back pain: a systematic review. <i>Phys Ther</i> 2009;89(1):9-25	Systematic review	Did not focus on chronic low back pain.
Madsen MV, Gotzsche PC, Hrobjartsson A. Acupuncture treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. <i>BMJ</i> 2009;338(a3115)	Systematic review	Did not focus on chronic LBP. Included multiple conditions.

Study	Study Type	Reason for Exclusion
Maier-Riehle B and Harter M. The effects of back schools - A meta-analysis. <i>Inter J Rehab Res</i> 2001;24(3):199-206	Systematic review (Meta-analysis)	Included studies of patients with acute and chronic pain.
Malanga G and Wolff E. Evidence-informed management of chronic low back pain with nonsteroidal anti-inflammatory drugs, muscle relaxants, and simple analgesics. <i>Spine J</i> 2008;8(1):173-84	Narrative review	Not a systematic review. Included multiple interventions.
Manheimer E, White A, Berman B, Forys K, Ernst E. Meta-analysis: acupuncture for low back pain. <i>Ann Intern Med</i> 2005;142(8):651-63	Systematic reviews (Meta-analysis)	The quality of RCTs included in the systematic review was assessed by one reviewer with random confirmation (approximately 30%) by another author.
Manchikanti L, Singh V, Vilims BD, Hansen HC, Schultz DM, Kloth DS. Medial branch neurotomy in management of chronic spinal pain: Systematic review of the evidence. <i>Pain Physician</i> , 2002;5(4):405-18	Systematic review	Included and pooled the results from studies of patients with different condition.
Margo K. Spinal manipulative therapy for low back pain. <i>Am Fam Phys</i> 2005;71(3):464-65	Brief review of a Cochrane publication	Not a systematic review.
Margo K. Cochrane for clinicians: putting evidence into practice. Spinal manipulative therapy for low back pain. <i>Am Family Phys</i> 2005;71(3):464-65	Brief review of a Cochrane publication	Not a systematic review. The brief review presents the systematic review by Assendelft et al. Spinal manipulative therapy for low-back pain. <i>Cochrane Database Syst Rev</i> 2004;(1):CD000447. That review was excluded because pooled the results from studies of patients with sub-acute and chronic pain.
May S and Johnson R. Stabilisation exercises for low back pain: a systematic review. <i>Physiotherapy</i> 2008;94(3):179-89	Systematic review	No definition of chronic pain is available for the selection of studies; the review potentially pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.
J. Mayer, V. Mooney, and S. Dagenais. Evidence-informed management of chronic low back pain with lumbar extensor strengthening exercises. <i>Spine J</i> 2008;8(1):96-113	Review	The quality of the included studies was not formally assessed with a quality tool.
McNeely ML, Torrance G, Magee DJ. A systematic review of physiotherapy for spondylolysis and spondylolisthesis. <i>Man Ther</i> 2003;8(2):80-91	Systematic review	Chronic LBP was not an inclusion criteria; one study included patients with subacute and chronic LBP with a duration of pain between 3 weeks and 5 years.

Study	Study Type	Reason for Exclusion
Milne S, Welch V, Brosseau L, Saginur M, Shea B, Tugwell P, et al. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. <i>Cochrane Database Syst Rev</i> 2000;(4):CD003008	Systematic review	Another systematic review published in 2005 was included: Khadilkar A, Milne S, Brosseau L, Robinson V, Saginur M, Shea B, Tugwell P, Wells G. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. <i>Cochrane Database Syst Rev</i> , 2005;(3):CD003008.
Mior S. Exercise in the treatment of chronic pain. <i>Clin J Pain</i> 2001;17(4 Suppl):S77-S85	Narrative review	Not a systematic review.
Mior S. Manipulation and mobilization in the treatment of chronic pain. <i>Clin J Pain</i> 2001;17(4 Suppl):S70-S76	Review	Included three old systematic reviews on LBP and studies on different conditions.
Nachemson A, Carlsson CA, Englund L, Goossens M. Back and neck pain. Stockholm: <i>The Swedish Council on Technology Assessment in Health Care</i> , 2000, pp. 417	Health technology assessment report	Included different interventions.
Nielson WR, Weir R. Biopsychosocial approaches to the treatment of chronic pain. <i>Clin J Pain</i> 2001;17(4 Suppl):S114-S127	Review	Did not specify the inclusion/exclusion criteria; Included different conditions of chronic pain.
Niemisto L, Kalso E, Malmivaara A, Seitsalo S, Hurri H. Radiofrequency denervation for neck and back pain. <i>Cochrane Database Syst Rev</i> 2002;(3):CD004058	Systematic review	Included studies on different conditions (neck and back pain).
O'Connell NE, Wand BM. Acupuncture for Low Back Pain: Interpretive Leaps of Faith. Re: Yuan J, Purepong N, Kerr DP, et al. Effectiveness of acupuncture for low back pain. A systematic review. <i>Spine</i> 2008;33:23:E887-900. <i>Spine J</i> 2009;34(7):752	Commentary	Not a systematic review.
Oesch P, Kool J, Hagen KB, Bachmann S. Effectiveness of exercise on work disability in patients with non-acute non-specific low back pain: systematic review and meta-analysis of randomised controlled trials. <i>Swiss Medical Weekly</i> 2009;139(31-32):9S	Abstract conference	This is an abstract presented to a conference. No details available about duration of pain and if the studies were formally assessed with a quality tool.
Pengel HM, Maher CG, Refshauge KM. Systematic review of conservative interventions for subacute low back pain. <i>Clin Rehabil</i> 2002;16(8):811-20	Systematic review	Included studies of patients with subacute LBP (pain <3 months).
Poitras S and Brosseau L. Evidence-informed management of chronic low back pain with transcutaneous electrical nerve stimulation, interferential current, electrical muscle stimulation, ultrasound, and thermotherapy. <i>Spine J</i> 2008;8(1):226-33	Review	Included multiple interventions.

