



## Evidence Summary 18-4

A Quality Initiative of the  
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

### Guidelines on Management of Pain in Cancer and/or Palliative Care

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# Guidelines on Management of Pain in Cancer and/or Palliative Care

## EVIDENCE SUMMARY

### THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC is a provincial initiative of CCO supported by the Ontario Ministry of Health and Long-Term Care (OMHLTC). All work produced by the PEBC and any associated programs is editorially independent from the OMHLTC.

### INTRODUCTION

The World Health Organization (WHO) [1] incorporates palliative care as a component of universal health coverage and urges palliative care policies integrating equitable palliative care services across all levels of care.

The WHO and the Worldwide Palliative Care Alliance [2,3] estimate that 40-60% of all deaths require palliative care, and that pain is one of the most frequent and serious symptoms. In higher income countries with aged populations, more than 60% of all deaths may require palliative care, while the proportion is lower in low/middle income countries due to higher mortality from infectious diseases and injuries. Pain relief for palliative care is considered an urgent humanitarian need.

Moderate to severe pain at the end of life is experienced in a large proportion of adult patients with cardiovascular disease (64%), cancer (84%), chronic obstructive pulmonary diseases (64%), AIDS (80%), diabetes (64%), kidney disease (50%), liver cirrhosis (34%), Alzheimer's disease and other dementias (47%), drug-resistant tuberculosis (90%), Parkinson's disease (82%), rheumatoid arthritis (89%), and multiple sclerosis (MS) (43%). These numbers vary according to geographic area and country income, with AIDS and tuberculosis much more prevalent in Africa.

### RESEARCH QUESTIONS

These research questions were developed to direct the search for clinical practice guidelines on assessment and management of pain:

- What are the most appropriate treatments for alleviation of pain in patients with cancer or in patients receiving palliative care?
- What are the most appropriate methods to assess or evaluate pain in patients with cancer or in patients receiving palliative care?

### TARGET POPULATION

Patients with cancer or other diseases requiring palliative care.

## INTENDED PURPOSE

This evidence summary was developed to assist the Patient Reported Outcomes and Symptom Management Program of CCO in revising the pain algorithm [4]. This algorithm is based on a review of guidelines until January 2009 [5], and used the Scottish Intercollegiate Guidelines Network (SIGN) 106 guideline on cancer pain [6] as its basis. The current evidence summary was also created as a source of information for the Ontario Palliative Care Network (OPCN).

## INTENDED USERS

The intended users of this evidence summary are staff of the Patient Reported Outcomes and Symptom Management Program of CCO and staff of the Ontario Palliative Care Network. This evidence summary may also be of interest to physicians, nurses, caregivers, and patients dealing with cancer or palliative care symptom management.

## METHODS

This evidence summary was developed by a Working Group at the request of the Patient-Reported Outcomes and Symptom Management program of CCO and the OPCN. The Working Group (see [Appendix A](#)) consisted of professionals with expertise in pain and palliative care (nurses and physicians) and a health research methodologist. The Working Group was responsible for reviewing the identified guidelines and drafting the summary. Conflict of interest declarations for all authors are summarized in [Appendix A](#), and were managed in accordance with the [PEBC Conflict of Interest Policy](#).

The sponsors and the Working Group agreed upon a list of diseases, in addition to cancer, for which palliative care is often required:

- Cardiovascular disease/congestive heart failure (CHF);
- Chronic obstructive pulmonary disease (COPD) ;
- Kidney failure (end-stage renal disease) ;
- Diabetes;
- HIV/AIDS ;
- Rheumatoid arthritis;
- MS;
- Stroke; and
- Neurodegenerative disease, including Parkinson's disease, amyotrophic lateral sclerosis (ALS), dementia.

This evidence summary is based on a systematic review on the topic of pain in cancer or palliative care (including the above diseases) in adults, limited to clinical practice guidelines which are based on systematic reviews of the literature.

## Literature Search Strategy

A systematic review was conducted using CINAHL on November 7, 2016 and using MEDLINE, Embase, and AMED on November 8, 2016. The search was for guidelines related to pain in cancer, palliative care, or in the diseases listed in the previous section. The search strategies are given in [Appendix B](#). Results were limited to publications since January 2009 (the date of the previous literature search).

After preliminary screening of the search results, searches were also conducted using websites of organizations related to the above diseases as identified from literature reviews or other guidelines, lists of organizations from earlier CCO symptom management guidelines,

and known cancer guideline developer websites. A list of organizations is provided in [Appendix C](#). For guidelines that appeared to have several versions, the latest version was used and earlier versions excluded. Reference lists from reviews were also used to identify guidelines. These searches were conducted December 2016 to February 2017. During data extraction and quality assessment, a few recent updates of already included guidelines were found.

### Study Selection Criteria and Process

For inclusion, publications needed to include recommendations regarding pain assessment or management in adult patients with cancer or specific diseases as listed under Methods, or undergoing palliative care. Only guidelines in English were included; guidelines with English summaries including the recommendations were considered if other details were also given and quality could be assessed. A systematic literature review had to be conducted and, where evidence was found, be the basis of the recommendations. Guidelines without a systematic review were excluded. In determining whether a systematic review was done, criteria such as an explicit statement of a systematic review along with databases searched, or databases searched plus time period, search terms, and results had to be reported. Some evidence-based guidelines included a literature search but it was unclear whether a systematic review was conducted. These guidelines were excluded at the final stage and are not in the Results tables or number of included studies; they are reported in [Appendix F](#) and some are referred to in the discussion.

It was considered outside the scope of the evidence summary to address in detail the management of patients experiencing acute adverse effects secondary to systemic therapy or radiation therapy (RT); however, chronic pain as a result of treatment was considered within scope. Guidelines dealing only with control or treatment of the disease were excluded. Also excluded were publications of clinical trials, case reports, non-systematic reviews, reviews without recommendations, or guidelines focused only on children. Guidelines focused on low/middle income countries or other resource-limited applications were also excluded. Publications focusing on headache, back pain, spinal pain, or other pain in a general population not associated with a life-limiting disease or cancer were excluded.

A review of the titles and abstracts that resulted from the search was conducted by one reviewer (GGF). For items that warranted full text review, one reviewer (GGF) reviewed each item.

### Guideline Assessment

The AGREE II is a tool to assess the quality and reporting of practice guidelines [7,8], and consists of 23 questions in 6 domains. The Rigour of Development (RoD) domain is sometimes used for an initial screening; for example, Walton et al. [9] used this domain and selected a threshold score of 50 for inclusion. This domain includes a set of questions related to the guideline development process (see headings in [Appendix G](#)) and was used in the current evidence summary. Lower marks may reflect that an item was not included in the guideline process, or that the publication(s) did not report sufficient details. When guidelines referred to other documents as part of the methods, such as separately published systematic reviews or guideline development procedures, these were considered in the evaluation. Domain scores were calculated as a percentage of the maximum possible score for that subset of questions:  $(\text{obtained score} - \text{minimum possible score}) / (\text{maximum possible score} - \text{minimum possible score})$ .

Because of the large number of guidelines, only one rater (RC) evaluated each guideline. Ratings for each question are subjective and scores may vary according to who is

conducting the rating. The scores reported, therefore, may be useful in giving a general grouping (e.g., high vs. low quality) but not an absolute ranking. Ratings were not used as a method of including or excluding guidelines from this literature review; however, as a result of internal review of the draft evidence summary it was decided to remove guidelines from the data tables if the RoD score was less than 50. These guidelines are summarized in [Appendix E](#). They may be useful to some readers, especially in cases where there are no other recent guidelines on the same topic.

## RESULTS AND DISCUSSION

### Overview

The results of the guideline search are illustrated in the flow diagram in [Appendix D](#). From the search of MEDLINE, Embase, CINAHL, and AMED there were 16,003 publications, of which 68 met the inclusion criteria. From the website searches and references in other publications there were an additional 70 publications, to give a total of 138 included publications. The guidelines applicable to pain management were divided into four major groups: (1) general pain management (not restricted to a specific disease); (2) specific to cancer pain; (3) specific cancers, provided there was at least one recommendation on pain; and (4) diseases as specified in the Methods section (other than cancer) that may require palliative care. In relation to the second research question, there were eight publications on assessment of pain. A list showing the number of publications in each category, as well as finer subcategories by disease, type of pain, or type of treatment is given in [Table 1](#). More than one publication has been included for a few guidelines, primarily when different aspects of pain assessment or management were reported separately. Results of the guideline assessment RoD are given in [Appendix G](#).

Characteristics of each guideline including the organization that created or approved the guideline, citation, and the general topic have been extracted and included in tables according to the categories in the preceding paragraph. Notes include more details of the topic and major pain concepts covered (to determine applicability), details of the systematic review including databases (an indication of how comprehensive the search was), and time period searched (indicating how recent the evidence is). These guidelines are discussed in the following sections. There is considerable overlap between some of the categories, and narrow topics may be covered in broader guidelines, although in less detail.

**Table 1. Number of Publications of Included Pain Guidelines.**

- 1. Guidelines that focus on pain (not specific to a particular disease) (32)**
  - Pain (general) (4)
  - Opioids (18)
  - Cannabinoids (2)
  - Cranial or neuro-stimulation (2)
  - Cognitive behavioural, psychological (1)
  - Neuropathic pain (3)
  - Palliative care (2)
- 2. Guidelines that focus on cancer pain (30)**
  - Cancer pain (general) (10)
  - Opioids for cancer pain, including breakthrough pain (3)
  - Complementary techniques (2)
  - Radiotherapy and bone-modifying agents for bone metastasis (10)



- Metastatic spinal cord compression (3)
- Mucositis (1)
- Palliative care or survivorship (1)
- 3. Guidelines that focus on specific cancers or issues (35)**
  - Bladder/kidney (5)
  - Breast (4)
  - Brain (1)
  - Gastric, hepatic (2)
  - Gynecologic (2)
  - Head and neck (2)
  - Hematologic (multiple myeloma) (1)
  - Lung (7)
  - Pancreas (4)
  - Prostate (7)
- 4. Guidelines that focus on specific diseases that may require palliative care (36)**
  - Cardiovascular/CHF (3)
  - Diabetes (6)
  - MS (3)
  - Neurodegenerative diseases (Parkinson's disease, ALS, dementia) (3)
  - Rheumatoid arthritis (12)
  - Stroke (4)
  - Restless leg, pressure ulcers (5)
- 5. Assessment of Pain (7)**

### Guidelines on Pain, Specific Types of Pain, or Specific Treatments

Guidelines that focus on pain, but not in relation to a specific disease, are summarized in [Table 2](#) [10-47]; there are 23 guidelines described in 29 publications [10-16,19-28,32-34,36-39,41,42,44,45,47], along with 9 supporting documents [17,18,29-31,35,40,43,46]

such as systematic reviews or methodology information. These guidelines often have recommendations for specific categories of disease, and may exclude others altogether. No guideline was identified that covered all aspects of pain. Additional guidelines meeting the inclusion criteria but with RoD scores less than 50 are summarized in [Appendix E](#).

