

# Healthy ageing in relation to chronic pain in the EU

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## List of abbreviations / glossary

<b>AHA</b>	Active and Healthy Ageing
<b>AMSTAR</b>	Instrument for assessing quality of systematic reviews
<b>AUSCAN</b>	Australian Canadian osteoarthritis pain score
<b>BPI</b>	Brief Pain Inventory, for measuring pain severity
<b>EC</b>	European Commission
<b>EIP</b>	European Innovation Partnership
<b>EFIC</b>	European Federation of International Association for the Study of Pain Chapters
<b>EQ-5D</b>	Instrument for measuring something similar to quality of life
<b>EU</b>	European Union
<b>FSH</b>	Facioscapulohumeral, type of muscular dystrophy
<b>FIQ</b>	Fibromyalgia Impact Questionnaire, quality of life instrument
<b>GFI</b>	Global Fatigue Index, for measuring fatigue
<b>(HR) QoL</b>	(Health related) quality of life
<b>IASP</b>	International Association for the Study of Pain
<b>RCT</b>	Randomised controlled trial
<b>SD</b>	Standard deviation
<b>SE</b>	Standard error
<b>SF-6D</b>	Instrument for measuring something similar to quality of life
<b>SF-12</b>	Short Form-12, quality of life instrument
<b>SF-36</b>	Short-Form-36, quality of life instrument
<b>SIP</b>	Strategic Implementation Plan
<b>STROBE</b>	Instrument to assess quality of reporting in observational studies
<b>SR</b>	Systematic review
<b>UK</b>	United Kingdom
<b>VAS</b>	Visual analogue scale, for measuring pain severity
<b>WHO</b>	World Health Organisation
<b>WHOQoL</b>	WHO quality of life (instrument)

## Introduction by Professor Hans G. Kress, MD PhD

### Dear Reader,

With the demographic changes of an ageing population the European Union and its member states are facing a tremendous challenge. One key policy response by the EU Commission<sup>1</sup> to manage this changing environment is “ensuring sustainable public finances to guarantee [...] health care and long-term care”.

With the European Innovation Partnerships the European Commission has developed a pilot project to enhance competitiveness in the EU and to tackle these societal challenges by fostering innovation and research. Under this innovation umbrella, the Healthy and Active Ageing Partnership has three major objectives<sup>2</sup>:

1. enabling EU citizens to lead healthy, active and independent lives while ageing;
2. improving the sustainability and efficiency of social and healthcare systems;
3. boosting and improving the competitiveness of the markets for innovative products and services, responding to the ageing challenge at both EU and global level, thus creating new opportunities for businesses.

The frame target of the partnership will be to “increase the average healthy lifespan by two years by 2020”<sup>2</sup>.

Following a period of pre-assessment and stakeholder involvement, in November 2011 a high-level steering group on behalf of the EU Commission finalised a strategic implementation plan, describing the commonly shared visions as well as operational activities to focus on in order to address the challenges of an ageing population.



<sup>1</sup> <http://ec.europa.eu/social/main.jsp?catId=502&langId=en>

<sup>2</sup> [http://ec.europa.eu/research/innovation-union/index\\_en.cfm?section=active-healthy-ageing](http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing)

<sup>3</sup> Referenz: e.g. König et al 2010

<sup>4</sup> EU Commission: EU Special Eurobarometer 272e / Wave 66.2 – TNS Opinion & Social\_Health in the European Union\_2006-2007

<sup>5</sup> [http://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/steering-group/operational\\_plan.pdf#view=fit&pagemode=none](http://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/steering-group/operational_plan.pdf#view=fit&pagemode=none)

During discussions with policy-makers on EU and national levels, EFIC® has raised the question of what can effectively be done in order to successfully gain two additional healthy years of life by 2020. Quality of life measures will be used to assess healthy years of life eventually gained by reducing the level of pain/discomfort<sup>3</sup> of a respective person. But so far, does pain play at all a role in determining the health status of the ageing population of EU member states?

According to EU Special Eurobarometer<sup>4</sup>, 44% of the EU population of + 55 years were affected by pain of muscles, joints, neck or back influencing their ability to carry out the activities of daily living. Exactly one quarter of all EU respondents stated that they had experienced chronic restrictive pain at some point in their life.

Chronic pain in the EU poses a substantial burden on the individual but also on the society, including enormous economic costs for health care systems. A structured programme is urgently needed to target these challenges and their long-term consequences. With the strategic implementation plan of the European Innovation Partnership on Active and Healthy Ageing the European Commission has developed a pilot project, where the improvement of pain management in Europe and addressing its societal challenges on EU-level have been identified as priorities<sup>5</sup>.

This systematic review looks at evidence found in the existing literature and evaluates the interrelation of ageing, quality of life and chronic pain in Europe. It will also elaborate whether prevention and treatment of chronic pain may have a significant effect on increasing the healthy lifespan by two years, as intended by the Active and Healthy Ageing Partnership project.

On behalf of EFIC®, I would like to wish you inspired reading,

**Professor Hans G. Kress, M.D., PhD**  
**President of EFIC®**



## Executive summary

Through the Europe 2020 strategy framework and its “Innovation Union” flagship initiative, the European Commission has committed to overcome the barriers to innovation, especially for addressing the major societal challenges. It put forward the novel concept of European Innovation Partnerships (EIPs). Active and Healthy Ageing (AHA) was chosen as the pilot area: ‘The European Commission has identified active and healthy ageing as a major societal challenge common to all European countries, and an area which presents considerable potential for Europe to lead the world in providing innovative responses to this challenge.’<sup>1</sup>

The Strategic Implementation Plan published by the European Commission refers to active and healthy ageing as “...the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age” (p.4, Strategic Implementation Plan 2011). The headline target of this pilot partnership will be to increase the average healthy lifespan by two years by 2020, including by: ‘... improving the health status and quality of life of European citizens, with a particular focus on older people...’ (p.6, Strategic Implementation Plan, 2011)<sup>2</sup>.

We know that people are living longer: in 2050 about 30% of the European population will be aged  $\geq 65$ <sup>3</sup>. The question is what can be done to improve their quality of life and specifically, for this report, what is the evidence that addressing chronic pain can help? This report addresses the relationship between chronic pain and quality of life and healthy ageing, and argues that prevention and treatment of chronic pain may be of significant help in reaching the aim to increase the healthy lifespan.

As the European Federation of IASP Chapters (EFIC) has highlighted<sup>4</sup>, everyone is familiar with acute pain as a symptom of some disease or injury. However, sometimes pain persists, often long after tissue healing. This chronic pain is often considered a separate entity in itself, with clear characteristics of symptoms, disability, and mental health aspects which are largely independent of the precipitating disease or trauma<sup>5,6</sup>. Therefore, as well as being part of many chronic diseases, such as stroke, it can be useful to consider it as a chronic disease in its own right. For example, we know that chronic pain is very common<sup>7</sup> but good data about prevalence, incidence, diagnosis, severity, treatment and utilisation of healthcare are scarce<sup>8</sup>. Indeed, lack of national statistics could be attributed partly to not seeing chronic pain as a separate entity, but as a symptom.

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One goal of this pilot in healthy ageing is to increase the average healthy lifespan by two years by 2020.

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## Impact of chronic pain on quality of life

There is reasonably strong evidence that chronic pain impairs quality of life. For example, a review of chronic pain<sup>9</sup> showed that in most moderate-to-severe chronic non-cancer pain sufferers, pain severely affected activities of daily living and many were less or no longer able to maintain relationships with family and friends. Also, those with any general chronic pain were more likely to rate their health status as fair-to-poor compared to those not experiencing persistent pain. Physical health scores of pain sufferers relative to non-sufferers are notably lower, especially in the cohorts of older adults and those with severe pain.<sup>10</sup>

Our report shows that there is also limited (only a few studies) evidence in that interventions, such as treatments e.g. pregabalin or gabapentin or hydrotherapy, can improve quality of life as well as reduce pain, although the extent to which improved quality of life is mediated by pain reduction is less clear.

There is stronger evidence of a correlation between pain severity and quality of life, which does not prove that reducing pain will improve quality of life, but is nevertheless consistent with this possibility. Moreover, the average age of study participants was no younger than in the 40s. Therefore, if reduced pain improves quality of life in middle-age then we have an opportunity for interventions that reduce pain to improve quality of life as people age. This might especially be the case in the over 50s, who have the highest prevalence of chronic pain<sup>7</sup>.

## Conclusions

1. Pain is a common health state. Once it is chronic it deserves to be treated like a separate disease.
2. Chronic pain is associated with reduced quality of life.
3. Chronic pain results in lost working days.
4. Chronic pain prevalence increases with age.
5. Pain influences the quality of life negatively for both individuals and population groups.
6. Chronic pain interventions reduce pain and improve quality of life.

## Relevance for policy makers

Based on the findings of this report policy makers are advised to consider pain care in future policies aiming at improving the quality of life for European citizens as part of the goals set within the Healthy Ageing framework.

## 1. What we already knew about chronic pain and quality of life

### 1.1 Chronic pain is common

From the report 'Reflection process on chronic diseases in the EU – the role of chronic pain'<sup>7</sup>, the prevalence of any chronic pain in the general adult population ranged from 16% in a study on Europe<sup>11</sup> to 46% in a study in Sweden<sup>12</sup>. This is high in comparison to some other chronic diseases, as shown in the latest European Union (EU) Major Chronic Diseases Report<sup>13</sup>. For example, the prevalence of dementia is no more than about 1.25% and, for depression and diabetes, these figures were estimated to be about 4.5% and 7.8% respectively.

### 1.2 Chronic pain prevalence increases with age

Seven out of 28 prevalence studies located in the review for the report 'Reflection process on chronic diseases in the EU – the role of chronic pain'<sup>7</sup> showed a strong link between increasing age and the prevalence of pain. Hensler (2009)<sup>14</sup>, Jakobsson (2010)<sup>12</sup>, Langley (2011)<sup>11</sup> and Raftery (2011)<sup>15</sup> all showed a general increase in the prevalence of chronic pain in the general adult population with increasing age. Fernandez-de-la-Penas (2011)<sup>16</sup> showed the same trend of increasing prevalence of pain with increasing age for neck pain and low back pain and Gerdle (2008)<sup>17</sup> for musculoskeletal pain. Also, in the study by Gialloreti (2009)<sup>18</sup>, 90.9% of those with post herpetic neuralgia were over 50.

### 1.3 Chronic pain is associated with reduced quality of life

From the 'Epidemiology of chronic non-cancer pain in Europe' report<sup>8</sup>, one medium quality study examined quality of life using the EQ-5D in Europeans with chronic neuropathic pain<sup>19-22</sup> and showed a poorer overall health status was significantly associated with increasing pain intensity in those with any general neuropathic pain, painful diabetic neuropathy, trigeminal neuralgia and post-herpetic neuralgia. Furthermore, chronic neuropathic pain sufferers felt their health status would significantly improve if they could achieve complete pain relief, indicating that chronic neuropathic pain contributed significantly to poor self-reported health status. Another study reported a trend towards lower health status among patients with any general chronic pain in seven out of eight European health centres reaching statistical significance in three health centres<sup>23</sup>.

Moreover, from the report 'Reflection process on chronic diseases in the EU – the role of chronic pain'<sup>7</sup>, unemployment attributed to pain ranged from 4% for back pain in Germany<sup>24</sup> to 6% for fibromyalgia in Spain<sup>25</sup>. From the same studies, this coincided with days off work of 13.6 and 73 respectively and the percentage of people claiming incapacity type benefits ranged from 3.7% for low back pain in Switzerland<sup>26</sup> to 29.9% for fibromyalgia in Spain<sup>27</sup>.