Study	Study Type	Reason for Exclusion
Rabago D, Best TM, Beamsley M, Patterson J. A systematic review of prolotherapy for chronic musculoskeletal pain. <i>Clinical Journal of Sport Medicine</i> 2005;15(5):376-80	Systematic review	Included studies on different conditions.
Rabinovitch DL, Peliowski A, Furlan AD. Influence of lumbar epidural injection volume on pain relief for radicular leg pain and/or low back pain. <i>Spine J</i> 2009;9(6):509-17	Systematic review	The review included studies of patients with chronic and acute/subacute (<3 months duration) pain.
Rainville J, Hartigan C, Martinez E, Limke J, Jouve C, Finno M. Exercise as a treatment for chronic low back pain. <i>Spine J</i> 2004;4(1):106-15	Review	Did not provide the search strategy, and inclusion and exclusion criteria for study selection.
Rackwitz B, de Bie R, Limm H, von Garnier K, Ewert T, Stucki G. Segmental stabilizing exercises and low back pain. What is the evidence? A systematic review of randomized controlled trials. <i>Clin Rehabil</i> 2006;20 (7):553-67	Systematic review	Only three studies included chronic LBP and presented results of segmental stabilizing exercises in combination with other treatment.
Reiman MP, Harris JY, Cleland JA. Manual therapy interventions for patients with lumbar spinal stenosis: a systematic review. <i>New Zealand Journal of Physiotherapy</i> 2009;37(1):17-36	Systematic review	Included patients with lumbar spinal stenosis; no definition of chronic pain is available.
Rooney L. Acupuncture in the treatment of non-specific low back pain in an adult population: a review of the evidence. <i>Internet Journal of Advanced Nursing Practice</i> 2008;9(2):6p	Narrative review	Not a systematic review.
Schofferman J and Mazanec D. Evidence-informed management of chronic low back pain with opioid analgesics. <i>Spine J</i> 2008;8(1):185-94	Narrative review	Not a systematic review.
Ginzburg R. Skeletal muscle relaxants. <i>Pharmacotherapy</i> 2008;28(2):207-13	Narrative review	Not a systematic review. Did not focus on chronic LBP.
Seers K. Review: intensive multidisciplinary biopsychosocial rehabilitation reduces pain and improves function in chronic low back pain. <i>Evidence-Based Nursing</i> 2002;5(4):116	Qualitative review (brief review of a Cochrane publication)	Not a systematic review.
Slade SC, Ther MM, Keating JL. Trunk-strengthening exercises for chronic low back pain: a systematic review. <i>J Manipulative Physiol Ther</i> 2006;29 (2):163-73	Systematic review	The review pooled results from studies of patients with LBP of 8 weeks or more.

Study	Study Type	Reason for Exclusion
Slipman CW, Bhat AL, Gilchrist RV, et al. A critical review of the evidence for the use of zygapophysial injections and radiofrequency denervation in the treatment of low back pain. <i>Spine J</i> 2003;3(4):310-6	Review	Did not clearly specified the inclusion/exclusion criteria for the studies included.
Staal JB, Hlobil H, van Tulder MW et al. Return-to-work interventions for low back pain: a descriptive review of contents and concepts of working mechanisms. <i>Sports Med</i> 2002;32(4):251-67	Review	Included studies on LBP with duration less than 12 weeks (<2 weeks and >8 weeks).
Standaert J, Weinstein SM, Rumpeltes J. Evidence-informed management of chronic low back pain with lumbar stabilization exercises. <i>Spine J</i> 2008;8(1):114-20	Review	Did not provide an explicit search strategy (that is the interval/date when search was conducted).
Tonkovich-Quaranta LA, Winkler SR. Use of epidural corticosteroids in low back pain. <i>Ann Pharmacother</i> 2000;34(10):1165-72	Review	Did not clearly specified the criteria used for searching literature and type (duration) of pain; pooled results from studies of different conditions.
Urrútia G, Burton AK, Morral A, Bonfill X, Zanoli G. Neuroreflexotherapy for non-specific low-back pain. <i>Cochrane Database Sys Rev</i> 2003;(2):CD003009	Systematic review	The review pooled results from studies of patients with sub-acute and chronic pain.
Vallano A, Fuentes I, Lopez A, Arnau JM. Efficacy and safety of analgesics and NSAIDs in chronic low back pain. Systematic review of randomized controlled trials. <i>Basic &amp; Clinical Pharmacology &amp; Toxicology</i> 2006;99:29	Abstract presentation	Describe results from a systematic review.
van Tulder M, Koes B. Low back pain and sciatica: chronic. <i>Clin Evid</i> 2002;(7):1032-48	Narrative Review	Not a systematic review; presented results from multiple systematic reviews.
van Tulder MW. Treatment of low back pain: myths and facts. <i>Schmerz</i> 2001;15(6):499-503	Narrative paper	Not a systematic review.
van Tulder MW, Jellema P, van Poppel MNM, Nachemson AL, Bouter LM. Lumbar supports for prevention and treatment of low-back pain. <i>Cochrane Database Syst Rev</i> 2000;(3):CD001823	Systematic review	Included studies of patients with non-specific LBP. Did not focus on chronic LBP.
van Tulder MW, Scholten RJPM, Koes BW, Deyo RA. Non-steroidal anti-inflammatory drugs for low-back pain. <i>Cochrane Database Syst Rev</i> 2000;(2):CD000396	Meta-analysis	Pooled results from studies of patients with acute and chronic LBP.

Study	Study Type	Reason for Exclusion
van Tulder MW, Ostelo RWJG, Vlaeyen JWS, Linton SJ, Morley SJ, Assendelft WJJ. Behavioural treatment for chronic low-back pain. <i>Cochrane Database Syst Rev</i> 2000;(2):CD002014	Meta-analysis	The updated search in March 2005 identified a new version of the systematic review which was included Ostelo RWJG, Tulder MW van, Vlaeyen JWS, Linton SJ, Morley SJ, Assendelft WJJ. Behavioural treatment for chronic low-back pain. <i>Cochrane Database Syst Rev</i> 2004;(3):CD002014. (see Appendix E: Data extraction)
van Tulder MW, Malmivaara A, Esmail R, Koes BW. Exercise therapy for low-back pain. <i>Cochrane Database Syst Rev</i> 2000;(2):CD000335	Qualitative review	The updated search in March 2005 identified a new qualitative systematic review which was included Liddle SD, Baxter GD, Gracey JH. Exercise and chronic low back pain: what works? <i>Pain</i> 2004;107(1-2):176-190. This review was updated in July 2006 by Hayden et al. Meta-analysis: Exercise therapy for nonspecific low back pain. <i>Ann Intern Med</i> 142 (9):765-775, 2005 (see Appendix E: Data extraction)
van Tulder M, Koes B. Low back pain (chronic). <i>Clin Evid</i> 2006;15:1634-53	Review	Synthesis of results (benefits, harms, and comments) from randomized controlled trials and systematic reviews on different interventions for chronic LBP.
Vohra S, Johnston BC, Cramer K, Humphreys K. Adverse events associated with pediatric spinal manipulation: a systematic review. <i>Pediatrics</i> 2007;119(1):e275-e283	Review	Did not focus on chronic LBP.
Vroomen PC, de Krom MC, Slofstra PD, Knottnerus JA. Conservative treatment of sciatica: a systematic review. <i>J Spinal Disord</i> 2000;13(6):463-9	Systematic review	Pooled the results from studies of patients with non-acute and acute pain.
Yuan J, Kerr D, Park J, Liu XH, McDonough S. Treatment regimens of acupuncture for low back pain-A systematic review. <i>Complementary Therapies in Medicine Churchill Livingstone</i> 2008;16(5):295-304	Review	The quality of the included studies was not formally assessed with a quality tool.
Yuan J, Purepong N, Kerr DP, Park J, Bradbury I, McDonough S. Effectiveness of acupuncture for low back pain: a systematic review. <i>Spine</i> 2008;33(23):E887-E900	Systematic review	The review pooled the results from studies of patients with chronic and acute/subacute (<3 months duration) pain.