#### General

The British Pain Society/ British Geriatrics Society guideline [10] focuses on pain in older people, and are thus of more limited scope than the current review. Cancer is mentioned in several sections. While approximately 9% of the publications found in their literature search were on the theme of palliative care, it is not discussed within the text. The guidelines by SIGN [12] on chronic pain and by Makris et al. [11] on persistent pain in elderly do not include cancer pain. The guideline by Wolff et al. [48] (see Appendix E) deals with phantom pain.

#### Opioids

Opioids appear to be the most common class of drugs for moderate to severe pain, and have the largest number of guidelines devoted to their use. Several guidelines address both cancer and other diseases. The WHO [49] and International Narcotics Control Board (INCB) [50] have noted the tension between ensuring availability and preventing abuse. The INCB reported that “the fear of drug abuse developing or spreading has led to the enactment of laws and regulations that may, in some cases, unduly impede the availability of opiates” (page 1). The WHO indicated that the “the obligation to prevent abuse of controlled



substances has received far more attention than the obligation to ensure their adequate availability for medical and scientific purposes, and this has resulted in countries adopting laws and regulations that consistently and severely impede accessibility of controlled medicines (page 16). Several of the recent guidelines focus on preventing misuse. Opioid-related deaths have had a large focus in the media in the past year, although the attention has mostly been on non-prescription (illegal) use.

The guideline by Veterans Affairs and the Department of Defense (USA) [20] is one of the most recent, but is of limited applicability for the current project. It focuses on unique needs of military members and veterans, considered a group with high risk of suicide, substance use disorders, and other medical and mental health conditions; these characteristics may make use of opioids more problematic than for other patient groups. The guideline also excludes patients receiving end-of-life care or with acute pain. Only nine key questions were updated since the previous 2010 version, and many questions and recommendations that are most relevant to the current project were deleted. There is a heavy focus on opioid misuse, and little consideration of effectiveness. Both the Center for Disease Control [21] and the Washington State Agency Medical Director's Group [22] guidelines are recent but exclude palliative care, end-of-life care, and cancer patients in active treatment. They are only of relevance to patients in clinical remission under surveillance.

The National Institute for Health and Care Excellence (NICE) guideline [13,14] focuses on the use of opioids in palliative care (adults with advanced and progressive disease including cancer), with the target audience being non-specialist healthcare professionals initiating strong opioids. Long-term opioid use is not addressed. Other identified guidelines deal with specific issues, such as methadone [16], monitoring sedation and respiratory depression when used for acute pain [15], and constipation or bowel dysfunction [19]. No guidelines were identified that cover all issues for both cancer and non-cancer patients.

There are several guidelines on opioid use for chronic non-cancer pain. They may have some relevance to other diseases, although as cancer is one of the major diseases requiring palliative care, its exclusion suggests there may be limited applicability. The guidelines by the National Opioid Use Guideline Group (Canada) [23-27], American Pain Society/American Academy of Pain Medicine [28], and the American Society of Interventional Pain Physicians (ASIPP) [32,33] are most comprehensive but do not include evidence published after 2009 (possibly up to 2012 for the ASIPP guideline). The German Pain Society guideline [34] covers postsurgical pain, diabetic neuropathy, rheumatoid arthritis and HIV. The National Pain Centre (McMaster University) guideline on opioids for chronic non-cancer pain [36] was published May 2017. This document was sponsored by Health Canada in response to revision of the National Anti-Drug Strategy, and has a focus on reduction of risks of adverse effects (including death). It excludes acute and subacute pain (less than three months), cancer pain, and end-of-life care.

### **Cannabinoids**

The National Academies of Sciences, Engineering, and Medicine (USA) 2017 report [37] indicates that cannabis or cannabinoids are effective for the treatment of chronic pain in adults and for improving MS spasticity symptoms. The authors indicate the meta-analysis by Whiting [51] was the primary source for effects on chronic pain. The American Academy of Neurology has a guideline on medical marijuana use in neurologic disorders including MS and movement disorders [38], and a guideline on complementary and alternative medicine in MS [52] which includes the use of cannabinoids for pain and spasticity. While no guidelines specifically on the use of cannabinoids for cancer pain were found, use of cannabinoids is covered in some broader cancer pain guidelines [6,53]. The College of Family Physicians of

Canada issued preliminary guidance on Authorizing Dried Cannabis for Chronic Pain or Anxiety [54], based on a non-systematic review by Kahan et al. [55].

### ***Cranial or Neurostimulation***

The European Academy of Neurology and the European Federation of Neurological Societies [39] have produced a recent guideline on central neurostimulation for chronic pain. The other major guidelines on this topic are by the Neurostimulation Appropriateness Consensus Committee of the International Neuromodulation Society (INS). These are evidence-based consensus guidelines (see Appendix F) on use of neurostimulation for pain [56-58], with additional guidelines on complications in 2017 [59-61] (see Appendix F). A group of European experts reported on the narrower topic of repetitive transcranial magnetic stimulation [62] (see Appendix E).

### ***Intraspinal/Intrathecal Analgesia***

Table 2 has no guidelines on this topic; the reader is referred to Guidelines in Appendix F. The Polyanalgesic Consensus Conference of the INS [65-67] produced consensus guidelines supported by literature searches on use of intraspinal/intrathecal analgesia. Safeguards to preventing neurologic complications when making epidural corticosteroid injections are important [68]. The American Society of Regional Anesthesia and Pain Medicine produced a guideline focusing on the delivery of neuraxial/interventional pain procedures including intrathecal analgesia in patients on antiplatelet and anticoagulant medicine [69].

### ***Cognitive Behavioural Therapy/Psychological Interventions***

The Italian Consensus Conference on Pain in Neurorehabilitation (see Appendix E) produced a guideline on use of psychological treatments and psychotherapies for pain neurorehabilitation [63].

### ***Neuropathic Pain***

Neuropathic pain Guidelines by the Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study of Pain (IASP) [41] and by NICE [42] address pharmacological management of neuropathic pain. The European Federation of Neurological Societies (EFNS) guideline [44] indicates symptoms and treatment of diabetic and non-diabetic painful polyneuropathy are similar, with the exception of HIV-induced neuropathy. Guidelines on neuropathic pain in specific diseases (diabetes, AIDS, cancer) are discussed in other sections.

### ***Headache***

No guidelines were located that met the inclusion criteria. SIGN guideline 107 [64] is relevant, but released in 2008 and is not included in the literature search results. As headache was not covered in the CCO treatment algorithm [4], this SIGN document may still be of use. The American College of Radiology (ACR) has a document on use of imaging in assessing headache [65]. Details on the literature search were not reported. This document is currently being updated, with planned completion in early 2018 (personal communication to GGF). The update is anticipated to be based on a systematic review as per current ACR methodology.

### ***Corticosteroids***

Guidelines on brain cancer and metastatic spinal cord compression ([66,67], see subsequent sections) recommend use of dexamethasone to reduce intracranial pressure, edema, and inflammation. Evidence for other applications appears limited. The guideline by

van den Beuken-van Everdingen et al. (National Guideline Working Group, The Netherlands [68]) includes a review of adjuvant analgesics in cancer pain. They make a weak recommendation that corticosteroids not be added to other analgesics for pain associated with cancer.

No other guidelines specifically on the use of corticosteroids in cancer or palliative care meeting the inclusion criteria were found. Systematic review of corticosteroids for cancer pain by Haywood et al. (Cochrane collaboration [69]) and by Paulsen et al. [70] indicated corticosteroids are frequently used to manage pain and other symptoms in patients with cancer, but conclude the evidence for efficacy of corticosteroids for pain control is weak, evidence exists for only short-term use, and adverse effects may be serious. The Therapeutic Guidelines: eTG Complete cited by Haywood et al. [69] indicates corticosteroids are used for relief of pain associated with space-occupying lesions in the liver and soft tissues (in addition to the brain and spinal cord mentioned above), being used when there may be inflammation and edema in confined spaces and prior to definitive treatment such as surgery or radiotherapy. A review by Leppert and Buss gives further background information [71]. Corticosteroids are often used for acute pain management during and after surgery [72].

Despite the limited evidence of efficacy for pain relief, corticosteroids are frequently used in palliative care. Adverse effects may include proximal myopathy, oral candidiasis, symptomatic hyperglycaemia, psychological disturbances, gastrointestinal irritation, increased susceptibility to infections, and the development of osteoporosis [69]. A retrospective study in Toronto reported 40% of patients with cancer attending a palliative care clinic received corticosteroids (dexamethasone being the most common) for appetite stimulation, fatigue, nausea, and pain [73].

A number of palliative care units and hospices have guidance on corticosteroid use [74-78]. Dexamethasone is the preferred choice in palliative care due to lower incidence of fluid retention (lack of mineralocorticoid effect), relatively high inflammatory potency (less tablets to take), long half-life, and option of subcutaneous injection. Dosage varies based on indication, with 4-8 mg/day being most often recommended for liver capsule pain or nerve compression pain [75-78], although the Northern England Clinical Networks suggests 8-16 mg/day for this use [74]. General considerations are that the lowest effective dose should be used for the shortest period of time, with discontinuation after five to seven days if no benefit. There should be monitoring for adverse effects.

### ***Palliative Care***

As indicated earlier, the WHO has released several documents [1,2,79] stressing the need for palliative care. The document on planning and implementing palliative care services [3] stresses the need for pain management, but refers the user to other guidelines for its management. Opioids are considered essential to the effective control of moderate-to-severe pain and are included on the list of essential medicines. Many guidelines refer to the WHO analgesic ladder [80,81], although there has also been significant discussion about whether it is still relevant [82-92].

Three guidelines on palliative care were found. The guideline by the Institute for Clinical Systems Improvement [47] discusses palliative care in detail, but has only a small section on pain. The NICE guideline [45] on care in the last days of life includes general principles of pain management. While it includes only pharmacological treatment, it does not provide guidance on specific drugs.