## 2. What is new in this report

### 2.1 Summary

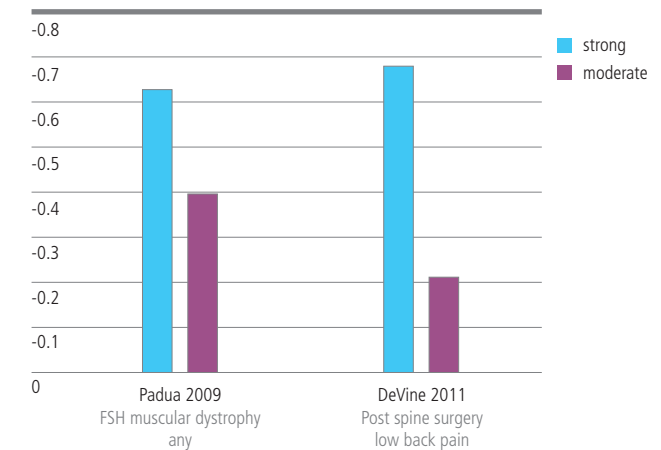
Briefly, there is some evidence that chronic pain is associated with reduced quality of life and that chronic pain interventions reduce pain and improve quality of life.

### 2.2 Chronic pain is associated with reduced quality of life

We identified six observational studies with a total of 5732 patients (estimated 82% female) that examined the relationship between pain and quality of life<sup>28-34</sup>. We also selected a single systematic review (1068 patients) that calculated study-level pooled mean differences from five studies that examined adults with low back pain who had undergone pain-relief surgery<sup>35</sup>. Details of their methods are described in Appendix 2.

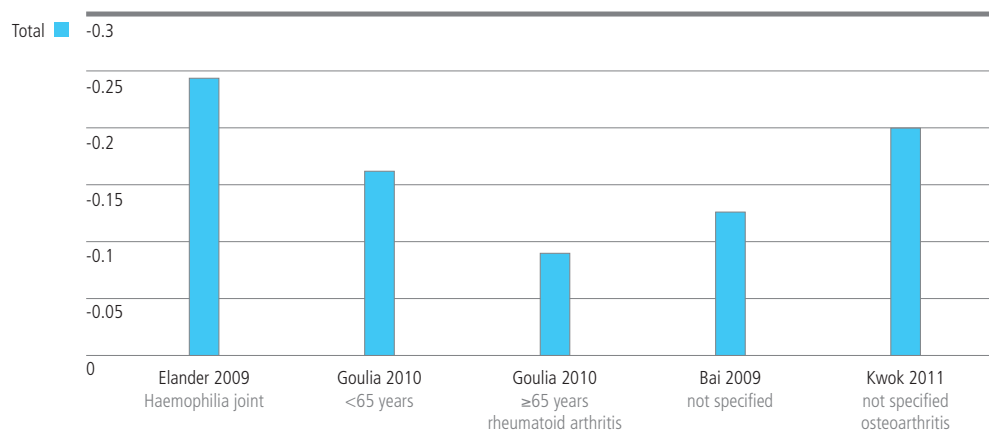
Figure 1 shows a summary of the results in terms of the amount of correlation between pain severity and QoL from the six studies that reported this information. A zero value would indicate that if pain increased or decreased then QoL is no more or less likely to change: the closer to 1 or -1 the more likely that there is a relationship.

There appears to be a negative (hence the negative values on the vertical axis) relationship between pain and QoL for most types of pain, which fits with the idea that if pain is relieved then QoL is improved.



**Figure 1** Correlation between QoL and pain severity (strong: 0.5-0.8, moderate: 0.2-0.5 (FSH=facioscapulohumeral))

Figure 2 shows what the size of the relationship is between pain severity and QoL i.e. not only whether QoL is likely to change with pain, but by how much QoL will as pain changes. These values have also been estimated by adjusting for other factors such as gender or disease duration. In essence, adjusting removes the effect of other factors to leave the 'pure' effect of pain on QoL. For example, in rheumatoid arthritis, it appears that QoL increases more with pain decrease below 65 than from 65 upwards. This would suggest that decreasing pain has a larger effect on QoL in younger people. However, the average (mean or median) age of participants in all studies was no younger than in the 40s. Moreover, even after adjusting for other factors, in most studies, pain and QoL were still highly correlated, as indicated by the size of this effect being statistically significantly different from zero i.e. unlikely that it could have occurred simply by chance. Only one study by Fernandez 2010<sup>30</sup> did not measure pain severity, but simply whether pain was present or not and again the relationship with QoL was statistically significant after adjusting for other factors.

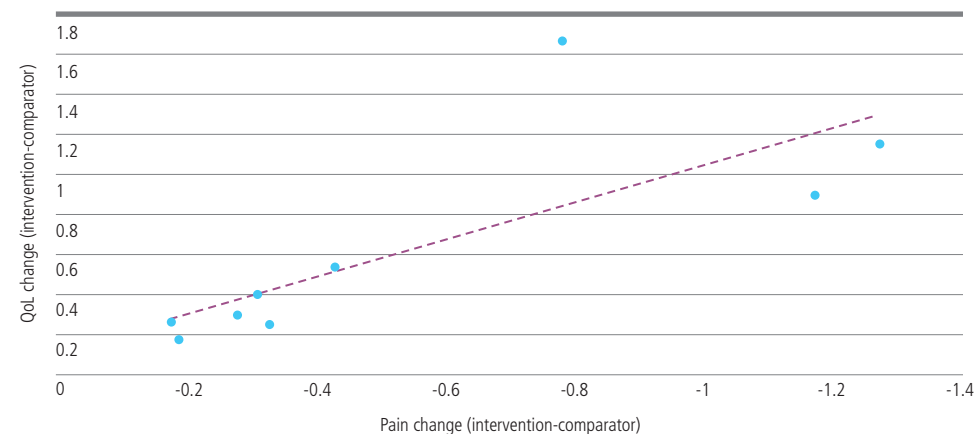


**Figure 2** size of effect in relationship between pain severity and QoL (e.g. -1 means 1 point decrease in pain produces 1 point increase in QoL)

### 2.3 Chronic pain interventions reduce pain and improve quality of life

From the search of systematic reviews of intervention in chronic pain, out of 23 full papers screened, eight were included<sup>36-43</sup>. Reasons for exclusion were inappropriate outcomes, largely due to lack of both pain and QoL data in all cases except two, which turned out not to be systematic reviews. Details of these studies are reported in Appendix 2.

Figure 3 shows the difference that the intervention (e.g. some drug or physical therapy) makes in comparison to the comparator treatment (usually placebo or no treatment) in terms of both pain and QoL. The dashed line shows that, albeit approximately, there is a clear relationship between such that as pain decreases then QoL increases. Moreover, in most studies, both the change in pain and QoL were statistically significantly different from zero, indicating that when pain decreases it is unlikely to be only by chance and the same is true for QoL. In terms of the relationship with ageing, the average age in all studies was no younger than the 40s.



**Figure 3** Relationship between change (intervention vs comparator treatment) in QoL and pain

### 3. Discussion

Other reports show that generally chronic pain is common, gets more common with age and decreases quality of life and that individuals with chronic pain would expect an improvement in quality of life if they had no pain.

What this study shows is that overall there is evidence from observational studies of an often statistically significant correlation between pain and QoL, even after controlling for other factors. This was also true regardless of age, although all the average age of participants in all studies was at least in the 40s. For example, there was evidence that chronic pain and pain associated with rheumatoid arthritis and haemophilia significantly impacted quality of life. Several studies showed statistically significant relationships between pain and QoL and were judged to have moderate to high quality of reporting.

Secondly, systematic reviews of interventions in chronic pain also show a relationship between reduction in pain and increase in quality of life. All systematic reviews of interventions to reduce chronic pain where both pain and QoL were reported showed both a decrease in pain as well as an increase in QoL, which was statistically significant in five out of nine results. Furthermore, the average age of participants was no younger than in the 40s.

There are some weaknesses with this study. Firstly, the search was pragmatic and as such limited observational data on quality of life to studies from 2009. However, the search of systematic reviews did go back to 2005. Also, the message seems to be consistent across studies regarding the effect of chronic pain on quality of life.

Secondly, no studies were found that focussed on those over 50. However, health ageing as defined in the Strategic Implementation Plan is about improving quality of life 'as people age', not beyond some arbitrary age cut-off. Therefore, evidence that quality of life can improve across a range of ages including older people is important.

Thirdly, just because quality of life and pain both changed does not imply causality i.e. that reducing pain will improve quality of life. However, the fact that quality of life improves by some intervention is clearly the most important thing, regardless of whether this is through actual decrease in pain or some other mechanism such as improved function.

Fourthly, all intervention studies were in fibromyalgia, although they were all of reasonable quality.

Strengths of this study include the transparent and reproducible search methods, even if they were pragmatic in terms of search date limits. Secondly, in our literature search we could find no other review that examined both the relationship between chronic pain severity and quality of life and the potential for improving quality of life by reducing pain.

## 4. Conclusions

1. The EU has decided to focus on Active and Healthy Ageing, which has a goal of increasing the average healthy lifespan by two years by 2020. Chronic pain is a common health state and results in lost working days and reduced quality of life.
2. The question is what can be done to improve quality of life, particularly of older people by addressing chronic pain? The aim of this study was therefore to review the evidence on the relationship between chronic pain and quality of life and the effect of interventions in terms of pain reduction and quality of life improvement.
3. Results showed that there is limited (only a few studies) evidence in that interventions, such as treatments e.g. pregabalin or gabapentin or hydrotherapy, can improve quality of life as well as reduce pain, although it is less clear the extent to which improved quality of life is mediated by pain reduction is less clear.
4. Results also showed that is stronger evidence of a correlation between pain severity and quality of life, which does not prove that reducing pain will improve quality of life, but is nevertheless consistent with this possibility. Moreover, the average age of study participants was no younger than in the 40s. Therefore, if reduced pain improves quality of life in middle-age then we have an opportunity for interventions that reduce pain to improve quality of life as people age. This might especially be the case in the over 50s, who have the highest prevalence of chronic pain.
5. In terms of the research questions, there appear to be sufficient grounds for further research and we could recommend that all intervention studies are appropriately designed to investigate differences in both pain and quality of life.

### **Relevance for policy makers**

Based on the findings of this report policy makers are advised to consider pain care in future policies aiming at improving the quality of life for European citizens as part of the goals set within the Healthy Ageing framework.

## Appendix 1

### List of references

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## Appendix 2

### Detailed methods and results

#### Background

The EU Commission is performing a project entitled "Pilot European Innovation Partnership on Active and Healthy Ageing" (see [http://ec.europa.eu/research/innovation-union/index\\_en.cfm?section=active-healthy-ageing&pg=implementation-plan](http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing&pg=implementation-plan)). The ambition of the EU Commission is to gain two quality life years by 2020. It is likely that pain plays an important role in relation to age (>50 years) and quality of life. We also see a strong need for enhanced policy making and budget reallocation in this area<sup>44</sup>.

To support future pain policy making in relation to healthy ageing and budget reallocation a report giving a fact base for the upcoming discussion is desired.

Kleijnen Systematic Reviews Ltd previously produced a number of reports about the epidemiology of chronic pain in Europe; these were commissioned by Grünenthal<sup>8</sup>. The impact of chronic pain on quality of life was part of that work. This new project uses the data from these previous reports but also provides an update of any new findings published in the last two and a half years as well as some new evidence on the relationship between pain and quality of life.