# **APPENDIX C.I: QUALITY ASSESSMENT CHECKLIST<sup>1-4</sup>**

## **Study Question**

The objective(s) of the review should be stated in the abstract, introduction, or methods section.

## **Inclusion/Exclusion Criteria**

Details of the participants, interventions, outcome measures, and types of studies considered for analysis should be stated in the abstract, introduction, or methods section of the review. If the first mention of any of these elements occurs in the results section, the review should be scored as 'not reported'. All of these elements are considered **mandatory for a quality review**, so if a review scores 'not reported' for any of these elements you do not need to assess the review further.

## **Search Strategy**

### **Electronic databases**

Any electronic databases used in the literature search should be listed. A review that used both Medline (and PubMed) and Embase is scored 'yes' in the quality subsection.

### **Other sources**

Any resources or methods used in the literature search other than searching of electronic databases (e.g. pearling, hand searching of journals).

## **Data Extraction**

### **Standardised method**

If the data categories extracted were listed or the use of a standardised data extraction form was mentioned then the review scores 'yes'.

### **Independent data extraction**

If data were extracted by at least two independent reviewers, the review should be scored 'yes'. In cases where data were extracted by one reviewer and checked by another, the study scores 'no'.

## **Quality Assessment**

### **Independent quality assessment**

If the quality of the included studies was assessed by at least two independent reviewers, the review should be scored 'yes'. In cases where the studies were assessed by one reviewer and checked by another, the study scores 'no'.

## **Inter-rater agreement**

Inter-rater agreement was considered to be reported if there was either a statement of the degree of difference/equivalence between the reviewers or a statistical measure of inter-rater agreement was provided.

## **Data Analysis/Synthesis**

### **Qualitative review**

A qualitative review is defined as a narrative summary of the study results with no statistical analysis or pooling of results. Reviews that analysed or discussed the results of the included studies in terms of their quality scored 'yes' in the quality subsection.

### **Semi-quantitative review**

A semi-quantitative review incorporates a statistical analysis of individual studies without pooling the results (e.g. relative risks calculated for individual study outcomes) and/or pooling of results using only descriptive statistics (e.g. median, mean, mode, frequency). A range or confidence interval must be reported for the review to score 'yes' in the quality subsection.

### **Meta-analysis**

This is defined as any analysis where a pooled effect estimate is calculated for at least two studies. Confidence intervals must be reported for the review to score 'yes' in the first quality subsection; results of a statistical analysis of study heterogeneity must be reported for the review to score 'yes' in the second quality subsection.

## **Conclusions**

### **Clinical application of results**

The clinical application of results was considered to be reported if all of the following four elements were present in the concluding section (includes discussion) or statement of the review: treatment, treatment effect, patient group, and comparator. If only three of the four elements were present the study was scored as 'partially reported'. A review was scored as 'not reported' if fewer than three of these elements were present.

### **Conclusions supported by results**

The review was scored as 'yes' if the conclusions drawn by the authors of the review were supported by the evidence presented in the results section.

## **Quality Rating**

Systematic reviews were rated on how well their methods excluded bias and confounding by examining the inclusion/exclusion criteria and search strategy used; how the data extraction, quality assessment of the included studies, and data analysis/synthesis were conducted; whether the conclusions of the review matched the results; and if conflicts of interest and funding sources were reported. The reviews were rated with respect to six essential quality criteria as follows:

*Good* – six criteria met, or five criteria met and one criterion only partially met;

**Average** – one criterion not met, or one criterion not met and one criterion only partially met, or two criteria only partially met;

**Poor** – at least two criteria not met.

## **Conflict/Funding**

A statement of conflict of interest (if any) and any funding sources should be present.

## **References**

1. Fishbain D, Cutler RB, Rosomoff HL, Rosomoff RS. What is the quality of the implemented meta-analytic procedures in chronic pain treatment meta-analyses? *Clinical Journal of Pain* 2000;16(1):73-85.
2. Aggressive Research Intelligence Facility - University of Birmingham. ARIF Critical Appraisal Checklist. Available at: <http://www.bham.ac.uk/arif/caprocess.htm> (accessed 2002 Feb 19).
3. University of Alberta. Evidence Based Medicine Tool Kit. University of Alberta. Available at: <http://www.med.ualberta.ca/ebm/main.htm> (accessed: 2000 Nov 1).
4. Greenhalgh T. How to read a paper. Papers that summarise other papers (systematic reviews and meta-analysis). *BMJ* 1997;315:672-5.

## APPENDIX D.I: CRITICAL APPRAISAL OF THE SYSTEMATIC REVIEWS

Table 3: Critical appraisal of reviews on opioids for non-malignant chronic pain

Review Characteristic		Chou et al. (2003) <sup>1</sup>	Furlan et al. (2006) <sup>2</sup>	Deshpande et al (2007) <sup>3</sup>
Study question formulated		•	•	•
Inclusion/ exclusion criteria	Participants	•	•	•
	Interventions	•	•	•
	Outcome measures	•	•	•
	Study type/design	•	•	•
Search strategy	Electronic databases	•	•	•
	<i>At least Medline and Embase</i>	✓	✓	✓
	Other sources	•	•	•
Data extraction	Data extraction method	•	•	•
	<i>Standardised method</i>	✓	✓	✓
	<i>Independent data extraction by at least two reviewers</i>	X	✓	✓
Quality assessment	Criteria used to assess the validity of included studies	•	•	•
	<i>Independent quality assessment by at least two reviewers</i>	✓	✓	✓
	Inter-rater agreement for quality assessment	•	○	•