### **Guidelines on Cancer Pain**

Guidelines that focus on cancer pain are summarized in [Table 3](#) [53,67,68,93-153] and discussed in the following subsections; there are 26 guidelines described in 28 publications

[6,53,67,68,93-96,98-100,103,104,126-131,133,135-140,142,144,153], along with 35 supporting documents [97,101,102,105-125,132,134,141,143,145-152] such as systematic reviews or methodology information. Additional guidelines meeting the inclusion criteria but with RoD scores less than 50 are summarized in [Appendix E](#). Some of the guidelines included in the previous section include a section on cancer pain management, or include information on pain treatment that is relevant to a broad range of diseases. Some aspects of cancer pain, including neuropathy, pain resulting from chemotherapy, radiotherapy, or surgical treatment, and pain due to metastasis are unique and may be dealt with better in specific guidelines focusing on pain in patients with cancer.

### ***Cancer Pain (General)***

The SIGN 106 guideline [6] released in 2008 (literature search until June 2007) is the basis of the previous pain treatment algorithm. For topics with inadequate or no coverage in more recent guidelines, this guideline may be a useful reference.

Two more recent guidelines on cancer pain were located. The Royal College of Physicians National Clinical Programme for Palliative Care (Ireland) guideline [93] uses the SIGN guideline as a basis [6], and conducted a literature search for the period 2007 to January 2015. It focuses mainly on pharmacologic treatment of cancer pain. The American Society of Clinical Oncology (ASCO) guideline [53] covers literature until November 2014, although the search was limited to only the PubMed database, and appears less comprehensive. There is a focus on opioids, although non-pharmacologic interventions are also included, and therefore may complement the Royal College guideline.

Several other guidelines on cancer pain focus on specific types of pain or interventions. For the topics covered, they likely contain more in-depth guidance than exists in the general pain guidelines. Guidelines were found on visceral pain [95], use of dipyrrone [96] (not available in Canada), and use of adjuvant analgesics [68]. There is also an ASCO guideline on chemotherapy-induced peripheral neuropathy [98]. The Japanese Society for Palliative Medicine has a guideline on cancer pain [99,100]; however, the most recent version is not available in English. The guideline by Visser et al. (see Appendix E) addresses interventional techniques [154].

The WHO [155] is working on a guideline on cancer pain, with expected completion in late 2017. This may be an important guideline on this topic, although the relevance to practice in Ontario compared with a global perspective cannot be ascertained at this time.

### ***Opioids for Cancer Pain, Including Breakthrough Pain***

Several of the guidelines in the preceding section have major sections on use of opioids in cancer. For guidelines specifically on opioid use in patients with cancer, the European Association for Palliative Care (EAPC) guideline prepared by European Palliative Care Research Collaborative (EPCRC) is the most comprehensive [104]. It considers literature published up to 2009 or 2010 (depending on the question). The systematic review by Carmona-Bayonas et al. [103] is more recent (search until 2015), although with a narrow scope and without a formal guideline process. Caraceni et al. [156] have compared guidelines on management of breakthrough pain, including the relevant portion of the EAPC guideline.

### ***Cannabinoids for Cancer Pain***

No guidelines specifically on the use of cannabinoids for cancer pain were found. Reviews [157-161] may be of interest. Use of cannabinoids is covered in some broader cancer pain guidelines [6,53] and general pain guidelines (see [Table 2](#)); these contain specific recommendations for use in treating cancer pain.

### ***Complementary Techniques***

The Society for Integrative Oncology has produced recent guidelines on complementary or integrative therapies for breast cancer [128] and lung cancer [127]. The lung cancer guideline was produced for the American College of Chest Physicians. They found evidence to support use of massage, mind-body modalities, and acupuncture.

### ***Radiotherapy, Radioisotopes, and Bone-Modifying Agents for Bone Metastasis***

Treatment of pain due to bone metastasis involves unique treatments that are not part of other types of pain management. Bone metastasis appears especially common for prostate cancer (see sections later in this review), breast cancer, and lung cancer. Guidelines specifically on lung and prostate cancers are described in subsequent sections. Palliative treatments include external beam radiotherapy (EBRT), bone-modifying agents (bisphosphonates or denosumab), and radiopharmaceuticals. Metastatic spinal cord compression is considered a medical emergency with its own unique treatment and is discussed in the next subsection. The Japanese guideline (Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for Radiation Oncology, [129]) appears to cover the most different treatments (EBRT, vertebroplasty, ablation, bone-modifying agents, opioids and non-opioids, radiopharmaceuticals).

Radiation treatment (generally EBRT) is often used for both treatment and palliation in patients with bone metastasis. The American Society for Radiation Oncology (ASTRO) and Alberta Health Services guidelines on this topic are the most recent. The NICE [133] document is older and discuss radiotherapy in breast cancer metastasis.

Use of radioisotopes/radionuclides/radiopharmaceuticals is recommended in the Alberta Health Services guideline for patients not candidates of other radiotherapy. While the original guideline does not meet our criteria due to being completed before 2009, the 2015 version (delegated to Education and Information status) indicates that a search in 2013 found no new guidelines, and that almost all new randomized controlled trials were in patients with prostate cancer. A new guideline specifically on prostate cancer was developed [132].  $^{223}\text{Ra}$  has been shown to both reduce pain and improve survival in metastatic prostate cancer (see later section), although utility in other cancers is unknown. While  $^{153}\text{Sm}$  and  $^{89}\text{Sr}$  appear the most common radioisotopes (and  $^{223}\text{Ra}$  for prostate cancer), this appears to be a topic of considerable interest and several recent reviews, such as the one by Guerra Liberal et al. [162], have been published.

Bisphosphonates and denosumab reduce bone resorption and therefore reduce or delay fractures, new metastasis, and bone pain. As the effect is not immediate, other standard pain management will be necessary at the onset of bone pain. ASCO [135,136] and Cancer Australia [138] have guidelines on use of bone-modifying agents, while the older NICE guideline [133] also has a section on this. A systematic review by the EAPC [137] will be used as part of the evidence base in updating this organization's guideline on cancer pain management.

Two additional guidelines were found. The European Palliative Care Research Network /EAPC guideline [139] focuses on vertebral bone pain and gives a recommendation for use of kiphoplasty (based on weak evidence) for patients with severe and disabling back pain refractory to other therapy. The Focused Ultrasound Foundation guideline [163] (see Appendix E) discusses the use of focused ultrasound for painful bone metastases.

### ***CNS Metastases and Metastatic Spinal Cord Compression***

Approximately 5% to 10% of cancer patients will develop metastatic spinal cord compression [67]. This is considered an oncologic emergency requiring rapid diagnosis and



immediate treatment. Spinal cord damage, including nerve damage, can result in back pain and motor or sensory deficits. Corticosteroids (dexamethasone) are often an initial treatment, followed by radiotherapy and/or surgery. Radiotherapy alone may be used for symptom relief in patients unsuitable for other treatments. Metastatic spinal cord suppression is the focus of the Comité de l'évolution des pratiques en oncologie guideline from Quebec [67], as well as a topic of the Alberta Health Services [131] and Cancer Australia guidelines. A 2008 NICE guideline [140] is also on this topic; the literature search included publications up to April 2008 and an evaluation in 2012 was that it would not be updated at that time.

### ***Mucositis***

The Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology prepared a guideline on mucositis in cancer [144] based on several systematic reviews on various aspects of this topic. This is the most extensive and up-to-date guideline on this topic. Some guidelines on Head and Neck cancer (see a latter section) are also relevant.

### ***Neuropathic Pain***

The EFNS guideline [44] indicates symptoms and treatment of diabetic and non-diabetic painful polyneuropathy are similar, with the exception of HIV-induced neuropathy.

### ***Palliative Care or Survivorship***

There were no comprehensive guidelines on palliative care in patients with cancer meeting our inclusion criteria. Alberta Health Services has a guideline on narrower topic of palliative radiotherapy in patients with advanced cancer and malignancy-associated urogenital or gastrointestinal for bleeding or gastrointestinal obstruction or compression [153]. Some of the guidelines in the previous section include components of palliative care.

### ***Other Guidelines Often Used (see Appendix F)***

Both the National Comprehensive Cancer Network (NCCN [164]) and the National Cancer Institute (NCI, USA) [165] have recent guidelines on cancer pain. The NCCN also has guidelines on palliative care [166] and on survivorship [167]. The survivorship guideline devotes several pages to pain management, while the palliative care guideline primarily refers the user to the NCCN Guidelines for Adult Cancer Pain [164], and only gives a few recommendations specific to patients in the last days to weeks of life. The NCI [165] also has a recent guideline on the last days of life [168]. Pain is a minor component of this guideline. These guidelines are widely used, but are not based on explicit systematic reviews, and therefore do not meet the inclusion criteria for the current systematic review of guidelines.

### ***Guidelines on Specific Types of Cancer***

Guidelines that focus on specific types of cancer are summarized in [Table 4](#) [66,127,128,132,169-202]; there are 30 guidelines described in 32 publications [66,127,128,132,169,171-173,175-183,185,187-200,202,203], along with 6 supporting documents [170,174,184,186,201] such as systematic reviews or methodology information. Additional guidelines meeting the inclusion criteria but with RoD scores less than 50 are summarized in [Appendix E](#). Pain is often only a small component of these guidelines. However, they do stress types of pain that may be unique to cancer, or specific types or stages of cancer, and therefore not covered adequately in general pain guidelines.

**Bladder and Kidney Cancer**

The NICE guideline [169] recommends percutaneous nephrostomy or retrograde stenting if ureteric obstruction; and RT, nerve block, or palliative chemotherapy for pelvic pain. The European Association of Urology guideline on renal cell carcinoma [171,172] recommends embolization in patients with flank pain but with non-resectable disease or unfit for surgery, RT if complete surgical removal is not feasible, and RT for bone and brain metastases. The EAU guideline [204,205] on bladder cancer (see Appendix E) indicates RT or radical cystectomy may be used as palliative treatment.

**Breast Cancer**

Pain in breast cancer is often related to bone metastasis, including spinal cord compression; these topics are addressed earlier in the document. Metastasis to the brain is covered in the next section. The American Cancer Society/ASCO guideline on survivorship care [175], and the Alberta Health Services guideline on follow-up care [176] include recommendations on assessment, and on symptoms with a pain component such as neuropathy, lymphedema, musculoskeletal symptoms, and frozen shoulder.