#### Objective of project

To undertake a literature review on the most recent epidemiological data on chronic pain in relation to quality of life in people over 50 years old. Countries to be included: any EU country and EU overall. The resulting report should form a basis for discussions about chronic pain as an issue of healthy ageing.

#### Patients

Patients over 50 years old with chronic pain from the EU.

#### Questions to be addressed

1. What is the impact of chronic pain on quality of life as part of healthy ageing?
2. What quality of life changes might be possible from adequately treating chronic pain in people over 50 years old?

## Population

The population is patients with a diagnosis of chronic pain who are over 50 years old.

## Intervention/comparators

These are not relevant to answer question (1). For question (2) there is no limit to the intervention or comparator except that they are successful in reducing pain.

## Outcomes

In order to estimate the potential for gaining quality of life by reducing pain in chronic pain sufferers we consider that any of the following sources might be useful. Note that an attempt has been made to list them in order of quality in terms of usefulness in addressing this question, but there are many factors that might promote or demote a particular study:

- Meta-analysis of some specific technology, which show evidence of improvement in QoL for a specific chronic pain population.
- Observational study, which estimates QoL as function of severity e.g. VAS such that one could assume if severity decreases then might obtain corresponding increase in QoL.
- Observational study, which estimates QoL in pain severity categories (including no pain) such that could assume if move from one category to another then have corresponding QoL change.
- Observational study, which estimates QoL in chronic pain population (single severity category or regardless of severity) such that could assume if pain relieved then QoL would improve and perhaps up to population average (excluding with pain).

Without specific data on effectiveness generally one could infer from evidence of under-treatment that if this was addressed that there might be a move from e.g. the severe to the moderate and moderate to mild according to this change or perhaps a move of e.g. one VAS point. Of course, one must be cautious with regards to causality i.e. the observation of variation in QoL between various levels of pain does not imply that movement between categories implies change in the measure.

This is largely because of the possibility of confounding i.e. that both measure and pain are associated with some other factor. An obvious example is the underlying cause of the pain, which might imply not only pain but disability such that a change in pain might not lead to a change in disability and thus might not change QoL or cost.

Confounding can be reduced by statistical models of the association between pain and QoL/cost as independent of other factors, such as disability. However, the extent to which the independent effect of pain is important also depends on the amenability (effectiveness and cost) of pain reduction to pain treatment e.g. by analgesia as opposed to treatment of the underlying disease, but this question is beyond the scope of this review. Therefore, in order to address question (1) we extracted any quantitative data, including summary statistics, on the relationship between chronic pain and quality of life. This was in the form of correlations between continuous measures of pain and quality of life or other measures of association between pain, however measured, and quality of life.

In order to address question (2) we extracted any quantitative data, including summary statistics on the effect of treatments, which reduce pain, on quality of life. The nature of these measures of effect depended on how quality of life is measured and so could be in the form of difference in means or medians, together with any other relevant statistics, such as confidence intervals.

## Study type

Study type for question (1) was any primary observational study, which estimates QoL in at least one pain category or the association between QoL and pain. Study type for question (2) was meta-analyses or, where pooling was not done, systematic reviews, as a range across all primary sources.

## Inclusion criteria

Any papers reporting data that fulfil criteria according to the population, outcomes and study type were included.

## Literature searches

### Search strategy

Searches were undertaken in multiple stages to identify relevant information, such as utilities data, health-related quality of life research and systematic reviews in the field of chronic pain. Searches were not limited by language or publication status (unpublished or published). The searches were limited to studies in humans.

### **Systematic reviews, guidelines and guidance**

These searches were a partial update of those undertaken in the broader Literature Review on the Epidemiology of Chronic Pain project previously undertaken for Grünenthal and date limits were employed accordingly.

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): 2009-2011/Issue 11
- Database of Abstracts of Reviews of Effects (DARE) (Wiley): 2009-2011/Issue 4
- Health Technology Assessment Database (HTA) (Wiley): 2009-2011/Issue 4
- NHS Economic Evaluation Database (NHS EED) (Wiley): 2009-2011/Issue 4
- GIN International Guidelines Library (Internet) 2009-2011/11/28
- NICE Guidance (Internet) 2009-2011/11/28
- National Guidelines Clearinghouse (Internet) 2009-2011/11/28
- INAHTA (International Network of Agencies for Health Technology Assessment) (Internet) 2009-2011/11/28

### **Observational studies**

Focused health-related quality of life search filters and EU countries filters were utilized where appropriate to pinpoint relevant studies. These searches were a partial update of those undertaken in the broader Literature Review on the Epidemiology of Chronic Pain project previously undertaken for Grünenthal and date limits were employed accordingly.

- Medline (OvidSP): 2009/08–2011/11/wk3
- Medline In-Process Citations (OvidSP): 2011/11/28
- Medline Daily Update (OvidSP): up to 2011/11/16
- Embase (OvidSP) 2009/wk36–2011/wk47

### **Intervention studies**

Searches were undertaken to find systematic reviews and health technology assessments. A study design search filter was utilised with date limits of 2005-2011.

- Medline (OvidSP): 2009/08–2011/11/wk3
- Medline In-Process Citations (OvidSP): 2005-2011/11/28
- Medline Daily Update (OvidSP): 2005-2011/12/06
- Embase (OvidSP) 2009/wk36–2011/wk48

Full search strategies for all databases are detailed in Appendix 3.

Identified references were downloaded in Endnote X4 software for further assessment and handling.

### **Methods of study selection, quality assessment and data extraction**

This literature review followed the methods and processes recommended in the Centre for Reviews and Dissemination (CRD) "Systematic Reviews: Guidance for undertaking systematic reviews in health care"<sup>45</sup>.

#### **Study selection**

Two reviewers independently inspected the abstract of each reference identified by the search and determine the potential relevance of each article. For potentially relevant articles, or in cases of disagreement, the full article was obtained, independently inspected, and inclusion criteria applied. Any disagreement was resolved through discussion and checked by a third reviewer. Justification for excluding studies from the review was documented.

#### **Assessment of methodological quality**

Quality assessment was carried out independently by two reviewers using appropriate checklists from CRD's guidance document and, for observational studies based on the STROBE<sup>46</sup> guidelines for reporting and on the AMSTAR checklist<sup>47</sup> for meta-analyses. Any disagreements were resolved by consensus. The results of the quality assessment were used for descriptive purposes to provide an evaluation of the overall quality of the included studies and to provide a transparent method of recommendation for design of any future studies. Based on the findings of the quality assessment, recommendations have been made for the conduct of future studies.

#### **Data collection**

For each study, data was extracted by one reviewer and checked by a second reviewer. Any disagreements were resolved by consensus. Data extraction was discussed and decisions documented. Studies are identified by the name of the first author and year in which the trial was first published.

#### **Data presentation**

We employed a narrative method to present the data and for any synthesis. Typically, narrative synthesis involves the use of narrative text and tables to summarise data in order to allow the reader to consider outcomes in the light of differences in study designs and potential sources of bias for each of the studies being reviewed. This involves organizing the studies by (as appropriate) intervention, population, or outcomes assessed, summarizing the results of the studies, summarizing the range and size of the associations these studies report, and describing the most important characteristics of the included studies. A detailed commentary on the major methodological problems or biases that affected the studies is included, together with a description of how this has affected the individual study results.

Reason for exclusion: in appropriate...	Count of Reason for exclusion
Country	7
Design	21
Outcomes	102
Population	9
<b>Grand Total</b>	<b>97</b>

Table 1

Reasons for exclusion

## Results: Chronic pain is associated with reduced quality of life

### Summary of study characteristics

For the purpose of finding studies that show the relationship between pain and quality of life, 145 full papers were screened and seven (Bai (2009)<sup>28</sup> and Goulia (2010)<sup>31</sup> are counted as two studies for reporting since they were different analyses of the same original data) were included because they estimated the relationship between quality of life and pain severity in a chronic pain population. Reasons for exclusion are shown below. Another study was obtained from the search for systematic reviews of interventions (see Chronic pain interventions section below)<sup>35</sup>.

Five studies were cross-sectional studies examining rheumatoid arthritis and related conditions (i.e. systemic lupus, scleroderma, and Sjogren's syndrome), hand osteoarthritis, facioscapulohumeral muscular dystrophy, haemophilia-related joint pain, and general chronic pain.<sup>28-32</sup> The remaining observational study was a retrospective analysis of pooled randomised controlled trials (RCTs) examining fibromyalgia<sup>33</sup>. We also selected a single systematic review (1068 patients) that calculated study-level pooled mean differences from five studies that examined adults with low back pain who had undergone pain-relief surgery<sup>35</sup>. The retrospective pooled analysis and the systematic review did not report their location whereas the remaining cross-sectional studies were located in European countries (Greece, United Kingdom (UK), Spain, Netherlands, and Italy).

With the exception of Padua (2009)<sup>34</sup>, all of the cross-sectional studies employed multiple regression analysis to determine the independent effect of pain on QoL. Padua (2009)<sup>34</sup> and DeVine (2011)<sup>35</sup> conducted a bivariate analysis using Spearman's rank coefficient test. Moore (2010)<sup>33</sup> reported mean change in pain levels and QoL using individual patient data pooled from four RCTs. Most of the studies used pain measuring tools that were independent of the QoL measure: the visual analogue scale (VAS), the

Brief Pain Inventory (BPI) or the Australian Canadian (AUSCAN) hand osteoarthritis Likert pain subscale. The one exception was Fernandez (2010)<sup>30</sup>, which measured both pain and QoL using a preference-based health-state utility index (SF-6D) with six attributes derived from the 12-item Short Form (SF-12) Health Survey. Apart from the two companion studies concerning rheumatoid arthritis and the study concerning general chronic pain, all studies employed the 36-item Short Form (SF-36) Health Survey to assess QoL. The retrospective analysis on fibromyalgia also used the Fibromyalgia Impact Questionnaire (FIQ) and Global Fatigue Index (GFI) to measure the impact of the disease on QoL.<sup>33</sup> In addition to the SF-36, DeVine (2011)<sup>35</sup> employed the Oswestry Disability Index (ODI) and the EuroQoL (EQ)-5D index. To measure impact on QoL, the study on rheumatoid arthritis employed the short version of the World Health Organisation QoL assessment (WHOQoL)<sup>28, 31</sup> and the study on general chronic pain employed the SF-6D survey<sup>30</sup>.

### Summary of results

Only one study stratified results by age. Among those aged 65 years or more, arthritis-related pain was significantly and independently associated with physical HRQoL ( $\beta=-0.207$ ,  $p=0.029$ ) after adjusting for sex, education level, and erythrocyte sedimentation rate (ESR)<sup>31</sup>. Arthritis-related pain was not found to be significantly associated with the social relationships domain of WHOQoL in this age group ( $\beta=0.026$ ,  $p=0.979$ ).

Chronic pain was found to be independently and significantly associated with SF-6D total score ( $\beta=-0.0761$ ,  $p<0.001$ ) after adjusting for sex, age, marital status, working status and education level<sup>30</sup>. Quantile regression analysis, which was employed to characterise the entire conditional distribution of QoL, indicated that the relationship between pain and QoL was significant regardless of the decile used. However, an inverse impact association was detected between chronic pain and QoL in that, as the SF-6D score increased, the predictive capability of chronic pain decreased: Between the first and ninth decile the difference between the coefficient of regression was  $+0.052$  ( $p<0.001$ ) and between the first and third the difference was  $+0.04$  ( $p=0.002$ ).