**Table 3: Critical appraisal of reviews on opioids for non-malignant chronic pain (cont'd)**

Review Characteristic		Chou et al. (2003) <sup>1</sup>	Furlan et al. (2006) <sup>2</sup>	Deshpande et al (2007) <sup>3</sup>
Data analysis/ synthesis	Qualitative review	●	N/A	N/A
	<i>Study quality used in analysis or discussion of study results</i>	✓		
	Semi-quantitative review	N/A	N/A	N/A
	<i>Confidence interval or range reported</i>			
	Meta-analysis	N/A	●	●
	<i>Precision of the results reported</i>		✓	✓
	<i>Test of homogeneity conducted</i>		✓	✓
Test for publication bias	○	○	○	
Concluding section	Potential methodological limitations	○	●	●
	Clinical application of results	●	●	●
	<i>Conclusions supported by results</i>	✓	✓	✓
Quality Rating	Six criteria (search at least 2 databases; independent data extraction and quality rating by 2 reviewer; appropriate data synthesis, conclusions supported by results)	5/6 Average	6/6 Good	6/6 Good
Conflict/ funding	Conflict of interest (if any)	○	●	●
	Source of funding	●	●	●

Key for quality of reporting: Reported: ●; Partially reported: ◐; Not reported: ○; Not applicable: N/A

**KEY FOR QUALITY OF REVIEW (GREY SECTIONS OF TABLE): YES = ✓; NO = X; UNCLEAR = ?**

**Table 4: Critical appraisal of reviews on treatments for chronic low back pain**

Review Characteristic		Ostelo et al. (2004) <sup>4</sup>	Furlan et al. (2008) <sup>5</sup>	Hayden et al. (2005) <sup>6</sup>	Lewis et al (2008) <sup>7</sup>	Dagenais et al. (2007) <sup>8</sup>
Study question formulated		•	•	•	•	•
Inclusion/ exclusion criteria	Participants	•	•	•	•	•
	Interventions	•	•	•	•	•
	Outcome measures	•	•	•	•	•
	Study type/design	•	•	•	•	•
Search strategy	Electronic databases	•	•	•	•	•
	<i>At least Medline and Embase</i>	✓	✓	✓	✓	✓
	Other sources	•	•	•	•	•
Data extraction	Data extraction method	•	•	•	•	•
	<i>Standardised method</i>	✓	✓	✓	✓	✓
	<i>Independent data extraction by at least two reviewers</i>	✓	✓	✓	✓	✓
Quality assessment	Criteria used to assess the validity of included studies	•	•	•	•	•
	<i>Independent quality assessment by at least two reviewers</i>	✓	✓	✓	✓	✓
	Inter-rater agreement for quality assessment	○	○	•	○	○

**Table 4: Critical appraisal of reviews on treatments for chronic low back pain (cont'd)**

Review Characteristic		Ostelo et al. (2004) <sup>4</sup>	Furlan et al. (2008) <sup>5</sup>	Hayden et al. (2005) <sup>6</sup>	Lewis et al (2008) <sup>7</sup>	Dagenais et al. (2007) <sup>8</sup>
Data analysis/ synthesis	Qualitative review	N/A	N/A	N/A	●	N/A
	<i>Study quality used in analysis or discussion of study results</i>				X	
	Semi-quantitative review	N/A	N/A	N/A	N/A	●
	<i>Confidence interval or range reported</i>					✓
	Meta-analysis	●	●	●	N/A	N/A
	<i>Precision of the results reported</i>	✓	✓	✓		
	<i>Test of homogeneity conducted</i>	✓	✓	✓		
	Test for publication bias	○	○	●	○	○
Concluding section	Potential methodological limitations	●	○	●	○	●
	Clinical application of results	●	●	●	●	●
	<i>Conclusions supported by results</i>	✓	✓	✓	✓	✓
Quality Rating	Six criteria (search at least 2 databases; independent data extraction and quality rating by 2 reviewer; appropriate data synthesis, conclusions supported by results)	6/6 Good	6/6 Good	6/6 Good	5/6 Average	6/6 Good
Conflict/ funding	Conflict of interest (if any)	●	●	●	●	●
	Source of funding	●	●	●	●	●

Key for quality of reporting: Reported: ●; Partially reported: ●; Not reported: ○; Not applicable: N/A

Key for quality of review (grey sections of table): Yes = ✓; No = X; Unclear = ?

**Table 4: Critical appraisal of reviews on treatments for chronic low back pain (cont'd)**

Review Characteristic		Ferreira et al. (2002) <sup>9</sup>	Khadilkar et al. (2008) <sup>10</sup>	van Tulder et al. (2002) <sup>11</sup>	Ammendolia et al. (2008) <sup>12</sup>
Study question formulated		•	•	•	•
Inclusion/ exclusion criteria	Participants	•	•	•	•
	Interventions	•	•	•	•
	Outcome measures	•	•	•	•
	Study type/design	•	•	•	•
Search strategy	Electronic databases	•	•	•	•
	<i>At least Medline and Embase</i>	✓	✓	✓	✓
	Other sources	•	•	•	•
Data extraction	Data extraction method	•	•	•	•
	<i>Standardised method</i>	?	✓	✓	✓
	<i>Independent data extraction by at least two reviewers</i>	✓	✓	✓	✓
Quality assessment	Criteria used to assess the validity of included studies	•	•	•	•
	<i>Independent quality assessment by at least two reviewers</i>	✓	✓	✓	✓
	Inter-rater agreement for quality assessment	○	○	•	○

**Table 4: Critical appraisal of reviews on treatments for chronic low back pain (cont'd)**

Review Characteristic		Ferreira et al. (2002) <sup>9</sup>	Khadilkar et al. (2008) <sup>10</sup>	van Tulder et al. (2002) <sup>11</sup>	Ammendolia et al. (2008) <sup>12</sup>
Data analysis/ synthesis	Qualitative review	N/A	N/A	N/A	●
	<i>Study quality used in analysis or discussion of study results</i>				✓
	Semi-quantitative review	N/A	●	N/A	N/A
	<i>Confidence interval or range reported</i>		✓		
	Meta-analysis	●	N/A	●	N/A
	<i>Precision of the results reported</i>	✓		✓	
	<i>Test of homogeneity conducted</i>	?		✓	
Test for publication bias	○	●	○	○	
Concluding section	Potential methodological limitations	○	●	●	○
	Clinical application of results	●	●	●	●
	<i>Conclusions supported by results</i>	✓	✓	✓	✓
Quality Rating	Six criteria (search at least 2 databases; independent data extraction and quality rating by 2 reviewer; appropriate data synthesis, conclusions supported by results)	5/6 Average	6/6 Good	6/6 Good	6/6 Good
Conflict/ funding	Conflict of interest (if any)	○	●	●	○
	Source of funding	○	●	●	●

Key for quality of reporting: Reported: ●; Partially reported: ◐; Not reported: ○; Not applicable: N/A

Key for quality of review (grey sections of table): Yes = ✓; No = X; Unclear = ?