Pain during intercourse (dyspareunia), vaginal dryness, and vulvovaginal atrophy are (premature) menopausal symptoms related primarily to use of hormonal (endocrine) therapy, although some chemotherapeutic regimens may contribute as well. These symptoms are addressed in guidelines on managing menopause by Cancer Australia [173]. The American Cancer Society/ASCO [175] and the Alberta Health Services [176] guidelines also include this topic. Systemic estrogen for symptom relief is generally contraindicated. Recommendations on use of topical (intravaginal) estrogen vary among guidelines, with guidelines by Alberta Health Services and the Society of Obstetricians and Gynecologists of Canada [206] (see Appendix F) suggesting it may be considered in cases not responding to non-hormonal options based on quality-of-life considerations and discussion of uncertain effects on breast cancer recurrence.

**Brain Cancer**

The Alberta Health Services guideline on gliomas [66] recommends use of dexamethasone for vasogenic edema and increased intracranial pressure. This is consistent with guidelines mentioned earlier on CNS metastasis and metastatic spinal cord compression. The German Society for Radiation Oncology (DEGRO)/Working Party of Gynecologic Oncology (AGO) guideline on palliative radiotherapy for brain metastases in patients with breast cancer [207] (see Appendix F) also mentions the use of dexamethasone and radiotherapy, along with pain medication and sedatives as supportive care.

**Gastric and Hepatic Cancer**

The guideline from the Korean Liver Cancer Study Group and the National Cancer Centre focuses on hepatocellular carcinoma [177], and states that dosage and intervals of analgesics must be based on liver function, and non-steroidal anti-inflammatory drugs (NSAIDs) should be used with caution. A Korean guideline on gastric cancer [178] recommends palliative RT to alleviate pain due to metastasis.

**Gynecologic Cancer**

A guideline on hyperbaric oxygen therapy by Alberta Health Services [179] recommends this treatment for late radiation tissue injury in cervical and other gynecologic cancers. The SIGN guideline on epithelial ovarian cancer [180] includes a section on pain in malignant bowel obstruction.



As the guidelines in Table 4 are not comprehensive, guidelines in Appendix F may be of interest. The WHO guideline [208] on cervical cancer is recent; however, it takes recommendations from a previous 1996 publication and notes a new guideline on cancer pain is being developed. It recommends RT as palliative therapy in very advanced/metastatic cancers, and use of national pain and palliative care guidelines, including opioids; non-pharmacological methods may supplement but not replace pharmacological methods. The Society of Obstetricians and Gynaecologists of Canada [209] suggests the use of vaginal dilators or sex for vaginal stenosis/fibrosis occurring after radiotherapy. This guideline also suggests lubricant or topically applied estrogen for atrophic vaginitis/dryness for surgically/chemically induced menopause in breast and gynecologic cancers (see also breast cancer section). The SIGN guideline on cervical cancer [203] was published in 2008 (and thus did not meet our inclusion criteria); it is consistent with the above guidelines in recommending vaginal stents/dilators, topical estrogens, and psychoeducational interventions after radiotherapy.

### ***Head and Neck Cancer***

An Italian guideline [182] focuses on pain in patients undergoing chemo-radiotherapy. As pain often persists (36% of patients still had pain after six months after the end of therapy), the guideline is considered relevant. Several of the recommendations encompass pain due to mucositis. The American Cancer Society has prepared a guideline on survivorship care [181] and includes recommendations on pain from cervical dystonia, shoulder dysfunction, and trismus.

### ***Hematologic Cancer***

The only included guideline for hematologic cancer is the NICE guideline on myeloma [183]. Interventional pain management is recommended for spinal bone disease, along with systemic pain control as described in other NICE guidelines. Radiotherapy may be used for pain relief if other measures are unsuitable or ineffective.

### ***Lung Cancer***

The ASTRO guideline is specific to palliative thoracic radiotherapy in lung cancer [190]. Several other guidelines on lung cancer also recommend palliative thoracic radiotherapy for control of symptoms [187], and palliative radiotherapy for symptomatic bone metastases [185,187-189]. Bisphosphonates [185,187,188] and radiopharmaceuticals [188] are also recommended for patients with bone metastases. These treatments are also discussed in the earlier section on bone metastases.

Both the American College of Chest Physicians guideline [185] and the Cancer Council Australia guideline [188] have recommendations on the use of pharmaceuticals for pain. The SIGN guideline refers the reader to SIGN 106 [6] for assessment and management of pain. For malignant pleural mesothelioma, the guideline by the European Respiratory Society and the European Society of Thoracic Surgeons [191] has similar recommendations as those for other lung cancers.

### ***Pancreatic Cancer***

ASCO has three recent guidelines on pancreatic cancer [192-194]. They recommend opioids, adjuvant medication for neuropathic pain (gabapentin, pregabalin, nortriptyline, duloxetine), and neurolytic celiac block. Palliative radiotherapy is also recommended in advanced or metastatic disease. The UK/Ireland Neuroendocrine Tumour Society guideline (see Appendix E) recommends radiotherapy for metastatic bone pain [210].

### **Prostate Cancer**

Several guidelines were found that focus on pain in patients with prostate cancer; they primarily discuss pain due to bone metastasis, as was covered in a previous section. The radionuclides  $^{153}\text{Sm}$ ,  $^{89}\text{Sr}$ ,  $^{186}\text{Re}$ , and  $^{223}\text{Ra}$  have been recommended for painful bone metastasis [132,196-200]. The more recent guidelines by PEBC/CCO [132], European Association of Urology/European Society for Radiotherapy & Oncology/European Society of Urogenital Radiology/International Society of Geriatric Oncology (EAU/ESTRO/ESUR/SIOG) [196], the American Urological Association [197,198], and ASCO/CCO [199] indicate that  $^{223}\text{Ra}$  has the additional benefit of improving overall survival. Several recent reviews, such as the ones by Guerra Liberal et al. [162] and Jessome [211], have been published discussing relative merits of various radioisotopes and may be useful as background information.

Docetaxel, bisphosphonates, and denosumab have also been recommended in management of bone pain. The EAU/ESTRO/ESUR/SIOG guideline recommends use of high-dose corticosteroids, surgery, and radiotherapy for spinal cord compression [196].

### **Guidelines on Diseases other than Cancer**

Guidelines on specific diseases for which patients are likely to require palliative care are summarized in [Table 5](#) [42,52,212-257]; there are 26 guidelines described in 27 publications [52,212,214,216-218,220-222,224,226,228,242-245,247-257], along with 24 supporting documents [42,213,215,219,222,223,225,227,229-241,246,258,259] such as systematic reviews or methodology information. Additional guidelines meeting the inclusion criteria but with RoD scores less than 50 are summarized in [Appendix E](#). Many of the guidelines are concerned with the management of the disease, with pain and symptom management being only a small portion. As mentioned in the exclusion criteria, guidelines covering only disease treatment were excluded.

### **Cardiovascular/Coronary Heart Failure**

The American Heart Association/American College of Cardiology (AHA/ACC) guideline on non-ST-elevation acute coronary syndromes [212] recommends sublingual nitroglycerin for patients with continuing ischemic pain in early hospital care, with intravenous nitroglycerin for persistent ischemia, and morphine sulphate intravenously if there is continued ischemic pain despite other medications. Sublingual or spray nitroglycerin is recommended for angina after discharge, with instructions to access emergency care. This is consistent with the NICE guideline for stable angina [214].

The AHA/ACC guideline [212] cautions that selective cyclooxygenase-2 (COX-2) inhibitors and other nonselective NSAIDs have been associated with increased cardiovascular risk, with greater risk in patients with established cardiovascular disease, and should only be used if other agents are ineffective. For musculoskeletal discomfort, they recommend acetaminophen, non-acetylated salicylates, tramadol, or small doses of narcotics; if these are not effective then nonselective NSAIDs such as naproxen are recommended. If there is still intolerable discomfort, then NSAIDs with increasing degrees of relative COX-2 selectivity at lowest effective dose for the shortest possible time are should be used.

A guideline on interventional pain medicine (see Appendix E) indicates spinal cord stimulation may be used for chronic refractory angina [260].

The SIGN guideline on chronic heart failure [261] indicates the prevalence of pain in patients with heart failure to be 24% to 35%. It suggests that management strategies used in other chronic pain conditions might be adapted, and refers the user to their guideline on management of chronic pain [12]. As there are no pain recommendations it is not included in the tables.

Implantable cardioverter-defibrillators (ICDs) are used to treat life-threatening cardiac arrhythmias and prevent sudden cardiac arrest. In terminally ill patients in the dying phase, repeated shocks can cause needless pain and ICD deactivation may allow a more peaceful death [262,263]. Some of the issues are discussed in the systematic review of clinical practice and provider and patient attitudes by Russo [263], and the literature review on barriers to deactivation by the Heart Rhythm Society [262]. Both cite the case of a home hospice patient in which the ICD activated 33 times and burned through the skin while the patient died in his wife's arms [264]. While the current literature review did not identify evidence-based practice guidelines, it is an issue for palliative care providers to consider.

### **Diabetes**

Neuropathy is a major issue in diabetes, with a prevalence of about 30%; up to 50% of patients with diabetes will eventually develop neuropathy [265]. This condition is often painful; diabetic neuropathic pain occurs in approximately 10% to 20% of diabetic patients, and in 40% to 60% of patients with documented neuropathy. The EFNS guideline [44] indicates symptoms and treatment of diabetic and non-diabetic painful polyneuropathy are similar, with the exception of HIV-induced neuropathy. General guidelines on neuropathic pain by NeuPSIG/IASP [41], NICE [42], and EFNS [44] as summarized in [Table 2](#) as well as the guideline on neuropathic pain in diabetes by the American Academy of Neurology<sup>1</sup> (AAN) [217] in [Table 5](#) are the most relevant.

The American Diabetes Association (ADA) recently released a 2017 update of standards of medical care in diabetes [216]. They include recommendations for prevention and assessment of neuropathy and management of pain. As the AAN guideline is the only guideline specific to painful diabetic neuropathy meeting the inclusion criteria, but covers literature only to 2008, the ADA neuropathy document may be useful for the recent literature. Two of the authors of the AAN guideline were among the authors of the ADA neuropathy document.

The NICE diabetes guideline [218] discusses management of acute painful neuropathy associated with rapid blood glucose control and refers to their neuropathic pain guideline [42] for other neuropathic pain treatment. The SIGN diabetes guideline [220] covers diabetes in general; while there is a small section on neuropathy related to foot disease, coverage of this topic is minor compared with the more specialized documents noted above. The Dutch/Belgium guideline on interventional pain medicine [221] recommends spinal cord stimulation as part of a study for patients with pain resistant to pharmacological management. For non-pharmacologic treatment, the AAN [266] recommends consideration of transcutaneous electric nerve stimulation (see Appendix E); this is noted in other guidelines as well.