In rheumatoid arthritis patients, pain was found to be a significant and independent predictor of impaired physical health-related QoL (HRQoL) ( $\beta=-0.624$ ,  $p<0.001$ ), after adjusting for major demographic variables (age, sex and education), pathology parameters (disease duration and ESR) and other physical impairment variables (number of tender and swollen joints and duration of morning stiffness)<sup>28</sup>. When the interaction between pain and personality was taken into consideration, a self-sacrificing defence style (i.e. the need to perceive one's self as being kind, helpful to others, and never angry) was found to be a significant moderator in the relationship between pain and physical HRQoL ( $\beta=-0.316$ ,  $p<0.001$ ).

After adjusting for psychological distress (General Health Questionnaire total score) and then for functional limitations (Health Assessment Questionnaire score), pain was no longer a significant independent predictor of physical HRQoL ( $\beta=-0.171$  and  $-0.127$ , respectively); although the interaction between pain and a self-sacrificing defence style remained a significant predictor ( $\beta=-0.331$ ,  $p<0.001$  and  $-0.298$ ,  $p<0.01$ , respectively).

Among patients with hand osteoarthritis, the self-reported AUSCAN pain measure was not found to be a significant independent predictor of either the SF-36 physical component score ( $\beta=-0.195$ ) or the mental component score ( $\beta=-0.395$ ), after adjusting for age, sex, marital state, education level, body mass index and smoking status.

Among those suffering from facioscapulohumeral muscular dystrophy, a significant correlation was found between pain and the SF-36 physical function ( $\beta=-0.34$ ,  $p<0.05$ ), role-physical ( $\beta=-0.65$ ,  $p<0.001$ ), bodily pain ( $\beta=-0.66$ ,  $p<0.001$ ), general health ( $\beta=-0.64$ ,  $p<0.001$ ), vitality ( $\beta=-0.71$ ,  $p<0.001$ ), social function ( $\beta=-0.51$ ,  $p<0.001$ ), role-emotional ( $\beta=-0.41$ ,  $p<0.01$ ), mental health ( $\beta=-0.43$ ,  $p<0.01$ ), physical component score ( $\beta=-0.60$ ,  $p<0.001$ ), and mental component score ( $\beta=-0.41$ ,  $p<0.05$ ).<sup>33</sup> The authors did not assess the independent effects of pain on QoL.

In those with haemophilia-related joint pain, pain intensity alone was found to be a significant and independent predictor for an impaired physical QoL ( $\beta=-0.51$ ,  $p<0.001$ ) but not for mental QoL ( $\beta=-0.05$ ) after adjusting for age, haemophilia severity, use of clotting factor, and measures of pain coping, negative thoughts and pain acceptance<sup>29</sup>. For physical QoL, pain willingness (i.e. the degree to which people have experiences of pain without trying to avoid or control them) was identified as a significant mediator of pain intensity (Sobel =  $-0.88$ ,  $p=0.0084$ ). As pain willingness increased, the impact of pain intensity on physical QoL was reduced (low pain willingness  $\beta$ [non-standardised] =  $-9.29$ ,  $p<0.001$ ; moderate pain willingness  $\beta=-7.36$ ,  $p<0.001$ ; and high pain willingness  $\beta=-5.43$ ,  $p<0.001$ ). Pain intensity alone was not a significant predictor of mental QoL but the interaction between pain intensity and negative thoughts was ( $\beta=0.14$ ,  $p<0.05$ ). In essence, negative thoughts were found to significantly mediate the impact of pain intensity on mental QoL (Sobel =  $-1.29$ ,  $p=0.0117$ ): As the intensity of negative thoughts increased, the impact of pain intensity on mental QoL also increased. However, these results did not reach statistical significance (low negative thoughts  $\beta=1.38$ ,  $p=0.18$ ; moderate negative thoughts  $\beta=-0.29$ ,  $p=0.71$ ; and high negative thoughts  $\beta=-1.95$ ,  $p=0.062$ ).

In the systematic review examining adults with low back pain who underwent pain-relieving spinal surgery, substantial improvements were observed in a 100-point standardized pain score (pooled mean (SD) change 24.5 (7.6)) and in the ODI lumbar spine functionality score (pooled mean (SD) change 15.4 (5.2)) as well as lesser improvements in SF-36 total score (pooled mean (SD) change 8.2 (4.6)), SF-36 physical composite score (pooled mean (SD) change 5.7 (2.1)), SF-36 mental composite score (pooled mean (SD) change 4.0 (2.3)) and EQ-5D index score (pooled mean (SD) change 0.29 (0.06))<sup>35</sup>. A statistically significant but weak correlation was observed between the change in pooled mean pain score and ODI score (Spearman rank correlation 0.69,  $p=0.04$ ). No significant correlations were noted between the change in pooled mean pain score and either the SF-36 physical or mental component summary pooled mean scores (0.67,  $p=0.22$  and 0.21,  $p=0.74$ , respectively). The sample sizes for the SF-36 total score and the EQ-5D index score were stated to be too small to allow for calculation of a correlation.

The authors suggested that the higher effect sizes of pain relief and physical functionality (as measured by the ODI) were unsurprising given that the clinical goal for spinal surgery was to improve low back pain and to improve lumbar spine function. In contrast, the SF-36 and EQ-5D QoL measures were less responsive to spinal surgery treatment and were likely more easily influenced by co-morbidities and psycho-social factors than either the VAS or ODI measures.

While the retrospective pooled analysis of fibromyalgia patients reported pain and QoL outcomes, the relationship between pain and QoL was not examined<sup>33</sup>.

In those who experienced marginal improvement in pain intensity (i.e. 0 to <15% reduction in VAS scores), a significant improvement was observed for the GFI, FIQ, and the SF-36 social functioning, bodily pain and vitality domains ( $p<0.05$ ). For those who experienced minimal improvement in pain intensity (i.e. 15 to <30% reduction in VAS scores), a significant improvement was observed for the GFI, FIQ and the SF-36 physical functioning, physical role, emotional role, social functioning, mental health, bodily pain and vitality domains ( $p<0.05$ ). For those with moderate or substantial improvements in pain intensity (i.e. 30 to <50% reduction or >50% in VAS scores), a significant improvement was noted for the GFI, FIQ and all SF-36 domains ( $p<0.05$ ). The main characteristics and results in terms of correlation are shown below.

Study	Country	Sample size	Age	Population or subgroup	Type of pain	Pain measure	QoL measure	Sub-scale	Statistically significant	Correlation between pain and QoL or Beta coefficient if adjusted	Adjusted			
DeVine 2011 <sup>35</sup>	Not reported	1168	39-76 (range of means)	Adults with chronic low back pain who had spine surgery	LBP	100mm VAS	ODI	physical function	yes	-0.69	no			
								SF-36	physical component summary	no	-0.67	no		
								SF-36	mental component summary	no	-0.21	no		
Bai 2009 <sup>28</sup>	Greece	320	54.9 (mean)	RA	RA	100mm VAS	WHOQOL	physical	no	-0.127	yes			
Elander 2009 <sup>29</sup>	UK	209	49.5 (mean)	Haemophilia	joint	100mm VAS	SF-36	physical component summary	yes	-0.52	yes			
								100mm VAS	SF-36	mental component summary	no	0.03	yes	
Fernandez 2010 <sup>30</sup>	Spain	2496	Not reported	General adult	any	SF-6D pain (1-5)	SF-6D	NA	yes	-0.0761	yes			
Goulia 2010 <sup>31</sup>	Greece	75	68 (median)	≥65 years	RA	VAS	WHOQOL	physical	yes	-0.207	yes			
								245	<65 years	WHOQOL	physical	yes	-0.291	yes
								75	≥65 years	WHOQOL	social relationships	no	0.026	yes
								245	<65 years	WHOQOL	social relationships	no	-0.035	yes
								320	all patients	WHOQOL	physical	yes	-0.0171	yes
Kwok 2011 <sup>32</sup>	Nether-lands	784	61 (mean)	OA	OA	0-20 AUSCAN Likert pain subscale	SF-36	physical component summary	yes	-0.1	yes			
								SF-36	mental component summary	no	-0.3	yes		
Padua 2009 <sup>34</sup>	Italy	65	40.9 (mean)	Facio-scapulo-humeral muscular dystrophy	any	VAS	SF-36	physical functioning	yes	-0.34	no			
								SF-36	role-physical	yes	-0.65	no		
								SF-36	bodily pain	yes	-0.66	no		
								SF-36	general health	yes	-0.64	no		
								SF-36	vitality	yes	-0.71	no		
								SF-36	social functioning	yes	-0.51	no		
								SF-36	role-emotional	yes	-0.41	no		
								SF-36	mental health	yes	-0.43	no		
								SF-36	physical component summary	yes	-0.6	no		
SF-36	mental component summary	yes	-0.41	no										
Moore 2010 <sup>33</sup>	NR	1858	Not reported		Fibromyalgia	100mm VAS	SF-36, FIQ	all	NA	NA	no			

Table 2

Summary of characteristics of observational studies

## Summary of quality

The quality of reporting for the observational studies included in this report was assessed using eight criteria derived from the STROBE<sup>46</sup> guidelines. Only Elander (2009)<sup>29</sup> was well-reported in that they met each criterion. Three observational studies had acceptable reporting levels in that they missed only one or two of the eight criteria<sup>28, 30-32</sup>. The study population examined in Bai (2009)<sup>28</sup> and Goulia (2010)<sup>31</sup> was judged to be not likely representative of the target population of rheumatoid arthritis patients since patients were recruited from a single hospital-based clinic that provided only secondary or tertiary care. The same can be said of Kwok (2011)<sup>32</sup>, which recruited osteoarthritis patients from a single University-based outpatient clinic. The study by Fernandez (2010)<sup>30</sup> and Kwok 2011<sup>32</sup> were missing key population characteristics (notably pain duration and severity). Fernandez (2010) also did not clearly indicate which factors were adjusted for to determine the independent effects of pain on QoL.

For the remaining two observational studies, the quality of reporting was judged as low<sup>33, 34</sup>. For both studies, key population characteristics were missing and it was unclear whether sample populations were representative of the target population because the sources for recruiting patients were not reported. For the retrospective analysis the losses to follow-up were not adequately reported. Moore (2010)<sup>33</sup> also did not elaborate on the study setting, although they referred the reader to previous publications of the relevant RCTs used in the analyses, plus they did not indicate whether or not results were adjusted for confounders.

Using the AMSTAR checklist<sup>47</sup> for methodological quality, the systematic review by DeVine (2011)<sup>35</sup> was assessed as low quality. An a priori design or a link to a protocol was not provided so it was difficult to determine whether the research question and inclusion criteria were established before the conduct of the review. The authors limited their search to published English studies and they did not report that they checked for publication bias. Key population characteristics were missing and it was not apparent that they checked for heterogeneity before combining study samples.