## APPENDIX E.I: DATA EXTRACTION

Table 5: Summary of data from reviews on opioids for non-malignant chronic pain

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Chou et al. (2003)<sup>1</sup></p> <p><b>Objective:</b> To determine if any long-acting opioid is superior to others in terms of efficacy and safety, and also whether long-acting opioids as a class are more efficacious or safer than short-acting opioids in the treatment of chronic non-cancer pain</p> <p><b>Studies Reviewed:</b> 16 RCTs and eight observational studies</p>	<p><b>Included Patients:</b> <u>Total number:</u> n = 1427 for RCTs n = 1190 for observational studies <u>Condition:</u> Chronic non-cancer pain of at least 6 months duration <u>Age:</u> &gt;18 years <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Not stated</p>	<p><b>Comparisons:</b> Head to head comparison of long-acting opioids; long-acting versus short-acting opioids.</p> <p><b>Outcomes Measured:</b> Pain intensity, pain relief, function, and adverse events; information about abuse or addiction; withdrawal rates.</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> Not stated <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> There was insufficient evidence to determine whether one long-acting opioid is superior to another in terms of efficacy or whether long-acting opioids are more effective than short-acting opioids in adult patients with non-malignant chronic pain. There was fair evidence from three studies that long-acting oxycodone and short-acting oxycodone are equally effective for pain control in adult patients with non-malignant chronic pain.</p> <p><b>Safety:</b> There was insufficient evidence to determine whether one long-acting opioid is safer than another in adult patients with non-malignant chronic pain.</p>

RCT – randomised controlled trial

**Table 5: Summary of data from reviews on opioids for non-malignant chronic pain (cont'd)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Furlan et al. (2006)<sup>2</sup></p> <p><b>Objective:</b> To determine in patients with chronic non-cancer pain: the efficacy/effectiveness of opioids compared with placebo and other drugs; which categories of chronic pain respond better to opioids; and the most common side effects and complications of opioid therapy</p> <p><b>Studies Reviewed:</b> 41 RCTs</p>	<p><b>Included Patients:</b> <u>Total number:</u> n = 1427 for RCTs <u>Condition:</u> Chronic non-cancer pain of at least 6 months duration <u>Age:</u> Not stated <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Patients with migraines, dental pain, abdominal pain, and ischemic pain from vascular disease.</p>	<p><b>Comparisons:</b> Any opioid administered for at least 7 days compared with placebo or other analgesics.</p> <p><b>Outcomes Measured:</b> Pain intensity, pain relief, function, and adverse events.</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> Not stated <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> Opioids reduced pain and improved function better than placebo in patients with nociceptive or neuropathic pain or fibromyalgia. Strong opioids (morphine, oxycodone) were superior to naproxen and nortriptyline only with respect to pain relief. Weak opioids (tramadol, propoxyphene, codeine) were less effective than tricyclic antidepressants or non-steroidal anti-inflammatory drugs in relieving pain and improving function.</p> <p><b>Safety:</b> Constipation and nausea were more common with opioids.</p>

RCT – randomised controlled trial

**Table 5: Summary of data from reviews on opioids for non-malignant chronic pain (cont'd)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Deshpande et al. (2007)<sup>3</sup></p> <p><b>Objective:</b> To determine the efficacy of opioids in adults with chronic LBP</p> <p><b>Studies Reviewed:</b> Four RCTs (three multicentre) conducted in: the USA (2), Canada (1), not stated (1)</p>	<p><b>Included Patients:</b> <u>Total number:</u> 944 <u>Condition:</u> Non-specific chronic LBP ≥3 months duration <u>Age:</u> ≥ 18 years <u>Race:</u> 90% white participants (three RCTs)</p> <p><b>Excluded Patients:</b> Cancer, infections, inflammatory arthritic conditions including osteoarthritis, compression fractures.</p>	<p><b>Comparisons:</b> Other pharmacological agents, non-pharmacological agents, placebo, no treatment.</p> <p><b>Outcomes Measured:</b> Primary: Pain ratings, function, global functioning, impairment and disability, side effects. Secondary: health care usage, non-opioid medication consumption, addiction prevalence, change in venue of treatment.</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> Outpatient setting <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> The benefits of opioids in clinical practice for the long-term management of chronic LBP remains questionable. Further high-quality studies that more closely simulate clinical practice are needed to assess the usefulness, and potential risks, of opioids for individuals with chronic LBP.</p> <p><b>Safety:</b> In studies comparing opioids with placebo: headache and nausea occurred more frequently in patients taking opioids (three studies). Other side effects associated with opioids included somnolence, constipation, dry mouth, and dizziness (two studies). In one study comparing opioids with naproxen, the most frequent side effects associated with opioids were dry mouth, drowsiness, headaches, constipation, and nausea.</p>

RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain**

**Intervention: BEHAVIOURAL TREATMENT\* (BT) FOR CHRONIC NON-SPECIFIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Ostelo et al. (2004)<sup>4</sup></p> <p><b>Objective:</b> To determine if BT is more effective than reference treatments for chronic non-specific low back pain. To determine which type of BT is most effective</p> <p><b>Studies Reviewed:</b> 21 RCTs published between 1982-2003 (one RCT was not included in the analysis)</p>	<p><b>Included Patients:</b> <u>Total number:</u> 1345 in 20 RCTs. (no. of patients with LBP unknown in one RCT) <u>Condition:</u> chronic LBP <u>Age:</u> 18-65 years <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Specific LBP caused by pathological entities such as: infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis or fractures</p>	<p><b>Comparisons:</b> Different types of BT BT versus: placebo no treatment other treatments waiting list controls</p> <p>BT plus another treatment (medication or physiotherapy) versus other treatment alone</p> <p><b>Outcomes Measured:</b> Overall improvement, back pain specific functional status, generic functional status, return to work, pain intensity, behaviour outcome: pain behaviour, cognitive errors, perceived or observed levels of tension, anxiety, depression.</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> Not stated <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> Seven trials were considered of high quality. Combined respondent-cognitive therapy and progressive relaxation therapy have a positive effect on pain intensity, in the short term compared to waiting list controls. Different types of behavioural treatments (cognitive, operant, respondent, and combination) did not differ in effectiveness. Adding a behavioural component to another treatment (physiotherapy and back education, inpatient pain management, pharmacotherapy, or exercise treatment) does not improve patient outcomes in the short or long-term. It is still unknown what type of patients benefit most from what type of behavioural treatment.</p> <p><b>Safety:</b> Not stated</p>

RCT – randomised controlled trial

\* Three behavioural treatment approaches can be distinguished: operant (positive reinforcement of healthy behaviours), cognitive (imagery and attention diversion, modification of maladaptive thoughts, feelings, and beliefs) and respondent (modify the physiological response system).