### **Multiple Sclerosis**

Spasticity is a chronic symptom in MS that can cause pain, spasms, and gait disorders [267]. Spasticity may be generalized or focal/regional, and this will influence treatment. The Italian guideline on pain in neurorehabilitation [268] (see Appendix E) indicates that in addition to pain due to enhanced muscle tone, there may also be neuropathic pain secondary to CNS damage, and nociceptive pain secondary to soft tissue damage or muscle ischemia. Mixed pain syndrome should be considered. The Italian guideline covers pain and spasticity in

<sup>1</sup> This is a joint guideline by the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation; it is often referred to as the AAN guideline.

patients with upper motor neuron syndrome, such as those with MS, stroke, spinal cord injury, and cerebral palsy. Results for each research question report on spasticity, and then on pain for each disease. In patients with MS, prevalence of pain was estimated to be 50% to 63%. This guideline appears to be the most recent and comprehensive.

The NICE guideline [224] is a broader document on management of MS. It covers spasticity in less detail and does not cover pain, other than to refer the reader to NICE CG173 [42] for neuropathic pain. It indicates Sativex® (nabiximols; a prescription oromucosal spray of cannabis extract containing delta-9-tetrahydrocannabinol (THC) and cannabidiol is not recommended for cost reasons. The AAN guideline on use of complementary and alternative medicine in MS [52] found cannabinoids may be effective for spasticity and pain. This is consistent with the Spanish and German consensus guidelines summarized by Gold and Oreja-Guevara [267], and a more recent systematic review by some of the same authors [269] which recommend nabiximols (Sativex®) in patients with poor response and/or tolerance to first-line oral treatments. As noted earlier, the National Academies of Sciences, Engineering, and Medicine (USA) 2017 report [37] indicates that cannabis or cannabinoids are effective for the treatment of chronic pain in adults and for improving MS spasticity symptoms.

### ***Neurodegenerative Diseases (Parkinson's Disease, ALS, Dementia)***

A recent review on pain in neurodegenerative disease [270] suggests pain is prevalent (38-75% in Alzheimer's disease, 40% to 86% in Parkinson's disease, 19% to 85% in motor neuron diseases) but often not addressed in treatment guidelines. In patients with Parkinson's disease, pain is often classified as musculoskeletal, radicular-neuropathic, dystonic, central neuropathic, and akathisia. It is thus difficult to diagnosis and has variable response to specific treatments. The only pain assessment scale specifically for Parkinson's disease is the King's Parkinson's Diseases Pain Scale (KPPS) [271]. While it has undergone international validation, due to its recent development it has not been recommended in clinical practice guidelines.

The NICE guideline [226] on motor neurone disease has recommendations on treatment of muscle problems such as cramps, stiffness, and spasticity (which may be painful) but does not explicitly discuss pain. The EFNS guideline [272] on ALS (see Appendix E) includes recommendations for management of cramps, spasticity, and intractable pain. The Italian Consensus Conference on Pain in Neurorehabilitation guideline [273] (see Appendix E) includes recommendations on assessing and treating pain in patients with movement disorders, including those with ALS and dementia, and mentions the KPPS assessment scale.

A recent systematic review [274] covers the topic of deep brain stimulation surgeries for nonmotor symptoms in Parkinson's disease and suggests it may relieve pain, although with other potential complications.

### ***Rheumatoid Arthritis***

A multinational guideline on pain management by pharmacotherapy in inflammatory arthritis by the 3e Initiative was found [228], as well as a publication of it by the New Zealand/Australian subgroup [229]. While the literature review search was complete only until April 2010, it is the most comprehensive on this topic. Most other guidelines are on general management and include a section on pain. Guidelines by the Turkish League Against Rheumatism [244] and Haute Autorité de Santé (France) [247]) may be useful for non-drug treatments. The SIGN guideline on early rheumatoid arthritis [243] and the NICE guideline [245] covered about the same time period, although focus is on management overall. There is also a German guideline on use of radiotherapy for non-malignant disorders including arthritis [275-277] (see Appendix E).

### **Stroke**

Pain in patients who have had a stroke is mainly due to spasticity, hemiplegic shoulder pain, and central post-stroke pain. An update of the guideline by the Stroke Foundation (Australia) was released September 2017 [250]. The New Zealand guideline [251] is based on the previous 2010 version, and therefore similar age as the SIGN guideline [252]. The Heart and Stroke Foundation of Canada guideline [249] discusses the broader area of stroke rehabilitation and includes some recommendations on pain. The recent Italian guideline [268] (see Appendix E) focuses specifically on pain and spasticity in patients with stroke, MS, cerebral palsy, spinal cord injury, and other conditions associated with spasticity. Pain management recommendations are provided for each disease.

Pain in the first 30 days following acute stroke is the subject of a best practice statement by the University of Glasgow and NHS Quality Improvement Scotland [278]. The authors of this consensus document indicated that no guidelines on this narrower topic were available.

### **Chronic Obstructive Pulmonary Disease**

No guidelines meeting our inclusion criteria were found that had recommendations regarding pain. However, better control of the disease and dyspnea are likely to reduce pain.

### **Kidney Failure (End-Stage Renal Disease)**

No recent guidelines were found that are based on systematic reviews. In patients with renal disease, drug metabolism is often significantly altered and toxicity of treatments may be increased. UpToDate [279] notes that non-pharmacologic treatments are generally the same as for the general population. Pharmacologic treatment, however, must consider the severity of kidney dysfunction and risk of toxicity due to accumulation of renally excreted drugs and metabolites.

### **HIV/AIDS**

No guidelines on treatment of pain in patients with HIV/AIDS were found.

### **Other**

#### **Restless Leg Syndrome**

Restless legs syndrome (RLS, Willis-Ekbom disease) is a neurologic disorder characterized by an urge to move the legs, with worsening symptoms at rest and in the evening/at night, and accompanied by unpleasant and often painful sensation in the legs (dysesthesias) [255,280]. The risk of RLS is elevated in patients with uremia or end-stage kidney disease and in patients with peripheral neuropathy [280]. It has also been linked to Parkinson's disease, rheumatoid arthritis, MS, and diabetes [280]. Guidelines on RLS specific to these diseases were not found, although more general guidelines on RLS are expected to be applicable. Selection of pharmaceutical agent for initial treatment depends on patient and disease characteristics [255]. A systematic review on RLS in end-stage renal disease indicates dosing and scheduling should be adjusted [281].

Three guidelines on RLS [254-256] have similar recommendations, although the relative order (strength of evidence) for individual agents varies among guidelines. The International Restless Legs Syndrome Study Group guideline focuses only on long-term treatment [255]. Generally dopamine agonists (pramipexole, ropinirole, rotigotine) or  $\alpha_2\delta$  ligands (gabapentin enacarbil, pregabalin, gabapentin) are recommended for first-line therapy, with the latter group preferable for patients with comorbid pain syndrome, painful restless legs [255], or polyneuropathy [282]. Augmentation may be a problem with dopaminergic agents [254]. Oxycodone/naloxone or other opioids are recommended for patients refractory to other



treatments [254,255] and may be the most likely to have pain reduction benefit. A fourth guideline, by the American Academy of Sleep Medicine [257], appears to have used a less comprehensive literature search and recommendations are not as consistent as for the other guidelines and recent systematic reviews.

### *Pressure Ulcers*

Pressure ulcers are common in immobilized patients. A review indicates 11% of nursing home residents and 14% to 28% of patients in hospice care had pressure ulcers [283]. These may be painful, especially in advanced stages. Pressure ulcers are especially common in patients with diabetes [284]. A guideline by the National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, and the Pan Pacific Pressure Injury Alliance addresses both assessment and treatment of pain in patients with pressure ulcers [253].

### **Pain Assessment**

Guidelines on the topic of pain or symptom assessment are summarized in [Table 6](#) [285-293]; there are six guidelines [285,286,288,291-293], along with three supporting documents [287,289,290] such as systematic reviews or methodology information. Two additional guidelines are summarized in [Appendix E](#) (RoD less than 50) and [Appendix F](#).

The Breast Cancer EDGE Task Force of the American Physical Therapy Association recommends eight measures (tools) for pain assessment in patients with breast cancer. Both NeuPSIG of the IASP [286] and the EFNS have guidelines on assessment of neuropathic pain [288]. The European Palliative Care Research Collaborative/European Association of Palliative Care Research Network (EPCRC/EAPCRN) guideline on cancer pain (see Appendix E) proposes use of the Cancer Pain Assessment and Classification System [294].

Assessment of pain in non-verbal patients, including those with dementia was addressed by the Nursing Home Pain Collaborative [291]. The PAINAD and PACSLAC tools were recommended. While not a guideline, Hadjistavropoulos et al. [295] provides a more recent summary of pain experience and assessment in patients with dementia, and this document may provide important background information in the absence of other comprehensive and recent guidelines on this topic. It covers literature in MEDLINE from January 1980 to October 2014.

Two guidelines by the American Physical Therapy Association deal with assessment (including pain) using patient-reported outcomes for neck dysfunction [292] and for shoulder dysfunction [293] in patients with head and neck cancer.

Some of the more general guidelines include a section on pain assessment. For example, the Royal College of Physicians National Clinical Programme for Palliative Care (Ireland) guideline [93] includes a section on pain assessment in patients with cancer.

### **SUGGESTIONS FOR USE OF THIS REVIEW**

For purposes of updating the pain algorithm by the Patient Reported Outcomes and Symptom Management, it is suggested that the most recent comprehensive guidelines be considered first, with recommendations then supplemented or modified by recommendations in guidelines of narrower scope, but which may be more appropriate in specialized circumstances. The reader should be aware of disease-specific aspects of pain and its management.

### **INTERNAL REVIEW**

The evidence summary was reviewed by the Assistant Director and the Director of the PEBC. The Working Group was responsible for ensuring the necessary changes were made.

### **Approval by Sponsors**

After internal review, the report was presented to the Patient Reported Outcomes and Symptom Management Program of CCO and the Ontario Palliative Care. These groups reviewed the document.

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- Ruth Chau for conducting an AGREE evaluation on the included guidelines.
- Sara Miller for copy editing.