Study ID	1. Was an 'a priori' design provided	2. Was there duplicate study selection and data extraction	3. Was a comprehensive literature search performed	4. Was the status of publication (i.e. grey literature) used as an inclusion criterion	5. Was a list of studies (included and excluded) provided	6. Were the characteristics of the included studies provided	7. Was the scientific quality of the included studies assessed and documented	8. Was the scientific quality of the included studies used appropriately in formulating conclusions	9. Were the methods used to combine the findings of studies appropriate	10. Was the likelihood of publication bias assessed	11. Was the conflict of interest stated
Bernardy 2011 <sup>36</sup>	yes	yes	yes	no	yes	no	yes	yes	yes	yes	no
DeVine 2011 <sup>35</sup>	no	yes	no	yes	yes	no	yes	yes	unclear	no	no
Doth 2010 <sup>37</sup>	no	yes	yes	no	yes	yes	no	no	unclear	no	yes
D'Sylva 2010 <sup>38</sup>	yes	yes	yes	no	yes	no	yes	yes	yes	no	no
Hauser 2009 <sup>39</sup>	no	yes	yes	no	yes	yes	yes	yes	yes	no	yes
Hauser 2010 Arthritis R&T <sup>40</sup>	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	yes
Hauser 2010 Rheumatology <sup>41</sup>	yes	yes	yes	no	yes	no	yes	yes	yes	yes	yes
Hoffman 2008 <sup>42</sup>	no	no	yes	yes	no	no	no	no	yes	no	yes
Langhorst 2009 <sup>43</sup>	no	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes

Table 3

Systematic reviews quality (according to AMSTAR)



## Results:

### Chronic pain interventions reduce pain and improve quality of life

#### Summary of study characteristics

We identified eight systematic reviews (SRs) of interventions in chronic pain that summarised both pain and quality of life data. Six examined populations with fibromyalgia<sup>36, 39-43</sup>, and one examined adults with neuropathic pain conditions<sup>37</sup>. Results from the eighth SR were reported above with the observational studies because the authors calculated study-level pooled mean change score<sup>35</sup>. For the remaining seven SRs, with the exception of Hoffman (2008)<sup>42</sup> which employed a narrative synthesis, data was assessed using meta-analysis as standardised mean difference (SMD) or study-level multivariate analysis. All studies reported data from European countries (including Austria, Germany, Italy, The Netherlands, Norway, Spain and Turkey) as well as the USA, Canada, Mexico, South American countries (notably Brazil), Israel, Asian countries and Australia.

Most of the SRs used pain measuring tools that were independent of the quality of life measure: the visual analogue scale (VAS), a numerical rating scale (NRS), the Brief Pain Inventory (BPI) and/or the Pain Rating Index of the McGill Pain Questionnaire (MPQ). The exception was Hoffman (2008)<sup>42</sup> which employed the 36-item Short Form (SF-36) Health Survey to measure both pain and QoL. Apart from Hoffman (2008), all SRs concerning fibromyalgia employed the Fibromyalgia Impact Questionnaire (FIQ) to measure the impact of the disease on quality of life as a total score and/or as individual domains. Hauser (2011)<sup>41</sup> used the Sickness Impact Profile (SIP) and the Sheehan Disability Scale (SDS) in addition to the FIQ. The EuroQoL (EQ)-5D index was used by the SRs that concerned neuropathic pain conditions<sup>37</sup>.

Study	Country	Sample size	Age	Type of pain	Pain measure	Comparator	Intervention	Pain change (intervention-comparator) (mean)	QoL measure	Sub-scale	QoL change (intervention-comparator) (mean)	Statistically significant
Bernardy 2011 <sup>36</sup>	Mexico, Spain, Norway, Netherlands, USA, Italy	Pain: 78 FIQ: 92	44-50 (range of means)	Fibromyalgia	0-10 VAS, 1-7 NRS, 0-10 NRS	usual care	Hypnosis /guided imagery	-1.17	FIQ	total	0.9	Pain-S, QoL-NS
Doth 2010 <sup>37</sup>		3824	57 (median)			placebo or usual care	duloxetine	NR	EQ-5D	total	0.09	QoL-S
		3824				placebo or usual care	spinal cord stimulation	NR	EQ-5D	total	0.22	QoL-S
		3824				placebo or usual care	ketamine	NR	EQ-5D	total	0.29	QoL-NS
D'Sylva 2010 <sup>38</sup>	NR	Pain: 112 NPQ: 94	Not reported	shoulder/neck	0-100 and 0-10 VAS, headache intensity change score	no treatment	manipulation and mobilisation	-0.34	NPQ change score (0-36)	function	0.39	NS
Hauser 2009 <sup>39</sup>	America, Europe, Asia, Australia	Pain: 4240 FIQ: 1229	48.7 (median)	Fibromyalgia	11 point pain scale: BPI, NRS, SF36 MPQ, VAS	placebo or usual care	pregabalin or gabapentin	-0.28	FIQ	total	0.3	S
Hauser 2010 <sup>40</sup>	North America, Europe, Brazil, and Turkey		45 (median)	Fibromyalgia	0-4, 0-10, 0-100 VAS and Pain Rating Index MPQ	usual care, active control or education	aerobic exercise	-0.31	FIQ	total	0.4	S
Hauser 2011 <sup>41</sup>	North America, South America, Europe	amitriptyline: 612 duloxetine: 1411 milnacipran: 4129	44.4 (mean)	Fibromyalgia	0-10 and 0-100 VAS, 0-3 NRS, MPQ, FIQ, BPI, pain electronic diary	placebo	amitriptyline	-0.43	FIQ	total	0.54	Pain-S, QoL-NS
			51 (mean)			placebo	duloxetine	-0.33	FIQ	total	0.25	S
			48.8 (mean)			placebo	milnacipran	-0.19	FIQ	total	0.18	S
Langhorst 2009 <sup>43</sup>	Austria, Turkey, Israel, Italy, Germany	Pain: 292 FIQ: 172	45 (median)	Fibromyalgia	0-10 or 0-100 VAS	usual care	Hydro-therapy	-0.78	FIQ	total	1.67	S

S = statistically significant (threshold varied, but no higher than p<0.05) for both pain change and QoL change unless stated otherwise  
NS = not statistically significant

Table 4

Summary of characteristics of observational studies

### Summary of results

Five out of nine results (from four studies) showed a statistically significant improvement in terms of both pain and QoL. Where pain was reported, intervention always reduced it and QoL always increased.

In adults with neuropathic pain conditions, from a meta-regression of RCTs, pain intensity was found to be a significant and independent study-level predictor of health utilities ( $p=0.001$ ) after adjusting for pain condition, mean age, sex, pain symptom duration and severity, the presence/absence of co-morbidities and health utility assessment method<sup>37</sup>.

While both pain and QoL outcomes were reported in the remaining SRs, the relationship between them was not examined. In those SRs that examined fibromyalgia, post-treatment pain and FIQ scores were significantly ( $p<0.001$ ) improved after 8-26 weeks of pregabalin/gabapentin treatment, although, at the latest follow-up (median 26 weeks; range 12-208 weeks), aerobic exercise had significantly improved FIQ score (SMD -0.27,  $p=0.01$ ) but no longer had a significant on pain intensity (SMD -0.18,  $p=0.08$ ). Treatment for 12 to 27 weeks with duloxetine or milnacipran resulted in significant improvement for pain ( $p<0.0001$ ) and QoL as measured by the FIQ, SIP and SDS indices (duloxetine (SMD -0.25,  $p=0.005$ ) and milnacipran (SMD -0.18,  $p<0.0001$ )) in those with fibromyalgia<sup>41</sup>. In contrast, from the same study, 4 to 26 weeks of treatment with amitriptyline resulted in a significant improvement for pain ( $p=0.008$ ) but not QoL ( $p=0.13$ ). Compared to controls, 1.5 to 3.5 weeks of hydrotherapy treatment significantly reduced pain (SMD -0.78,  $p=0.02$ ) and improved FIQ score (SMD -1.67,  $p=0.008$ ), which were both maintained up to the latest follow-up (median 14 weeks; range 6-36)<sup>43</sup>. In a narrative synthesis, Hoffman (2008)<sup>42</sup> reported that fibromyalgia

outpatients had significantly lower scores than healthy controls on all eight SF-36 health status domains, including the sub-scale Bodily Pain, and the two SF-12 physical and mental component summary scores.

### Summary of quality

After using the AMSTAR checklist<sup>47</sup> to assess methodological quality, five of the seven SRs may be considered of moderate quality in that they missed only one or two out of eleven criteria<sup>36, 39-41, 43</sup>. Hauser (2009)<sup>39</sup> did not provide an a priori design or a link to a protocol so it was difficult to determine whether the research question and inclusion criteria were established before the conduct of the review. Also, they did not check for publication bias and explicitly made the assumption that their search strategy was inclusive enough such that no RCTs concerning pregabalin or gabapentin were missed. Langhorst (2009)<sup>43</sup> also did not provide an a priori design or link to a protocol and they required studies to be published in full paper form, which lent a potential for publication bias; however, the fail-safe-N's calculations suggested that publication bias was not evident although there were too few studies to allow interpretation of the funnel plot. The quality of two publications by Hauser (2010)<sup>40</sup> and Hauser (2011)<sup>41</sup> and Bernardy (2011)<sup>36</sup> were lowered because of missing study characteristics such as duration and severity of pain and socioeconomic status. Bernardy (2011) also was missing a statement concerning conflicts of interest or lack thereof.

For the remaining two SRs, methodological quality was judged as low<sup>37, 42</sup>. For both, an a priori design or a link to a protocol was not provided, the quality of the studies was not assessed and they did not report that they checked for publication bias.

Study ID	Adequate description of study design and setting	Adequate description of eligibility criteria	Study population is representative of target population	Adequate description of outcomes (and how / how often measured), exposures, predictors	Adequate description of statistical methods	Adequate description of study participants	Adequate description of losses to follow-up (for longitudinal studies), loss to follow-up less than 10% at 12 months or less than 25% for longer follow-up	Results reported as unadjusted and confounder-adjusted including precision
Bai 2009 <sup>28</sup> /Goulia 2010 <sup>31</sup>	yes	yes	no	yes	yes	yes	na	yes
Elander 2009 <sup>29</sup>	yes	yes	yes	yes	yes	yes	na	yes
Fernandez 2010 <sup>30</sup>	yes	yes	yes	yes	no	no	na	yes
Kwok 2011 <sup>32</sup>	yes	yes	no	yes	yes	no	na	yes
Moore 2010 <sup>33</sup>	no	yes	unclear	yes	yes	no	no	no
Padua 2009 <sup>34</sup>	yes	yes	unclear	no	no	no	na	yes

Table 5

Observational studies quality (based on STROBE)

## Appendix 3 Search strategy

### Systematic reviews, guidelines and guidance

**Cochrane Database of Systematic Reviews (CDSR): 2009-2011/Issue 11**

**Database of Abstracts of Reviews of Effects (DARE): 2009-2011/Issue 4**

**Health technology Assessment Database (HTA): 2009-2011/Issue 4**

**NHS Economic Evaluation Database (NHS EED): 2009-2011/Issue 4**

**Date searched: 29.11.11**

- #1 ((Chronic\* or longterm or long term or sustained or long standing or permanent\* or intractable\* or persistent\* or unremitting or unrelenting or continual\* or continuous\* or constant\* or unending or unceasing) near (back\* or muscl\* or neck or shoulder\*) near (pain or pains or painful\* or sore\* or tender\* or discomfort or ache\* or aching or strains or strained or sprain or sprains or sprained or injur\* or damag\*)):ti,ab 1701
- #2 MeSH descriptor Diabetic Neuropathies, this term only 629
- #3 MeSH descriptor Polyneuropathies explode all trees 234
- #4 MeSH descriptor Mononeuropathies explode all trees 587
- #5 (neuropath\* or arthralg\* or neuralg\* or fibromyalg\* or DPN or mononeuropath\* or polyneuropath\* or nerve\* pain\* or cancer\* or neoplas\* or malignan\* or tumor\* or tumour\* or paraneoplas\*):ti,ab or (rheumatoid arthrit\* or osteoarthritis\*):ti,ab,kw 70584
- #6 MeSH descriptor Neoplasms explode all trees 42019
- #7 MeSH descriptor Arthritis, Rheumatoid, this term only 3471
- #8 MeSH descriptor Osteoarthritis explode all trees 2835
- #9 (#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) 83586
- #10 MeSH descriptor Pain explode all trees 28322
- #11 (pain or pains or painful\*):ti,ab 47585
- #12 (#10 OR #11) 56070
- #13 (#9 AND #12) 10824
- #14 MeSH descriptor Muscle, Skeletal explode all trees 5925
- #15 muscl\*:ti,ab 15515
- #16 (#14 OR #15) 17224
- #17 (pain or pains or painful\* or sore\* or tender\* or discomfort or ache\* or aching or strains or strained or sprain or sprains or sprained or injur\* or damag\*):ti,ab 71099
- #18 (#10 OR #17) 79023
- #19 (#16 AND #18) 4587
- #20 MeSH descriptor Chronic Disease explode all trees 9766
- #21 ((longterm or chronic\* or long term or sustained or long standing or permanent\* or intractable\* or persistent\* or unremitting or unrelenting or continual\* or continuous\* or constant\* or unending or unceasing) near (disorder\* or condition\* or illness\* or illhealth\* or ill health\* or malad\* or sickness or disease\*)):ti,ab,kw 23094
- #22 (#20 OR #21) 23094