Cognitive-behavioural treatment is based on a multidimensional model of pain that includes physical, affective, cognitive, and behavioural components. Treatment may include: education about a multidimensional view of pain, identification and modification of maladaptive cognition, the use of coping strategies, hypnosis, relaxation, and electromyographic (EMG) biofeedback.

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Intervention: MASSAGE FOR CHRONIC LOW-BACK PAIN (LBP)\***

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Furlan et al. (2008)<sup>5</sup></p> <p><b>Objective:</b> To assess the effectiveness of massage therapy in patients with non-specific LBP compared with other procedures or medical treatment. To assess the effectiveness of different techniques of massage.</p> <p><b>Studies Reviewed:</b> Thirteen RCTs Seven RCTs focuses on chronic LBP. Studies were conducted in: the USA (4), Germany (1), Thailand (2); published between 2000 and 2005.</p>	<p><b>Included Patients:</b> <u>Total number:</u> 693 patients with chronic and 102 patients with subacute and chronic LBP at randomization <u>Condition:</u> non-specific LBP. A subgroup analysis included patients with chronic LBP (pain longer than 12 weeks). <u>Age:</u> &gt;18 years <u>Race:</u> 67% Caucasian, 8% Hispanic, 17% African American, 8% Asian (2 RCTs); 85% white participants (2 RCTs)</p> <p><b>Excluded Patients:</b> Specific cause of LBP such as: infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, fracture, inflammatory process or radicular syndrome</p>	<p><b>Comparisons:</b> Sham or placebo massage Relaxation therapy, exercise, joint mobilization Different techniques of massage (classic, Swedish massage, traditional Thai massage, acupuncture massage, muscle energy technique)</p> <p><b>Outcomes Measured:</b> Primary outcomes: pain, overall improvement, back-specific functional status, well being (e.g. quality of life), disability (e.g. activities of daily living, work absenteeism) return to work or work status, subjective change of symptoms, functional status Secondary outcomes: range of motion, spinal flexibility, muscle strength</p>	<p><b>Provider:</b> Physical therapist (two RCTs), massage therapist (two RCTs), licensed therapist (two RCTs)</p> <p><b>Setting:</b> Physical therapy department (one RCT), rehabilitation clinic (one RCT), HMO.</p> <p><b>Cost:</b> In one RCT the cost of massage was US\$377 per patient, acupuncture cost US\$352 and self-care education cost US\$50 per patient. The number of provider visits, pain medication and costs of outpatient HMO back care services were about 40% lower in the massage group than in the other groups.</p>	<p><b>Efficacy/Effectiveness:</b> Massage was superior to joint mobilization, relaxation therapy, physical therapy, acupuncture, and self-care education. The beneficial effects of massage in patients with chronic low back pain lasted at least one year after the end of the treatment. Acupuncture massage produces better results than classic (Swedish) massage but this need confirmation. Thai massage produces similar results to classic (Swedish) massage. Massage might be beneficial for patients with chronic non-specific low back pain especially when combined with exercise and education.</p> <p><b>Safety:</b> Adverse events reported in two RCTs: soreness after treatment (11% on day one and 12% after treatment in week 3), allergic reaction such as rashes and pimples (6%) to the massage oil (one RCT); significant discomfort or pain during or shortly after treatment (one RCT). The other five RCTs did not measure/report adverse events.</p>

\* Massage is defined as soft-tissue manipulation using hands or a mechanical device. Types of massage techniques, duration, and frequency of treatments varied among the studies. RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Intervention: EXERCISE FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Hayden et al. (2005)<sup>6</sup></p> <p><b>Objective:</b> To evaluate the effectiveness of exercise therapy in adult non-specific acute, subacute, and chronic LBP compared to no treatment and other conservative treatments</p> <p><b>Studies Reviewed:</b> 61 RCTs on LBP published between 1990-2001: Acute: 11 RCTs, Subacute: 6 RCTs, Chronic: 43 RCTs. Unclear: 1 RCT</p>	<p><b>Included Patients:</b> <u>Total number:</u> 3907 with chronic LBP <u>Condition:</u> non-specific LBP. A subgroup analysis included patients with chronic LBP (pain longer than 12 weeks). <u>Age (mean):</u> 42 years (chronic LBP patients) <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> LBP caused by specific pathologies or conditions</p>	<p><b>Comparisons:</b> No treatment, sham treatment, other conservative treatments, usual general practitioner care, other exercise therapy.</p> <p><b>Outcomes Measured:</b> Self-reported pain intensity, condition-specific physical functioning, global improvement, return to work or absenteeism.</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> group exercise in a health care setting (secondary or tertiary care), individual exercise program at home <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> Evidence that exercise therapy reduces pain and functional limitations in patients with chronic LBP (meta-analysis of 23 exercise groups). Effects were maintained over longer follow up (≥12 months). Evidence that strengthening exercise is at least as effective as other conservative interventions for managing pain and functional improvement, in adults with chronic LBP. A greater improvement was found in trials investigating health care populations. Future intervention studies should be conducted in populations that are seeking care and therefore best represent LBP patients.</p> <p><b>Safety:</b> A total of 16 studies reported adverse events (the population involved: acute, subacute, or chronic was not specified). Twelve studies reported mild negative reactions to the exercise program such as increased low back pain and muscle soreness in some patients.</p>

RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Intervention: EXERCISE THERAPY FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Lewis et al. (2008) <sup>7*</sup></p> <p><b>Objective:</b> To determine the effectiveness of physiotherapy exercises (general fitness and aerobic exercises, flexibility regimes, stretches, muscle strengthening, spinal stabilizing exercises) in reducing chronic low back pain</p> <p><b>Studies Reviewed:</b> 15 RCTs published between 1994 and 2006. One RCT focused on fitness program versus yoga.</p>	<p><b>Included Patients:</b> <u>Total number:</u> 1695 with chronic LBP; 101 chronic LBP patients in the RCT that focuses on fitness program versus yoga <u>Condition:</u> non-specific chronic LBP <u>Age:</u> 18 to 65 years <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Co-morbidity or conditions of an inflammatory or infectious nature, LBP related to pregnancy, depression.</p>	<p><b>Comparisons:</b> Different physiotherapy exercises, surgical stabilisation, yoga, hydrotherapy, back care education booklets, placebo</p> <p><b>Outcomes Measured:</b> Pain, functional status</p>	<p><b>Provider:</b> Physiotherapist (all 15 RCTs)</p> <p><b>Setting:</b> Physiotherapy outpatient departments, occupational health centre, physiotherapy private practice, medical and pain management clinics, hospital orthopaedic clinic, rehabilitation centres, spine program</p> <p><b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> Preliminary evidence that physiotherapy exercises are effective for the treatment of chronic LBP, although no particular treatment modality (specific technique or exercise format) was found to optimise therapy outcomes to a much greater extent than others. A yoga group intervention reported some superior outcomes compared to the fitness group in one RCT. The fitness group included: warm-up, aerobics, strengthening, stretches, ergonomic education.</p> <p><b>Safety:</b> Not stated.</p>