Table 2. Guidelines on Pain (Not Disease-Specific)

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Organization	Citation	Topic	Notes	AGREE RoD <sup>2</sup>
<b>General</b>				
British Pain Society/British Geriatrics Society	British Pain Society, 2013 [10]	Pain in older people	Systematic Review: PubMed and CINAHL 1997-2009; also AMED, PsycINFO, Scopus for specific topics; English only, adults over 65 years with chronic pain living in the community; search strategy and results reported	73
<b>General: non-cancer pain only</b>				
none	Makris, 2014 [11]	Persistent pain in older patients	Systematic Review: MEDLINE and Cochrane Jan 1990-May 2014, search terms reported, English only; reported review results	52
SIGN	Healthcare Improvement Scotland, 2013 [12]	Chronic non-malignant pain	Management -Systematic review: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2007-2012 -Excludes interventions delivered in secondary care, headache, children, treatment of underlying conditions	75
<b>Opioids</b>				
NICE	NICE, 2012 [13,14] [evaluated 2016]	Palliative care	Systematic Review: Cochrane reviews and RCTs, DARE, HTA, CINAHL, Embase, MEDLINE, PsycINFO, Web of Science 1950-2011; search strategy reported	71
American Society for Pain Management Nursing	Jarzyna, 2011 [15]	Acute pain: monitoring sedation and respiratory depression	Focus on hospitalized medical-surgical populations receiving opioids for acute pain (postsurgical, trauma, acute pain from medical conditions) and may not be applicable to chronic pain or end of life -Systematic review: MEDLINE to 2009 plus others for some questions(PubMed, CINAHL, Cochrane); reported search terms and outcomes for some questions	60
American Pain Society and College on Problems of Drug Dependence; Heart Rhythm Society	Chou, 2014 [16]	Methadone safety	Methadone for chronic pain and opioid addiction -Systematic reviews on MEDLINE, Cochrane, PsycINFO from their start date until Jul 2012 [17] or Jan 2014 for overdose and arrhythmia [18]	85
(10 authors from several European countries)	Muller-Lissner, 2016 [19]	Constipation, bowel dysfunction	Management of opioid-induced bowel dysfunction -Systematic Review: MEDLINE 1946-Sept 2014, Embase and Embase Classic 1947-Sept 2014, Cochrane (RCTs); search terms reported; description of search results -Level of evidence reported for statements (recommendations)	65

<sup>2</sup> AGREE II Rigor of Development sub-scale score (see Methods section and Appendix G)

# Evidence Summary 18-4

Veterans Affairs and Department of Defense (USA)	The Opioid Therapy for Chronic Pain Work Group, 2017 [20]	Chronic pain (cancer and non-cancer)	<p>Management of opioid therapy. Update of 2010 guideline.</p> <ul style="list-style-type: none"> <li>-Systematic review: MEDLINE, CINAHL, Embase, PsycINFO, DARE, HTA, Cochrane reviews and RCTs, 2009-Nov/Dec 2015; Search terms reported; evidence rated and recommendations graded; English only</li> <li>-Focus on unique needs of service members, veterans, and their families, a group with high risk of suicide, substance abuse, and other medical/mental health conditions; excludes acute pain or end-of-life care</li> <li>-Updated 9 questions from 2010 and deleted many relevant ones; heavy focus on opioid misuse and little information on effectiveness</li> <li>-Limited relevance/applicability to current evidence review</li> </ul>	71
Center for Disease Control (USA)	Dowell, 2016 [21]	Chronic pain prescribing guideline for primary care clinicians	<p>Chronic pain outside of active cancer treatment, palliative care, end-of-life care</p> <ul style="list-style-type: none"> <li>-Based on 2014 AHRQ report which included a systematic review on MEDLINE, Cochrane (RCTs and reviews), PsycINFO, CINAHL Jan 2008-Aug 2014; conducted update until Apr 2015</li> <li>-Excludes patients undergoing active cancer treatment, palliative care, or end-of-life care</li> <li>-Include cancer survivors with chronic pain in clinical remission, and are under cancer surveillance only</li> <li>-Limited relevance/applicability to current evidence review</li> </ul>	71
Washington State Agency Medical Director's Group	Washington State Agency Medical Director's Group, 2015 [22]	Prescribing opioids	<p>Includes cancer and non-cancer pain; acute and chronic</p> <ul style="list-style-type: none"> <li>-Systematic reviews: March 2014 or later using PubMed and also MEDLINE for some topics; also National Guideline Clearinghouse for guidelines on chronic non-cancer pain; starting date varied depending on topic</li> <li>-Excludes opioids for hospice and palliative care during active cancer or terminal conditions but includes chronic pain in cancer survivors</li> <li>-Limited relevance/applicability to current evidence review</li> </ul>	67
<b>Opioids: Non-cancer pain only</b>				
National Opioid Use Guideline Group (NOUGG) (Canada); National Pain Centre (McMaster)	National Opioid Use Guideline Group, 2010 [23,24]; Kahan, 2011 [25,26]; Furlan, 2010 [27]	Chronic non-cancer pain	<p>Systematic review: Cochrane RCTs, MEDLINE and Embase to 2009 (starting year varied for different searches), strategies listed</p> <ul style="list-style-type: none"> <li>-Included neuropathic pain, rheumatoid arthritis, plus others not relevant to current review</li> <li>-Excludes end-of-life and acute pain</li> <li>-Target audience is primary-care physicians and medical and surgical specialists</li> </ul>	81

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American Pain Society and American Academy of Pain Medicine	Chou, 2009 [28]	Chronic non-cancer pain	Systematic review [29]: MEDLINE, Cochrane until July 2008; see also associated documents on adverse effects [30] and research gaps [31]	85
American Society of Interventional Pain Physicians (ASIPP)	Manchikanti, 2012 [32,33]	Chronic non-cancer pain	Responsible opioid prescribing; chronic moderate to severe pain of non-cancer origin. Focus to curtail abuse of opioids without jeopardizing non-cancer pain management -Systematic Review based on multiple published reviews by ASIPP plus additional screening of over 10,000 abstracts; analysis of evidence according to US Preventive Services Task Force criteria, described guideline development process	60
German Pain Society (an S3 guideline)	Hauser, 2014 [34]	Chronic non-cancer pain	Systematic review (see AWMF manual [35]); search: CENTRAL, MEDLINE, Scopus, Oct 2008 - Oct 2013 -Diabetic polyneuropathy, rheumatoid arthritis, other polyneuropathy such as HIV, chronic postoperative pain including mastectomy	60
National Pain Centre (McMaster University, Hamilton, ON)	Busse, 2017 [36]	Chronic non-cancer pain	Systematic reviews: Embase, MEDLINE (AMED, PubMed, Cochrane, CINAHL, PsycINFO for some questions), search strategies available online <a href="http://nationalpaincentre.mcmaster.ca/guidelines.html">http://nationalpaincentre.mcmaster.ca/guidelines.html</a> ; search until 2016 (varied from May to Nov depending on question) -High level/general principles, doesn't address issues of who should receive opioids, which ones to use, etc. -Guideline for policy makers, patients, prescribers -Excludes cancer-related pain, acute or sub-acute pain (less than 3 months), pain associated with end-of-life care	77
<b>Cannabinoids (see also complementary and alternative medicine, multiple sclerosis, cancer pain)</b>				
National Academies of Sciences Engineering and Medicine (USA)	National Academies of Sciences Engineering and Medicine, 2017 [37]	Health effects	Is section on pain, with conclusion of effectiveness for chronic pain in adults, and for improving MS spasticity. -Systematic review: MEDLINE, Embase, Cochrane reviews 1999-June 2016; additional search in PsycINFO on mental health and psychosocial endpoints; additional search update until Aug 2, 2016 (see Appendix B) -Full search strategies and summary of results	65
American Academy of Neurology (Guideline Development Subcommittee)	Koppel, 2014 [38]	Neurologic disorders	Systematic review of MEDLINE, Embase, PsycINFO, Web of Science, Scopus: 1948 - Nov 2013; symptoms of MS, epilepsy, movement disorders. Search strategy reported	58
<b>Cranial or neuro-stimulation</b>				
European Academy of Neurology (EAN);	Cruccu, 2016 [39]	Central neurostimulation	Update of European Federation of Neurological Societies (EFNS) 2007 guideline [40] for neurostimulation for neuropathic pain;	69

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European Federation of Neurological Societies (EFNS)		for chronic pain	expanded to other chronic pain conditions -Systematic review: PubMed/MEDLINE, Embase, Cochrane, 2006-Dec 2014 (back to 1966 for question not included in previous guideline) -Neuropathic pain, complex regional pain syndrome, post-surgical chronic back and leg pain	
<b>Neuropathic Pain</b>				
Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study of Pain (IASP)	Finnerup, 2015 [41]	Pharmacotherapy for neuropathic pain	Systematic review: MEDLINE, PubMed, Cochrane trials, Embase 1966 until Apr 2013; additional search in PubMed and clinicaltrials.gov up to Jan 31 2014 -Neuropathic pain, including diabetic, post-amputation, post-surgical, central post-stroke, MS, cancer	65
National Institute for Health and Care Excellence (NICE)	NICE, 2013 [42]	Pharmacological management in non-specialist settings	Systematic review [43]: CINAHL, Cochrane, DARE, Embase, HEED, HTA, MEDLINE, NHS Economic Evaluations until July 2012; MEDLINE strategy, inclusion and exclusion criteria reported	90
European Federation of Neurological Societies (EFNS)	Attal, 2010 [44]	Pharmacological treatment of neuropathic pain	Systematic review: Cochrane; MEDLINE, other electronic databases including Web for questions with no top-level study in Cochrane, Jan 2005-Sept 2009. Inclusion/exclusion criteria and results reported	60
<b>Palliative Care</b>				
NICE	NICE, 2015 [45]	Dying adults in last days of life	Systematic review [46]: MEDLINE, Embase to Jan 2015; Cochrane, PsycINFO and CINAHL for specific questions. Full search strategies reported	85
Institute for Clinical Systems Improvement (ICSI)	McCusker, 2013 [47]	Palliative care for adults	Literature search July 2011 to July 2013 (earlier publications in previous editions of guideline) to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature; some search terms reported - This literature is evaluated based on the GRADE methodology by work group members -National Guidelines Clearinghouse indicates this is based on a systematic review conducted using PubMed	60

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; AWMF, German Association of Scientific Medical Societies; HEED, Health Economic Evaluations Database; HTA, Health Technology Assessment Database; NICE, National Institute for Health and Care Excellence; RCT, randomized controlled trials; RoD, Rigour of Development; SIGN, Scottish Intercollegiate Guidelines Network

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Table 3. Guidelines that Focus on Cancer Pain