#23 (#12 AND #22) 3213

#24 ((Chronic\* or longterm or long term or sustained or long standing or permanent\* or intractable\* or persistent\* or unremitting or unrelenting or continual\* or continuous\* or constant\* or unending or unceasing) near (pain or pains or painful\*)):ti,ab 4237 0

#25 MeSH descriptor Pain, Intractable, this term only 222

#26 MeSH descriptor Pain, Referred, this term only 8

#27 MeSH descriptor Back Pain explode all trees 2345

#28 MeSH descriptor Neuralgia explode all trees 595

#29 MeSH descriptor Neck Pain, this term only 437

#30 MeSH descriptor Arthralgia explode all trees 614

#31 MeSH descriptor Fibromyalgia, this term only 483

#32 low\* back pain\*:ti,ab,kw 4135

#33 (#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) 6496

#34 (#1 OR #13 OR #19 OR #23 OR #33) 20775

#35 (sf36 or "sf 36" or "short form 36" or "shortform 36"):ti,ab 2510

#36 ("sf thirtysix" or "sf thirty six" or "shortform thirtysix" or "shortform thirty six" or "short form thirty six" or "short form thirtysix"):ti,ab 0

#37 (sf6 or "sf 6" or "short form 6" or "shortform 6" or "sf six" or sfsix or "shortform six" or "short form six"):ti,ab 66

#38 (sf20 or "sf 20" or "short form 20" or "shortform 20" or "sf twenty" or sftwenty or "shortform twenty" or "short form twenty"):ti,ab 41

#39 (sf6D or "sf 6D" or "short form 6D" or "shortform 6D" or "sf six D" or sfsixD or "shortform six D" or "short form six D"):ti,ab 57

#40 (sf12 or "sf 12" or "short form 12" or "shortform 12" or "sf twelve" or sftwelve or "shortform twelve" or "short form twelve"):ti,ab 286

#41 (euroqol or "euro qol" or eq5d or "eq 5d"):ti,ab 621

#42 ("Time trade off" or "time tradeoff" or TTO or "Standard gamble"):ti,ab 161

#43 (hql or hrql or hqol or "h qol" or hrqol or "hr qol"):ti,ab 1109

#44 (hye or hyes):ti,ab 1

#45 (health\* near/2 year\* near/2 equivalent\*):ti,ab 2

#46 (health near/2 utilit\* near/2 ind\*):ti,ab 94

#47 (hui or hui1 or hui2 or hui3 or hui4 or "hui 4" or "hui 1" or "hui 2" or "hui 3"):ti,ab 67

#48 ("quality of well being" or "quality of wellbeing" or qwb):ti,ab 63

#49 (Disability adjusted life year\* or health adjusted life year\* or "years of healthy life" or "years of potential life lost" or "years of health life lost" or quality adjusted life year\*):ti,ab 913

#50 ((health) near/2 (state\*) near/2 (utilit\* or value\* or preference\*)):ti,ab 47

#51 (qald\* or qale\* or qtime\*):ti,ab 11

#52 (QALY\* or DALY\* or HALY\* or YHL or HYES or YPLL or YHLL or QOL):ti,ab 2959

#53 ("Brief Pain Inventory" or BPI or "FACT Bone" or "Family Pain Questionnaire" or FPQ or "Survey Regarding Pain"):ti,ab 184

#54 ((McGill near/2 Pain) or (Abbey near/2 Pain)):ti,ab 458

#55 ("Discomfort Behavior Scale" or DBS or Nottingham Health Profile\* or NHP or Sickness Impact Profile\* or SIP or WHOQOL or "Maastricht Utility Measurement" or MUMQ or "Aberdeen Back Pain"):ti,ab 729

#56 (#35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55) 8132

#57 (#34 AND #56) 1389

#58 (#57), from 2009 to 2011 367

CDSR: 12 references  
DARE: 0 references  
HTA: 0 references  
NHS EED: 0 references

#### NICE Guidance (National Institute for Health and Clinical Excellence)

<http://guidance.nice.org.uk/>  
Searched 28.11.11  
Search term: Pain  
Limits: Publication period: 01.09.2009 – 28.11.11  
Search type: Guidance  
38 references retrieved

#### Guidelines International Network (Internet)

<http://www.g-i-n.net/>  
Searched 28.11.11  
Date limit: 2009-2011

Terms searched	Hits
Chronic AND pain*	58
Pain	52
Cancer pain*	20
referred pain*	0
intractable pain*	3
phantom pain*	0
<b>Total before deduplication</b>	<b>133</b>
<b>Total after deduplication</b>	<b>113</b>

## National Guidelines Clearinghouse (Internet) 2009-2011

<http://www.guideline.gov/>

Searched 28.11.11

Advanced search

Terms searched	Hits
Chronic AND pain: limit to 2009, 2010, 2011	256
<b>Total</b>	<b>256</b>

## International Network of Agencies for Health Technology Assessment (INAHTA)

<http://www.inahta.org/>

Searched 28.11.11

Date limit: 2009-2011

Search terms	Hits
pain	17
<b>Total</b>	<b>17</b>

## Observational studies

### Medline (OvidSP) 2009/08–2011/11/wk3

Date searched: 29.11.11

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (6174)
- 2 Diabetic Neuropathies/ or exp polyneuropathies/ or exp Mononeuropathies/ or exp neoplasms/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (2709315)
- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (99897)
- 4 exp osteoarthritis/ or Arthritis, Rheumatoid/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (129683)
- 5 or/2-4 (2896176)

- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (467857)
- 7 5 and 6 (110967)
- 8 exp muscle, skeletal/ or muscl\$.ti,ab. (541861)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$).ti,ab. (1462166)
- 10 8 and 9 (71006)
- 11 chronic disease/ (207208)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (322306)
- 13 or/11-12 (322306)
- 14 13 and 6 (30590)
- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (31900)
- 16 pain, intractable/ or pain, referred/ (5394)
- 17 exp Back Pain/ (25320)
- 18 exp neuralgia/ (10979)
- 19 Neck Pain/ (3489)
- 20 exp Arthralgia/ (5828)
- 21 Fibromyalgia/ (5292)
- 22 low\$ back pain\$.mp. (17966)
- 23 or/15-22 (81089)
- 24 or/1,7,10,14,23 (237746)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (11861)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (1)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (881)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (304)
- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (262)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (1805)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (2429)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (1238)

33 (hq| or hrq| or hqol or h qol or hrqol or hr qol).ti,ab. (7075)

34 (hye or hyes).ti,ab. (50)

35 health\$ year\$ equivalent\$.ti,ab. (36)

36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (863)

37 (quality of well being or quality of wellbeing or qwb).ti,ab. (307)

38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (5192)

39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (319)

40 (qald\$ or qale\$ or qtime\$).ti,ab. (81)

41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (18253)

42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (1406)

43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (1291)

44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sickness Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (7267)

45 or/25-44 (47929)

46 24 and 45 (5706)

47 European Union/ or EU.ti,ab. (17560)

48 (Europe\$ adj3 (union or community)).ti,ab. (8574)

49 (Austria\$ or vienn\$ or austro\$).ti,ab,in,hw. (78342)

50 (Belgium or belgian\$ or Brussels or Antwerp\$ or ghent\$).ti,ab,in,hw. (108106)

51 (bulgaria\$ or sofia).ti,ab,in,hw. (15848)

52 (Cyprus or Cypriot\$ or Lefkosia or nicosia).ti,ab,in,hw. (1669)

53 (Czech\$ or prague or praha).ti,ab,in,hw. (59816)

54 (denmark or Danish or copenhagen or Aarhus).ti,ab,in,hw. (116752)

55 (Estonia\$ or Tallinn).ti,ab,in,hw. (4431)

56 (finland or finnish or finns or finn or Helsinki).ti,ab,in,hw. (93800)

57 (france or French or paris\$ or Marseille or Lyon or Toulouse or nantes or Strasbourg or lille).ti,ab,in,hw. (478495)

58 (Germany or german\$ or berlin\$ or hamburg or munich or munchen or cologne or koln or Frankfurt or Stuttgart or dusseldorf).ti,ab,in,hw. (628192)

59 (Greece or greek\$ or Athens or Athenian or Thessaloniki).ti,ab,in,hw. (79933)

60 (hungary or Hungarian\$ or Budapest).ti,ab,in,hw. (47266)

61 (Ireland or irish or Dublin\$ or eire).ti,ab,in,hw. (72041)

62 (Italy or Italian\$ or rome or roman or Milan or naples or turin).ti,ab,in,hw. (396177)

63 (Latvia\$ or riga).ti,ab,in,hw. (1900)

64 (Lithuania\$ or Vilnius).ti,ab,in,hw. (4991)

65 (Luxembourg\$ or luxemburg\$).ti,ab,in,hw. (1795)

66 (malta or maltese or Mdina or Notabile or Imdina).ti,ab,in,hw. (1446)

67 (netherland\$ or Holland or dutch or Amsterdam or Rotterdam or hague or Utrecht or Eindhoven).ti,ab,in,hw. (257657)

68 (polish or Poland or warsaw or Krakow or lodz or Wroclaw).ti,ab,in,hw. (99528)

69 (portug?ese or Portugal or Lisbon or porto).ti,ab,in,hw. (40136)

70 (Romania\$ or Bucharest).ti,ab,in,hw. (15599)

71 (Slovakia\$ or Bratislava or pozsony).ti,ab,in,hw. (12821)

72 (slovenia\$ or Ljubljana).ti,ab,in,hw. (9480)

73 (Spanish or spain or Madrid or Barcelona or Valencia or Seville or Zaragoza or Malaga or Mallorca or iberia\$).ti,ab,in,hw. (253593)

74 (Swedish or Sweden or swede\$ or Stockholm or norrland or svealand or gotaland).ti,ab,in,hw. (208162)

75 (Britain or british or wales or welsh or Scottish or scots or Scotland or England or English or Birmingham or leeds or London or Liverpool or Manchester or Glasgow or Edinburgh or Cardiff or Belfast or GB or UK or aberdeen).ti,ab,in,hw. (2764338)

76 Austria/ or Belgium/ or exp france/ or exp Germany/ or Bulgaria/ or Cyprus/ or Czech Republic/ or Denmark/ or Estonia/ or Finland/ or Greece/ or hungary/ or Ireland/ or exp Italy/ or Latvia/ or Lithuania/ or Luxembourg/ or malta/ or Netherlands/ or Poland/ or portugal/ or Romania/ or Slovakia/ or Slovenia/ or spain/ or Sweden/ or exp Great Britain/ (821907)