\*The systematic review (SR) used an additional comparator (yoga) to those of the original SR by Hayden et al. (2005)<sup>6</sup>, hence the new intervention is included in the Evidence in Brief summary. RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Intervention: PROLOTHERAPY INJECTIONS FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Dagenais et al. (2007)<sup>8*</sup></p> <p><b>Objective:</b> To determine the efficacy of prolotherapy (ligament sclerotherapy) injections in adults with chronic LBP</p> <p><b>Studies Reviewed:</b> Five RCTs conducted in: the USA (2), Australia (1), the UK (2).</p>	<p><b>Included Patients:</b> <u>Total number:</u> 366 <u>Condition:</u> Non-specific chronic LBP &gt;3 months duration. <u>Age:</u> ≥18 years. <u>Race:</u> Not stated.</p> <p><b>Excluded Patients:</b> Lumbar/sacral radiculopathies and pathological causes of back pain such as: infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, fractures.</p>	<p><b>Comparisons:</b> Control injections or non-injection therapy.</p> <p><b>Outcomes Measured:</b> Low-back pain; low-back-related disability; overall improvement or satisfaction with treatment; well-being; return to work; days of absenteeism or days of reduced activity; physical examination (range of motion, spinal flexibility, or muscle strength), side effects; medication use; and healthcare use.</p>	<p><b>Provider:</b> Not stated.</p> <p><b>Setting:</b> Departments of rheumatology and orthopaedic surgery Medical clinic Hospital Health centre general practice.</p> <p><b>Cost:</b> Not stated.</p>	<p><b>Efficacy/Effectiveness:</b> There is conflicting evidence regarding the efficacy of prolotherapy injections for patients with chronic LBP. When used alone, prolotherapy is not an effective treatment for chronic low back pain. When combined with spinal manipulation, exercise, and other co-interventions, as part of a multimodal treatment program, prolotherapy may improve chronic LBP and disability. Conclusions are confounded by clinical heterogeneity amongst studies and by the presence of co-interventions.</p> <p><b>Safety:</b> The most commonly reported adverse event was a temporary increase in back pain and stiffness following injections. Some patients (2% to 4%) had severe headaches suggestive of lumbar puncture, but no serious or permanent adverse events were reported.</p> <p>No study reported any significant differences in the incidence of adverse events between treatment and control groups.</p>

RCT – randomised controlled trial.

\* This is an updated review of the following systematic review: Yelland MJ, Del Mar C, Pirozzo S, Schoene ML, Vercoe P. Prolotherapy injections for chronic low-back pain. *Cochrane Database Syst Rev* 2004;(2):CD004059.

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**  
**Intervention: SPINAL MANIPULATIVE THERAPY FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Ferreira et al. (2002)<sup>9</sup></p> <p><b>Objective:</b> To determine the efficacy of spinal manipulative therapy in the treatment of chronic LBP</p> <p><b>Studies Reviewed:</b> Eight randomised or quasi-randomised controlled trials</p>	<p><b>Included Patients:</b> <u>Total number:</u> Not stated <u>Condition:</u> Non-specific low back pain &gt;3 months <u>Age:</u> Not stated <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Not stated</p>	<p><b>Comparisons:</b> Spinal manipulative therapy versus placebo, short wave diathermy, acupuncture, or back school Manual therapy versus NSAIDs, physiotherapy, or no treatment</p> <p><b>Outcomes Measured:</b> Disability, pain, quality of life, adverse events, return to work, global perceived effect, or patient satisfaction</p>	<p><b>Provider:</b> Not stated <b>Setting:</b> Not stated <b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> Spinal manipulative therapy is not more effective than sham treatment in reducing pain, nor is it more effective than NSAIDs in improving disability of patients with chronic low back pain. It is unclear if spinal manipulative therapy is more effective than NSAIDs in reducing pain in chronic low back pain patients. All other treatment comparisons were inconclusive.</p> <p><b>Safety:</b> Not stated.</p>

NSAIDs – non-steroidal anti-inflammatory drugs

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Intervention: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/ Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Khadilkar et al. (2008)<sup>10</sup></p> <p><b>Objective:</b> To determine whether TENS is more effective than placebo for the management of chronic LBP</p> <p><b>Studies Reviewed:</b> Four RCTs published between 1990 and 2005</p>	<p><b>Included Patients:</b> <u>Total number:</u> 585 patients with chronic LBP at randomization (59 withdrawals) <u>Condition:</u> Chronic low back pain lasting longer than 12 weeks <u>Age:</u> 18 to 70 years <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Malignancy, infection, fracture, inflammatory disorder, neurological syndrome; mix of chronic and acute LBP or subacute LBP (less than 12 weeks duration), mix of LBP and middle or upper back pain</p>	<p><b>Comparisons:</b> Placebo TENS or sham TENS (Note: studies were excluded if the active or/and placebo groups received TENS percutaneously with acupuncture needles)</p> <p><b>Outcomes Measured:</b> Pain, back specific functional status, generic health status, work disability, patient satisfaction, treatment side-effects, physical examination measures, medication use, use of medical services</p>	<p><b>Provider:</b> Researcher in clinic, self-administration at home.</p> <p><b>Setting:</b> Outcomes measured in the clinic setting or at home.</p> <p><b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> There is conflicting evidence about whether TENS improves chronic pain intensity and consistent evidence that does not improve back-specific functional status regardless of whether conventional or acupuncture-like TENS is used. There is conflicting evidence on the effects of TENS on generic health status. There is moderate evidence that work status and the use of medical services did not change with treatment. In general, patients treated with acupuncture-like TENS responded similarly to those treated with conventional TENS. Optimal treatment schedules could not be reliably determined based on the available data.</p> <p><b>Safety:</b> Adverse effects reported in one RCT (N = 145) included skin irritation at the site of electrode placement in 1/3 of subjects (equal proportions affected in the TENS and placebo groups), one out of 72 patients who received sham TENS developed severe dermatitis 4 days after therapy.</p>

RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**

**Indication: MUSCLE RELAXANTS (antispasmodics) FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/ Outcome	Provider/ Setting/ Cost	Relevant Results/ Authors' Conclusions
<p>van Tulder et al. (2002)<sup>11</sup></p> <p><b>Objective:</b> To determine if muscle relaxants are effective in the treatment of non-specific LBP</p> <p><b>Studies Reviewed:</b> 30 RCTs and double-blinded control trials (five RCTs on chronic LBP)</p>	<p><b>Included Patients:</b> <u>Total number:</u> 497 <u>Condition:</u> chronic LBP <u>Age:</u> 18-80 years (in one RCT), mean age 44.4 to 50.8 in 3 RCTs) <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> infection, neoplasm, metastasis, osteoporosis, fractures, rheumatological disorders, neurological disorders, etc.</p>	<p><b>Comparisons:</b> Placebo</p> <p><b>Outcomes Measured:</b> Pain intensity, global measure (overall improvement, patients recovered), back pain specific functional status, return to work, physiological outcomes</p>	<p><b>Provider:</b> Not stated</p> <p><b>Setting:</b> secondary care (outpatient, rehabilitation centres)</p> <p><b>Cost:</b> Not stated</p>	<p><b>Efficacy/Effectiveness:</b> <u>Benzodiazepine (tetrazepam) vs. placebo</u> There is a strong evidence that tetrazepam 50mg t.i.d. is more effective on short-term pain relief and overall improvement. (based on two high quality trials, 222 patients) There is moderate evidence (one high quality trial, 50 patients) that tetrazepam is more effective on short-term decrease of muscle spasm.</p> <p><u>Non-benzodiazepine vs. placebo</u> There is moderate evidence that flupirtin is more effective on short-term pain relief and overall improvement after 7 days, but not on reduction of muscle spasm (based on one high quality trial, 107 patients). There is moderate evidence that tolperisone is more effective on short-term overall improvement after 21 days, but not on pain relief and reduction of muscle spasm (based on information from one high quality trial, 112 patients).</p> <p><b>Safety:</b> Muscle relaxants are associated with adverse events: drowsiness and dizziness (central nervous system events). For this reason they must be used with caution, respecting the guidelines available.</p>

RCT – randomised controlled trial

**Table 6: Summary of data from reviews on treatments for chronic low back pain (cont'd)**  
**Intervention: ACUPUNCTURE FOR CHRONIC LOW-BACK PAIN (LBP)**

Systematic Review	Study Population	Comparison/Outcome	Provider/Setting/Cost	Relevant Results/ Authors' Conclusions
<p>Ammendolia et al. (2008)<sup>12</sup></p> <p><b>Objective:</b> To assess the effects of needle acupuncture for the treatment of chronic non-specific low back pain</p> <p><b>Studies Reviewed:</b> 19 RCTs conducted in Australia (3), Germany (4), Hong Kong China (2), Ireland (1), Japan (1), Sweden (2), United Kingdom (2), USA (4), published between 1980 and 2006</p> <p><i>Note: Fifty per cent of the included RCTs were considered to be of low quality. Two RCTs had fatal flaws and were excluded from the analysis.</i></p>	<p><b>Included Patients:</b> <u>Total number:</u> 4998 with chronic LBP; in four studies that included 709 patients with subacute and chronic LBP, at least 50% of patients were diagnosed with chronic LBP <u>Condition:</u> non-specific chronic LBP <u>Age:</u> &gt;18 years <u>Race:</u> Not stated</p> <p><b>Excluded Patients:</b> Specific pathological entities; impossibility to determine whether at least 50% of the study population included patients with chronic LBP; studies that compared different forms of acupuncture</p>	<p><b>Comparisons:</b> No treatment, sham therapy or placebo, other therapies, addition of acupuncture to other therapies</p> <p><b>Outcomes Measured:</b> Pain, global measure, functional status, return to work, complications</p>	<p><b>Provider:</b> Acupuncturist (one RCT), physician (two RCTs)</p> <p><b>Setting:</b> Acupuncture centre, pain clinic, outpatient pain clinic in a hospital setting, physiotherapy clinic, health maintenance organization, multidisciplinary inpatient clinic, university hospital, private clinic</p> <p><b>Cost:</b> Not stated in the included RCTs</p>	<p><b>Efficacy/Effectiveness:</b> There is some evidence of the effects of acupuncture for chronic LPB. Compared with no treatment, there is evidence for pain relief and functional improvement with acupuncture immediately after a series of treatment and in the short-term follow-up. There is inconclusive evidence for the effectiveness of acupuncture when compared with sham acupuncture. Compared with other conventional therapies, acupuncture is no better for improvement of pain and function. There is consistent evidence that acupuncture added to other conventional therapies relieves pain and improves function better than conventional therapies alone.</p> <p><b>Safety:</b> No serious complications or side effects related to acupuncture were reported in 12 RCTs: local bleeding and hematoma (6% patients, one RCT); worsening of the chronic LBP, tiredness, drowsiness, light-headedness, dizziness, local bleeding, hematoma (7.8% patients, 11 RCTs). No adverse effects resulted in death, permanent disability or hospitalization.</p>

RCT – randomised controlled trial

## References (Appendix D.I and Appendix E.I)

1. Chou R, Clark E, Helfand M. Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: a systematic review. *Journal of Pain and Symptom Management* 2003;26(5):1026-48.
2. Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. *CMAJ* 2006;174(11):1589-94.
3. Despante et al. Opioids for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2007;(3):CD004959
4. Ostelo RWJG, van Tulder MW, Vlaeyen JWS, Linton SJ, Morley SJ, Assendelft WJJ. Behavioural treatment for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2004;(3):CD002014.
5. Furlan AD, Imamura M, Dryden T, Irvin E. Massage for low-back pain. *Cochrane Database of Systematic Reviews* 2008;(4): CD001929.
6. Hayden JA, van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: exercise therapy for nonspecific low back pain. *Annals of Internal Medicine* 2005;142(9), 765-75.
7. Lewis A, Morris ME, Walsh C. Are physiotherapy exercises effective in reducing chronic low back pain? *The Physical Therapy Review* 2008;13(1), 37-44.
8. Dagenais S, Yelland MJ, Del Mar C, Schoene ML. Prolotherapy injections for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2007;(2):CD004059.
9. Ferreira ML, Ferreira PH, Latimer J, Herbert R, Maher C. Does spinal manipulative therapy help people with chronic low back pain? *Australian Journal of Physiotherapy* 2002;48:277-84.
10. Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2008;(4):CD003008.
11. van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM. Muscle relaxants for non-specific low-back pain. *Cochrane Database of Systematic Reviews* 2003;(1):CD004252.
12. Ammendolia C, Furlan AD, Imamura M, Irvin E, van Tulder M. Evidence-informed management of chronic low back pain with needle acupuncture. *Spine Journal* 2008;8(1):160-72.