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Organization	Citation	Topic	Notes	AGREE RoD <sup>3</sup>
<b>General Cancer Pain Guidelines</b>				
Royal College of Physicians National Clinical Programme for Palliative Care (Ireland)	National Clinical Effectiveness Committee, 2015 [93]	Cancer pain - pharmacological  -Includes breakthrough pain	Searched for guidelines published Nov 2008-Nov 2011 using the ADAPTE process -Systematic reviews: Cochrane reviews and RCTs, MEDLINE, CINAHL, PsycINFO June 2007-Nov 2011 and updated Jan 2015 Health questions that had already been addressed by European Association for Palliative Care/European Palliative Care Research Collaborative (EAPC/EPCRC) reviews and guideline (see opioids section ) were not included in initial searches, but were included in update search	77
American Society of Clinical Oncology (ASCO)	Paice, 2016 [53]	Chronic pain in survivors of adult cancer	Systematic review: PubMed 1995- Nov 5, 2014, searched for specific interventions (large focus on opioids; searched other specific terms by title/abstract but not indexing; includes non-pharmacologic); listed search strategy -Evaluation: search is not as comprehensive as in some other guidelines, but includes non-pharmacologic treatments that are not included in the Royal College guideline [93]; consider together with specialized guidelines and general (not cancer-specific) guidelines	94
<b>General Cancer Pain: Subset of techniques or agents</b>				
Health Quality Ontario	Health Quality Ontario, 2016 [94]	Intrathecal - cancer pain	Health technology assessment -Systematic Review: MEDLINE, Embase, Cochrane, 1994-Apr 2014; full search strategy reported	60
European Association for Palliative Care (EAPC)	Mercadante, 2015 [95]	Visceral cancer pain	Sympathetic blocks for visceral cancer pain -This work was done within the European Palliative Care Research Network(EPCRN) as part of the project to update the European Association for Palliative Care (EAPC) recommendations -Systematic review: MEDLINE, Embase, Cochrane RCTs until Feb 3 2014; search strategy provided by author (cited but inadvertently omitted from publication); results reported	63
German Guideline Program in Oncology	Gaertner, 2016 [96]	Cancer pain - Dipyrrone	Dipyrrone (metamizole, novaminsulfone) -Systematic review: MEDLINE, Embase, Cochrane 1948-Sept 27	63

<sup>3</sup> AGREE II Rigor of Development sub-scale score (see Methods section and Appendix G)

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			2012, updated to Sept 12 2013; search strategy and results reported -Withdrawn from use in Canada, USA, UK, parts of Europe, Japan, India, due to reports of potentially life-threatening agranulocytosis; but widely used (and steadily increasing) in other parts of Europe Middle East, Asia, South Africa, Latin America -Is among the most extensively used analgesics in Germany, and may be safer than NSAIDs	
National Guideline Working Group (The Netherlands)	van den Beuken-van Everdingen, 2017 [68]	Cancer pain - adjuvant analgesics	Systematic review: MEDLINE, Embase, Cochrane trials Jan 2005-May 2014; search terms reported -“Adjuvant analgesics are defined as drugs with a primary indication other than pain, but with analgesic properties under certain circumstances.” -Part of a larger Dutch guideline from 2016 on diagnosis and treatment of pain in patients with cancer [97] but not available in English	58
American Society of Clinical Oncology (ASCO)	Hershman, 2014 [98]	Cancer - neuropathy	Chemotherapy-induced peripheral neuropathy -Systematic review: MEDLINE, Embase, AMED to April 2013; search strategy and results reported	73
Japanese Society for Palliative Medicine	Yamaguchi, 2012, 2013 [99,100]	Cancer pain	Pharmacological management of cancer pain -Recommendations and short summary of development process; details including search strategy are in full guideline [101] -Systematic review: PubMed until July or Dec 2008, Cochrane (Pain, Palliative and Supportive care category); limited to drugs available in Japan -Authors note that key messages and recommendations in EAPC guideline [104] are essentially the same -Note: this is based on the 2010 version of the guideline [101]; there is now a 2014 version (Japanese only) with literature update until Dec 2012 [102]. -Evaluation: Good guideline but do not use because search only until 2008; the more recent version is not available in English. This should be reassessed if the current version is released in English.	54
<b>Opioids for cancer pain</b>				
None (7 medical/radiation oncologists in Spain)	Carmona-Bayonas, 2017 [103]	Chronic opioid therapy	Long-term cancer survivors; does not include breakthrough pain -PubMed, Embase, Cochrane, Google Scholar 1980-2015; include search terms and results -Evaluation: Primarily a systematic review with recommendations by authors; not a formal guideline process	56

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European Association for Palliative Care (EAPC); prepared by European Palliative Care Research Collaborative (EPCRC)	Caraceni, 2012 [104]	Opioids in cancer pain  -Includes section on breakthrough pain	Based on 19 published (and 3 unpublished) systematic reviews [105-123]; also an editorial about it [124] and background/method document [125] -Systematic search for guidelines: MEDLINE, CINAHL, Cochrane reviews, Embase, Google 2001-2008; English only -Systematic reviews for each question include evidence up to 2009-2010 (depending on question): MEDLINE; Embase also for most, some also used CINAHL, Cochrane	67
None (nurses in Australia and UK)	Handsaker, 2013 [126]	Transmucosal fentanyl for breakthrough pain	Used systematic review by Zeppetella et al.2011 [106] for the EAPC/EPCRC guideline for cancer pain [104]. [Searched MEDLINE until 2009 July 31; search terms and results reported. Note that the EAPC updated the search to June 2010 for the corresponding section of their guideline] -Evaluation: Do not use as it is based on same but not-updated review as used by EAPC; guideline is not by an association/guideline group	58
<b>Complementary techniques (see also breast cancer and lung cancer in Table 4)</b>				
American College of Chest Physicians guideline; it was developed for the ACCP by the Society for Integrative Oncology	Deng, 2013 [127]	Complementary, integrative: lung cancer	Complementary therapies and integrative medicine in lung cancer; see lung cancer table -Systematic review: MEDLINE, PubMed, Web of Science 2000-2011 for mind-body modalities; searched further back for exercise and for acupuncture -More limited search for massage: PubMed until 2011, reviews/meta-analyses only -Recommend mind-body modalities for acute or chronic pain; massage; acupuncture for peripheral neuropathy	88
Society for Integrative Oncology (initially USA, expanded to 29 countries)	Greenlee, 2014 [128]	Integrative therapies in breast cancer	Supportive care in breast cancer -Systematic review: Embase, MEDLINE, PubMed, CINAHL, PsycINFO, Web of Science, SCOPUS, AMED, Acutrial1990-Dec 31 2013 -Energy/sleep enhancement, massage, music therapy, physical training + mind-body modality, hypnosis, acupuncture, electro-acupuncture	79
<b>Radiotherapy and bone-modifying agents for bone metastasis (see also prostate and lung in Table 4)</b>				
Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for	Shibata, 2016 [129]	Bone metastasis	Systematic review (see methods [296]): PubMed, Cochrane, CINAHL, Japan Medical Abstracts Society, 2003-2013; search strategy on website <a href="http://www.jsmo.or.jp/about/doc/150317_GL.pdf">www.jsmo.or.jp/about/doc/150317_GL.pdf</a> -EBRT, vertebroplasty, ablation, bone-modifying agents, opioids and non-opioid, radiopharmaceuticals	56



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Radiation Oncology				
ASTRO	Lutz, 2017 [130]	Bone metastasis	Palliative radiation; update of 2011 guideline -Systematic review: PubMed, since previous search (Dec 2009) to Jan 7 2015; search terms and results reported -Focus mainly on EBRT	79
Alberta Health Services	Alberta Health Services, 2016 [131]	Palliative radiotherapy for bone metastasis, spinal cord compression	Systematic review: Original guideline in 2008, updated 2010; new search 2012 but not updated. Current version: update searched PubMed Jan 2012-Dec 2014; search strategy and results reported; additional studies after 2014 as they became available -Includes EBRT and radioisotopes <sup>89</sup> Sr, <sup>153</sup> Sa; <sup>223</sup> Ra for prostate cancer -See also spinal cord compression (next section)	65
NICE	NICE, 2009 [133]	Breast cancer, advanced	Diagnosis and treatment -Systematic review [134]: MEDLINE, Embase, Cochrane, CINAHL, AMED, etc. until June 30 2008. Evaluated 2012; lymphedema section updated in 2014: MEDLINE until Oct 2013 -Bisphosphonates + RT for bone metastasis	77
ASCO	Van Poznak, 2011 [135] Focused update submitted [136]	Breast cancer, metastatic	Bone-modifying agents -Systematic review: MEDLINE and Cochrane 2003 to July 15 2009	71
European Association for Palliative Care	Porta-Sales, 2016 [137]	Bone metastasis	Analgesic role of bisphosphonates and denosumab -Systematic review: MEDLINE, Embase, Cochrane until Jan 31 2014; reported search terms (though may be too restrictive); reported results -This review will be one of those used to update EAPC guidelines on cancer pain management	60
Cancer Australia	Cancer Australia, 2011 [138]	Breast cancer, advanced	Use of bisphosphonates -Systematic review: Cochrane review and separate review for more recent literature until April 2010 -Bone pain	65
European Palliative Care Research Network, European Association of Palliative Care (EAPC)	Mercadante, 2016 [139]	Vertebral bone pain	Minimally invasive procedures for management of vertebral bone pain -Systematic review: MEDLINE, Embase, Cochrane trials searched to 3 February 2015; search terms not reported but gave inclusion criteria; results were reported	56
<b>Metastatic Spinal Cord Compression</b>				
Alberta Health Services	Alberta Health Services, 2016 [131]	Palliative radiotherapy for bone	Systematic review: Original guideline in 2008, updated 2010; new search 2012 but not updated. Current version: update searched PubMed Jan 2012-Dec 2014; search strategy and results reported;	65

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		metastasis, spinal cord compression	additional studies after 2014 as they became available -Includes EBRT and radioisotopes <sup>89</sup> Sr, <sup>153</sup> Sa, <sup>223</sup> Ra for prostate cancer -See also bone metastasis (previous section)	
Comité de l'évolution des pratiques en oncologie (CEPO), Quebec	L'Esperance, 2012 [67]	Metastatic spinal cord compression	Treatment -Systematic review: PubMed until Feb 2011; search terms reported, results reported. -Dexamethasone, then surgery ± RT	54
NICE	NICE, 2008 [140]	Metastatic spinal cord compression	Reviewed 2012 but decided not to update -Risk assessment, diagnosis and management -Systematic Review as separate document [141] -MEDLINE, Embase, Cochrane, CINAHL, BNI, PsycINFO, SIGLE, Web of Science, ISI proceedings, Biomed Central: search until 2007 and updated to April 2008; search strategy and results reported	79
Cancer Australia	Cancer Australia, 2014 [142]	CNS metastases in secondary breast cancer	Systematic review: MEDLINE, Embase, PubMed Jan 2001-April 2012; search strategy reported in separate publication of the systematic review [143]; results reported -Spinal cord compression: dexamethasone, surgery ± RT	67
<b>Mucositis, Oral or Gastrointestinal</b>				
Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO)	Lalla, 2014 [144]	Mucositis in cancer	Mucositis secondary to cancer therapy, based on several systematic reviews [145-150]; method described separately [151,152]	79 <sup>4</sup>
<b>Palliative care or survivorship</b>				
Alberta Health Services	Alberta Health Services, 2016 [153]	Palliative radiotherapy for bleeding and gastrointestinal obstruction	-Palliative oncology patients with advanced cancer and malignancy-associated urogenital or gastrointestinal bleeding or gastrointestinal compression or obstruction -Systematic review: PubMed Jan 2012 (since previous version) to Sept 2014; search strategy and results reported	63

Abbreviations: ASTRO, American Society for Radiation Oncology; EBRT, external beam radiation therapy; NICE, National Institute for Health and Care Excellence; RT, radiation therapy

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<sup>4</sup> Original rating was 48, however this was revised to 79 by a second rater. The original score may not have taken into account additional information in accompanying methods documents and systematic reviews which were the foundation for the guideline.