77 Mediterranean Islands/ or Baltic States/ (890)

78 or/47-77 (5428359)

79 46 and 78 (2610)

80 (200908\$ or 200909\$ or 20091\$ or 2010\$ or 2011\$).ed. (1869690)

81 79 and 80 (686)

82 exp animals/ not humans.sh. (3722514)

83 81 not 82 (686)

84 remove duplicates from 83 (640)

#### Medline In-Process & Other Non-Indexed Citations (OvidSP) up to 2011/11/28

#### Medline Daily Update (OvidSP) up to 2011/11/16

Date searched: 29.11.11

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (562)
- 2 Diabetic Neuropathies/ or exp polyneuropathies/ or exp Mononeuropathies/ or exp neoplasms/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (71815)

- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (4543)
- 4 exp osteoarthritis/ or Arthritis, Rheumatoid/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (4399)
- 5 or/2-4 (79695)
- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (19690)
- 7 5 and 6 (4637)
- 8 exp muscle, skeletal/ or muscul\$.ti,ab. (16940)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damage\$).ti,ab. (67711)
- 10 8 and 9 (3523)
- 11 chronic disease/ (108)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (7599)
- 13 or/11-12 (7599)
- 14 13 and 6 (523)
- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (2292)
- 16 pain, intractable/ or pain, referred/ (3)
- 17 exp Back Pain/ (8)
- 18 exp neuralgia/ (18)
- 19 Neck Pain/ (5)
- 20 exp Arthralgia/ (8)
- 21 Fibromyalgia/ (3)
- 22 low\$ back pain\$.mp. (1076)
- 23 or/15-22 (3255)
- 24 or/1,7,10,14,23 (10479)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (768)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (0)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (292)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (8)
- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (22)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (155)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (236)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (65)
- 33 (hql or hrql or hqol or h qol or hrqol or hr qol).ti,ab. (535)
- 34 (hye or hyes).ti,ab. (1)
- 35 health\$ year\$ equivalent\$.ti,ab. (1)
- 36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (70)
- 37 (quality of well being or quality of wellbeing or qwb).ti,ab. (17)
- 38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (404)
- 39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (26)
- 40 (qald\$ or qale\$ or qtime\$).ti,ab. (7)
- 41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (1367)
- 42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (113)
- 43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (71)
- 44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sickness Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (702)
- 45 or/25-44 (3853)
- 46 24 and 45 (338)
- 47 European Union/ or EU.ti,ab. (2147)
- 48 (Europe\$ adj3 (union or community)).ti,ab. (543)
- 49 (Austria\$ or vienn\$ or austro\$).ti,ab,in,hw. (4673)
- 50 (Belgium or belgian\$ or Brussels or Antwerp\$ or ghent\$).ti,ab,in,hw. (7115)
- 51 (bulgaria\$ or sofia).ti,ab,in,hw. (1025)
- 52 (Cyprus or Cypriot\$ or Lefkosia or nicosia).ti,ab,in,hw. (198)
- 53 (Czech\$ or prague or praha).ti,ab,in,hw. (3170)
- 54 (denmark or Danish or copenhagen or Aarhus).ti,ab,in,hw. (6146)
- 55 (Estonia\$ or Tallinn).ti,ab,in,hw. (348)
- 56 (finland or finnish or finns or finn or Helsinki).ti,ab,in,hw. (4508)
- 57 (france or French or paris\$ or Marseille or Lyon or Toulouse or nantes or Strasbourg or lille).ti,ab,in,hw. (33053)
- 58 (Germany or german\$ or berlin\$ or hamburg or munich or munchen or cologne or koln or Frankfurt or Stuttgart or dusseldorf).ti,ab,in,hw. (51325)
- 59 (Greece or greek\$ or Athens or Athenian or Thessaloniki).ti,ab,in,hw. (10352)
- 60 (hungary or Hungarian\$ or Budapest).ti,ab,in,hw. (2582)
- 61 (Ireland or irish or Dublin\$ or eire).ti,ab,in,hw. (9698)



- 62 (Italy or Italian\$ or rome or roman or Milan or naples or turin).ti,ab,in,hw. (27310)
- 63 (Latvia\$ or riga).ti,ab,in,hw. (145)
- 64 (Lithuania\$ or Vilnius).ti,ab,in,hw. (330)
- 65 (Luxembourg\$ or luxemburg\$).ti,ab,in,hw. (163)
- 66 (malta or maltese or Mdina or Notabile or Imdina).ti,ab,in,hw. (120)
- 67 (netherlands\$ or Holland or dutch or Amsterdam or Rotterdam or hague or Utrecht or Eindhoven).ti,ab,in,hw. (16300)
- 68 (polish or Poland or warsaw or Krakow or lodz or Wroclaw).ti,ab,in,hw. (6904)
- 69 (portuguese\$ or Portugal or Lisbon or porto).ti,ab,in,hw. (4339)
- 70 (Romania\$ or Bucharest).ti,ab,in,hw. (1092)
- 71 (Slovakia\$ or Bratislava or pozsony).ti,ab,in,hw. (644)
- 72 (slovenia\$ or Ljubljana).ti,ab,in,hw. (993)
- 73 (Spanish or spain or Madrid or Barcelona or Valencia or Seville or Zaragoza or Malaga or Mallorca or iberia\$).ti,ab,in,hw. (23058)
- 74 (Swedish or Sweden or swede\$ or Stockholm or norrland or svealand or gotaland).ti,ab,in,hw. (10159)
- 75 (Britain or british or wales or welsh or Scottish or scots or Scotland or England or English or Birmingham or leeds or London or Liverpool or Manchester or Glasgow or Edinburgh or Cardiff or Belfast or GB or UK or aberdeen).ti,ab,in,hw. (110513)
- 76 Austria/ or Belgium/ or exp france/ or exp Germany/ or Bulgaria/ or Cyprus/ or Czech Republic/ or Denmark/ or Estonia/ or Finland/ or Greece/ or hungary/ or Ireland/ or exp Italy/ or Latvia/ or Lithuania/ or Luxembourg/ or malta/ or Netherlands/ or Poland/ or portugal/ or Romania/ or Slovakia/ or Slovenia/ or spain/ or Sweden/ or exp Great Britain/ (469)
- 77 Mediterranean Islands/ or Baltic States/ (1)
- 78 or/47-77 (319728)
- 79 46 and 78 (156)
- 80 exp animals/ not humans.sh. (1559)
- 81 79 not 80 (156)
- 82 remove duplicates from 81 (156)

**Embase (OvidSP) 2009/wk36–2011/wk47**

**Date searched: 29.11.11**

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (8444)
- 2 peripheral neuropathy/ or diabetic neuropathy/ or exp polyneuropathy/ or exp mononeuropathy/ or neuropathy/ or exp neoplasm/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (3156325)

- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (125365)
- 4 exp osteoarthritis/ or rheumatoid arthritis/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (183440)
- 5 or/2-4 (3386315)
- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (790299)
- 7 5 and 6 (226573)
- 8 exp skeletal muscle/ or muscl\$.ti,ab. (568329)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$).ti,ab. (1897339)
- 10 8 and 9 (89807)
- 11 chronic disease/ (137148)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (332829)
- 13 or/11-12 (332829)
- 14 6 and 13 (34024)
- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (43179)
- 16 chronic pain/ or intractable pain/ or phantom pain/ or referred pain/ or cancer pain/ (38898)
- 17 exp backache/ (52103)
- 18 exp neuralgia/ (57048)
- 19 neck pain/ (9330)
- 20 arthralgia/ (27221)
- 21 fibromyalgia/ (10135)
- 22 low\$ back pain\$.mp. (31491)
- 23 or/15-22 (193601)
- 24 or/1,7,10,14,23 (424245)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (15780)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (1)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (1245)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (268)



- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (399)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (2487)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (3809)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (1515)
- 33 (hql or hrql or hqol or h qol or hrqol or hr qol).ti,ab. (9574)
- 34 (hye or hyes).ti,ab. (60)
- 35 health\$ year\$ equivalent\$.ti,ab. (41)
- 36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (1089)
- 37 (quality of well being or quality of wellbeing or qwb).ti,ab. (347)
- 38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (6679)
- 39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (462)
- 40 (qald\$ or qale\$ or qtime\$).ti,ab. (113)
- 41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (27180)
- 42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (2004)
- 43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (1630)
- 44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sickness Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (9785)
- 45 or/25-44 (66080)
- 46 24 and 45 (9348)
- 47 European-Union/ or EU.ti,ab. (25036)
- 48 (Europe\$ adj3 (union or community)).ti,ab,hw. (20593)
- 49 (Austria\$ or vienn\$ or austro\$).ti,ab,in,ad,hw. (155844)
- 50 (Belgium or belgian\$ or Brussels or Antwerp\$ or ghent\$).ti,ab,in,ad,hw. (211251)
- 51 (bulgaria\$ or sofia).ti,ab,in,ad,hw. (35735)
- 52 (Cyprus or Cypriot\$ or Lefkosia or nicosia).ti,ab,in,ad,hw. (3819)
- 53 (Czech\$ or prague or praha).ti,ab,in,ad,hw. (114584)
- 54 (denmark or Danish or copenhagen or Aarhus).ti,ab,in,ad,hw. (195973)
- 55 (Estonia\$ or Tallinn).ti,ab,in,ad,hw. (7509)
- 56 (finland or finnish or finns or finn or Helsinki).ti,ab,in,ad,hw. (144381)
- 57 (france or French or paris\$ or Marseille or lyon or Toulouse or nantes or Strasbourg or lille).ti,ab,in,ad,hw. (944727)
- 58 (Germany or german\$ or berlin\$ or koln or hamburg or munich or munchen or cologne or Frankfurt or Stuttgart or dusseldorf).ti,ab,in,ad,hw. (1280026)
- 59 (Greece or greek\$ or Athens or Athenian or Thessaloniki).ti,ab,in,ad,hw. (127629)
- 60 (hungary or Hungarian\$ or Budapest).ti,ab,in,ad,hw. (84158)
- 61 (Ireland or irish or eire or Dublin\$).ti,ab,in,ad,hw. (184171)
- 62 (Italy or Italian\$ or rome or roman or Milan or naples or turin).ti,ab,in,ad,hw. (747755)
- 63 (Latvia\$ or riga).ti,ab,in,ad,hw. (4133)
- 64 (Lithuania\$ or Vilnius).ti,ab,in,ad,hw. (7699)
- 65 (Luxembourg\$ or luxemburg\$).ti,ab,in,ad,hw. (4286)
- 66 (malta or maltese or Mdina or Notabile or Imdina).ti,ab,in,ad,hw. (2887)
- 67 (netherlands\$ or Holland or dutch or Amsterdam or Rotterdam or hague or Utrecht or Eindhoven).ti,ab,in,ad,hw. (448348)
- 68 (polish or Poland or warsaw or Krakow or lodz or Wroclaw).ti,ab,in,ad,hw. (184806)
- 69 (portuguese\$ or Portugal or Lisbon or porto).ti,ab,in,ad,hw. (78208)
- 70 (Romania\$ or Bucharest).ti,ab,in,ad,hw. (29066)
- 71 (Slovakia\$ or Bratislava or pozsony).ti,ab,in,ad,hw. (28224)
- 72 (slovenia\$ or Ljubljana).ti,ab,in,ad,hw. (18307)
- 73 (Spanish or spain or Madrid or iberia\$ or Barcelona or Valencia or Seville or Zaragoza or Malaga or Mallorca).ti,ab,in,ad,hw. (470566)
- 74 (Swedish or Sweden or swede\$ or Stockholm or norrland or svealand or gotaland).ti,ab,in,ad,hw. (331391)
- 75 (Britain or british or wales or welsh or Scottish or scots or Scotland or England or English or Birmingham or leeds or London or Liverpool or Manchester or Glasgow or Edinburgh or Cardiff or Belfast or UK or GB or aberdeen).ti,ab,in,ad,hw. (1483042)
- 76 Austria/ or Belgium/ or Benelux/ or france/ or exp Germany/ or Bulgaria/ or Cyprus/ or Czech-Republic/ or Denmark/ or Estonia/ or Finland/ or Greece/ or hungary/ or Ireland/ or Italy/ or Latvia/ or Lithuania/ or Luxembourg/ or malta/ or Netherlands/ or Poland/ or portugal/ or Romania/ or Slovakia/ or Slovenia/ or spain/ or Sweden/ or United-Kingdom/ (846478)
- 77 Southern-Europe/ or Scandinavia/ or Western-Europe/ or Baltic-States/ (13540)
- 78 or/47-77 (6683744)
- 79 46 and 78 (4367)
- 80 ("200936" or "200937" or "200938" or "200939" or 20094\$ or 20095\$ or 2010\$ or 2011\$).em. (2383365)
- 81 79 and 80 (1647)
- 82 animal/ or animal experiment/ (3123853)
- 83 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).mp. (4830062)
- 84 82 or 83 (4830062)
- 85 exp human/ or human experiment/ (12738143)
- 86 84 not (85 and 84) (3870815)

- 87 81 not 86 (1647)
- 88 limit 87 to embase (1499)
- 89 remove duplicates from 88 (1486)

## Intervention studies

### Medline (OvidSP) 2009/08–2011/11/wk3

Date searched: 07.12.11

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (6174)
- 2 Diabetic Neuropathies/ or exp polyneuropathies/ or exp Mononeuropathies/ or exp neoplasms/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (2709315)
- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (99897)
- 4 exp osteoarthritis/ or Arthritis, Rheumatoid/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (129683)
- 5 or/2-4 (2896176)
- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (467857)
- 7 5 and 6 (110967)
- 8 exp muscle, skeletal/ or muscl\$.ti,ab. (541861)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$).ti,ab. (1462166)
- 10 8 and 9 (71006)
- 11 chronic disease/ (207208)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (322306)
- 13 or/11-12 (322306)
- 14 13 and 6 (30590)
- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (31900)
- 16 pain, intractable/ or pain, referred/ (5394)
- 17 exp Back Pain/ (25320)
- 18 exp neuralgia/ (10979)
- 19 Neck Pain/ (3489)
- 20 exp Arthralgia/ (5828)
- 21 Fibromyalgia/ (5292)
- 22 low\$ back pain\$.mp. (17966)
- 23 or/15-22 (81089)
- 24 or/1,7,10,14,23 (237746)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (11861)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (1)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (881)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (304)
- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (262)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (1805)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (2429)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (1238)
- 33 (hql or hrql or hqol or h qol or hrqol or hr qol).ti,ab. (7075)
- 34 (hye or hyes).ti,ab. (50)
- 35 health\$ year\$ equivalent\$.ti,ab. (36)
- 36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (863)
- 37 (quality of well being or quality of wellbeing or qwb).ti,ab. (307)
- 38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (5192)
- 39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (319)
- 40 (qald\$ or qale\$ or qtime\$).ti,ab. (81)
- 41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (18253)
- 42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (1406)
- 43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (1291)
- 44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sickness Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (7267)
- 45 or/25-44 (47929)
- 46 24 and 45 (5706)

- 47 meta analysis.mp,pt. or review.pt. or search:.tw. (1842501)
- 48 46 and 47 (366)
- 49 limit 48 to yr="2005 -Current" (238)
- 50 remove duplicates from 49 (221)

SRs filter from:

Montori VM, Wilczynski NL, Morgan D, Haynes RB for the Hedges Team. Optimal search strategies for retrieving systematic reviews from MEDLINE: an analytical survey. *BMJ*. 2005 Jan 8;330(7482):68.

**Medline In-Process & Other Non-Indexed Citations (OvidSP) 2005-2011/12/06**

**Medline Daily Update (OvidSP) 2005- 2011/11/16**

**Date searched: 07.12.11**

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (582)
- 2 Diabetic Neuropathies/ or exp polyneuropathies/ or exp Mononeuropathies/ or exp neoplasms/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (74427)
- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (4667)
- 4 exp osteoarthritis/ or Arthritis, Rheumatoid/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (4570)
- 5 or/2-4 (82563)
- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (20326)
- 7 5 and 6 (4792)
- 8 exp muscle, skeletal/ or muscl\$.ti,ab. (17501)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$).ti,ab. (69893)
- 10 8 and 9 (3631)
- 11 chronic disease/ (108)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (7919)
- 13 or/11-12 (7919)
- 14 13 and 6 (542)

- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (2363)
- 16 pain, intractable/ or pain, referred/ (3)
- 17 exp Back Pain/ (8)
- 18 exp neuralgia/ (18)
- 19 Neck Pain/ (5)
- 20 exp Arthralgia/ (8)
- 21 Fibromyalgia/ (3)
- 22 low\$ back pain\$.mp. (1110)
- 23 or/15-22 (3357)
- 24 or/1,7,10,14,23 (10821)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (805)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (0)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (295)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (8)
- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (26)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (163)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (247)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (69)
- 33 (hql or hrql or hqol or h qol or hrqol or hr qol).ti,ab. (550)
- 34 (hye or hyes).ti,ab. (1)
- 35 health\$ year\$ equivalent\$.ti,ab. (1)
- 36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (72)
- 37 (quality of well being or quality of wellbeing or qwbl).ti,ab. (17)
- 38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (414)
- 39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (29)
- 40 (qald\$ or qale\$ or qtime\$).ti,ab. (7)
- 41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (1411)
- 42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (120)
- 43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (73)

- 44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sickness Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (720)
- 45 or/25-44 (3983)
- 46 24 and 45 (354)
- 47 meta analysis.mp,pt. or review.pt. or search:.tw. (18150)
- 48 46 and 47 (7)
- 49 limit 48 to yr="2005 -Current" (7)
- 50 remove duplicates from 49 (7)

SRs filter from:

Montori VM, Wilczynski NL, Morgan D, Haynes RB for the Hedges Team. Optimal search strategies for retrieving systematic reviews from MEDLINE: an analytical survey. *BMJ*. 2005 Jan 8;330(7482):68.

#### Embase (OvidSP) 2009/wk36–2011/wk48

Date searched: 07.12.11

- 1 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj3 (back\$ or muscl\$ or neck or shoulder\$) adj3 (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$)).ti,ab. (8459)
- 2 peripheral neuropathy/ or diabetic neuropathy/ or exp polyneuropathy/ or exp mononeuropathy/ or neuropathy/ or exp neoplasm/ or (cancer\$ or neoplas\$ or malignan\$ or tumo?r\$ or paraneoplas\$).ti,ab. (3161516)
- 3 (neuropath\$ or arthralg\$ or neuralg\$ or fibromyalg\$ or DPN or mononeuropath\$ or polyneuropath\$ or nerve\$ pain\$).ti,ab. (125559)
- 4 exp osteoarthritis/ or rheumatoid arthritis/ or (rheumatoid arthrit\$ or osteoarthritis).mp. (183655)
- 5 or/2-4 (3391785)
- 6 exp Pain/ or (pain or pains or painful\$).ti,ab. (791826)
- 7 5 and 6 (227086)
- 8 exp skeletal muscle/ or muscl\$.ti,ab. (568962)
- 9 exp Pain/ or (pain or pains or painful\$ or sore\$ or tender\$ or discomfort or ache\$ or aching or strains or strained or sprain or sprains or sprained or injur\$ or damag\$).ti,ab. (1900895)
- 10 8 and 9 (89958)
- 11 chronic disease/ (137284)
- 12 ((longterm or chronic\$ or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or

- continuous\$ or constant\$ or unending or unceasing) adj2 (disorder\$ or condition\$ or illness\$ or illhealth\$ or ill health\$ or malad\$ or sickness or disease\$)).mp. (333656)
- 13 or/11-12 (333656)
- 14 6 and 13 (34119)
- 15 ((Chronic\$ or longterm or long term or sustained or long standing or permanent\$ or intractable\$ or persistent\$ or unremitting or unrelenting or continual\$ or continuous\$ or constant\$ or unending or unceasing) adj2 (pain or pains or painful\$)).ti,ab. (43272)
- 16 chronic pain/ or intractable pain/ or phantom pain/ or referred pain/ or cancer pain/ (38984)
- 17 exp backache/ (52192)
- 18 exp neuralgia/ (57128)
- 19 neck pain/ (9355)
- 20 arthralgia/ (27296)
- 21 fibromyalgia/ (10163)
- 22 low\$ back pain\$.mp. (31527)
- 23 or/15-22 (193946)
- 24 or/1,7,10,14,23 (425107)
- 25 (sf36 or sf 36 or short form 36 or shortform 36).ti,ab. (15829)
- 26 (sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six or short form thirtysix).ti,ab. (1)
- 27 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab. (1246)
- 28 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab. (268)
- 29 (sf6D or sf 6D or short form 6D or shortform 6D or sf six D or sfsixD or shortform six D or short form six D).ti,ab. (401)
- 30 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab. (2499)
- 31 (euroqol or euro qol or eq5d or eq 5d).ti,ab. (3825)
- 32 (Time trade-off or time tradeoff or TTO or Standard gamble).ti,ab. (1518)
- 33 (hql or hrql or hqol or h qol or hrqol or hr qol).ti,ab. (9613)
- 34 (hye or hyes).ti,ab. (60)
- 35 health\$ year\$ equivalent\$.ti,ab. (41)
- 36 (health utilit\$ ind\$ or hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3).ti,ab. (1092)
- 37 (quality of well being or quality of wellbeing or qwb).ti,ab. (349)
- 38 (Disability adjusted life year\$ or health adjusted life year\$ or years of healthy life or years of potential life lost or years of health life lost or quality adjusted life year\$).ti,ab. (6705)

- 39 (health state\$ utilit\$ or health state\$ value\$ or health state\$ preference\$).ti,ab. (464)
- 40 (qald\$ or qale\$ or qtime\$).ti,ab. (113)
- 41 (QALY\$ or DALY\$ or HALY\$ or YHL or HYES or YPLL or YHLL or QOL).ti,ab. (27306)
- 42 (Brief Pain Inventory or BPI or FACT Bone or Family Pain Questionnaire or FPQ or Survey Regarding Pain).ti,ab. (2010)
- 43 ((McGill adj2 Pain) or (Abbey adj2 Pain)).ti,ab. (1631)
- 44 (Discomfort Behavior Scale or DBS or Nottingham Health Profile\$ or NHP or Sicknes Impact Profile\$ or SIP or WHOQOL or Maastricht Utility Measurement or MUMQ or Aberdeen Back Pain).ti,ab. (9818)
- 45 or/25-44 (66317)
- 46 24 and 45 (9368)
- 47 (meta-anal\$ or metaanal\$ or systematic review\$).mp. or (search or medline).tw. (258192)
- 48 46 and 47 (370)
- 49 limit 48 to yr="2005 -Current" (319)
- 50 limit 49 to embase (283)
- 51 remove duplicates from 50 (277)

Systematic reviews adapted from SR filter:

Wilczynski NL, Haynes RB, The Hedges Team. EMBASE search strategies achieved high sensitivity and specificity for retrieving methodologically sound systematic reviews. J Clin Epidemiol 2007;60:29-33.