Table 4. Guidelines on Specific Cancers which Include Pain Recommendations

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Organization	Citation	Topic	Notes	AGREE RoD <sup>5</sup>
<b>Bladder/Kidney</b>				
NICE	NICE, 2015 [169]	Bladder cancer	Diagnosis and management -Percutaneous nephrostomy or retrograde stenting if ureteric obstruction; RT, nerve block, or palliative chemotherapy for pelvic pain -Systematic review posted separately [170]: Cochrane, MEDLINE, Embase, Web of Science (CINAHL, AMED, PsycINFO for some topics) until June 2014	92
European Association of Urology	Ljungberg, 2016, 2017 [171,172]	Renal cell carcinoma	Embolization in patients with flank pain but with non-resectable disease or unfit for surgery -RT to bone and brain metastases -RT if complete surgical removal is not feasible -Systematic Review: MEDLINE, Embase, Cochrane 2013-July 30 2015; limited update on website version until June 30 2016, search strategy given	54
<b>Breast (see also RT/bone-modifying agents, complementary techniques, spinal cord compression in Table 3; brain cancer in this table)</b>				
Cancer Australia	Cancer Australia, 2016 [173]	Breast cancer	Management of menopausal symptoms -Pain during intercourse (dyspareunia); dryness and vaginal atrophy -Systematic review: PubMed, MEDLINE, Embase, PsycINFO, CINAHL, Cochrane 2001-Nov 2015; full details in separate report [174]	69
American Cancer Society / ASCO	Runowicz, 2016 [175]	Breast cancer	Survivorship care -Musculoskeletal symptoms, joint and muscle pain, neuropathy, sexual health, lymphedema, frozen shoulder -Systematic review: PubMed through April 2015 -For sexual health in text includes dilators and pelvic floor relaxation exercise; estrogen if not on AI; against estrogen if on AIs. These are not mentioned in actual recommendation	77
Alberta Health Services	Alberta Health Services, 2015 [176]	Breast cancer, early	Follow-up care -Includes assessment, neuropathy, painful intercourse, lymphedema -Systematic search: MEDLINE, Embase 2001-Sept 2011; terms	65

<sup>5</sup> AGREE II Rigor of Development sub-scale score (see Methods section and Appendix G)

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			given; refers to “Guideline Resource Unit Handbook” for methodology [297] [this refers to “Guideline Development Literature Searching Checklist”; a copy was requested and received from GURU]	
Society for Integrative Oncology (initially USA, expanded to 29 countries)	Greenlee, 2014 [128]	Integrative therapies in breast cancer	Supportive care in breast cancer (also see Complementary Techniques in Table 3) -Systematic review: Embase, MEDLINE, PubMed, CINAHL, PsycINFO, Web of Science, SCOPUS, AMED, Acutrial1990-Dec 31 2013 -Energy/sleep enhancement, massage, music therapy, physical training + mind-body modality, hypnosis, acupuncture, electro-acupuncture	79
<b>Brain</b>				
Alberta Health Services	Alberta Health Services, 2014 [66]	Gliomas	Use of dexamethasone for vasogenic edema and increased intracranial pressure. -Systematic review: MEDLINE, PubMed, Cochrane reviews, CINAHL to Nov 2012; search terms given. Also searched guideline websites	69
<b>Gastric, Hepatic</b>				
Korean Liver Cancer Study Group and the National Cancer Center, Korea	Park, 2015 [177]	Hepatocellular carcinoma	Systematic review: MEDLINE up to 2014, search terms given, evidence graded -EBRT -Dosage and intervals of analgesics (including opioids) must be based on liver function; use NSAIDs with caution; lower the dose of acetaminophen	60
Several professional organizations <sup>6</sup>	Lee, 2014 [178]	Gastric cancer	Gastric cancer in Korea -Systematic review: PubMed, MEDLINE, Cochrane, KoreaMed 1980-2011 -Palliative RT to alleviate symptoms including pain due to metastasis	63
<b>Gynecologic, Cervix</b>				
Alberta Health Services	Alberta Health Services, 2009 [179]	Cervical; other gynecologic	Hyperbaric oxygen therapy for late radiation tissue injury -Systematic review: MEDLINE, Embase, Cochrane 1965-June 25, 2009	54

<sup>6</sup> Korean Academy of Medical Sciences, the Korean Association of Internal Medicine, the Korean Society for Radiation Oncology, the Korean Society of Pathologists, the Korean College of Helicobacter and Upper Gastrointestinal Research, the Korean Society of Gastrointestinal Endoscopy, the Korean Society of Gastroenterology, the Korean Cancer Association, the Korean Society of Radiology, the Korean Gastric Cancer Association, and the Korean Society of Nuclear Medicine, along with the participation of experts in the guideline development methodology

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SIGN	Healthcare Improvement Scotland, 2013 [180]	Epithelial ovarian cancer	Management. Version modified May 2014 Systematic review: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2003-2012 -Pain in malignant bowel obstruction	71
<b>Head and Neck</b>				
American Cancer Society	Cohen, 2016 [181]	Head and neck cancer	Survivorship care -Systematic review: PubMed to April 2015 -Cervical dystonia, neuropathy, shoulder dysfunction, trismus	75
(Italian multidisciplinary group of head and neck cancer specialists)	Mirabile, 2016 [182]	Pain in head and neck cancer	Patients undergoing chemo-radiotherapy; consensus recommendations based on systematic review -Systematic review: MEDLINE 1994- March 2013, terms given -Recommendations primarily (but not only) on mucositis	50
<b>Hematologic</b>				
NICE	NICE, 2016 [183]	Multiple myeloma	Diagnosis and management -Systematic review published separately [184]: MEDLINE, Cochrane, Embase, Web of Science; CINAHL, PsycINFO, AMED for some topics, until June 8 2015 -RT if others not effective -Interventional pain management for spinal bone disease, along with systemic pain control as in other NICE guidelines on opioids in palliative care (CG140) and on neuropathic pain (CG173) -Bisphosphonates recommended, though not specifically for pain [use is not covered in detail and other guidelines need to be referred to for this topic]	90
<b>Lung</b>				
American College of Chest Physicians	Simoff, 2013 [185]	Lung cancer	Symptom management -Systematic review (more detailed methodology published separately [186]: MEDLINE, CINAHL, PsycINFO, Cochrane, Embase, Web of Science, Google Scholar; searches until 2012 (based on date of included articles) and extended back more than 10 years (stated in methodology) -Assessment; pharmaceuticals for chronic pain; RT, bisphosphonates, surgery for pain due to bone metastasis; dexamethasone, surgery, RT for brain metastasis	73
SIGN	Healthcare Improvement Scotland, 2014 [187]	Lung cancer	Management -Systematic review: MEDLINE, Embase, CINAHL, PsycINFO and the Cochrane Library 2005-2012 -Palliative RT if not suitable for radical RT -Bisphosphonates for symptomatic bone metastases -See SIGN 106 for assessment and management of pain	75

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American College of Chest Physicians guideline; it was developed for the ACCP by the Society for Integrative Oncology	Deng, 2013 [127]	Complementary, integrative: lung cancer	Complementary therapies and integrative medicine in lung cancer; also see Complementary Techniques in Table 3 -Systematic review: MEDLINE, PubMed, Web of Science 2000-2011 given for mind-body modalities; searched further back for exercise and for acupuncture -More limited search for massage: PubMed until 2011, reviews/meta-analyses only -Recommend mind-body modalities for acute or chronic pain; massage; acupuncture for peripheral neuropathy	56
Cancer Council Australia	Cancer Council Australia, 2012 [188]	Lung cancer	Treatment -Document on Wiki in sections; cannot download or search full document -Systematic review: in different appendix for each question -Palliative care section: Cochrane Library, PubMed, Embase up to 2011 and monthly updates until Dec 2014, excluded RT, postoperative pain; recommends bisphosphonates and radiopharmaceuticals for multiple bony metastasis and NSAIDs and opioids for pain in NSCLC; psychological interventions -Palliative RT for bony metastasis in metastatic NSCLC: Embase search to April 2011 then monthly updates until Feb 2015	85
NICE	NICE, 2011 [189]	Lung cancer	Diagnosis and management -Systematic review: Cochrane, MEDLINE, Embase, CINAHL, AMED, British Nursing Index, PsycINFO, Web of Science, Sci-expanded, Social Sciences Citation Index, Biomed Central until August 2010 -Radiotherapy for palliation of bone metastasis if standard analgesic treatments are inadequate (not updated since 2005 version) -A surveillance report in 2016 resulted in a plan to conduct a partial update; for the topic of palliative radiotherapy new evidence was identified but not thought to have an effect on current recommendations	81
American Society for Radiation Oncology (ASTRO)	Rodrigues, 2011 [190]	Lung cancer	Palliative radiotherapy -Systematic review: PubMed 1966-March 2010	56
European Respiratory Society and the European Society of Thoracic Surgeons	Scherpereel, 2010 [191]	Malignant pleural mesothelioma	Management -Systematic review: MEDLINE, Embase, 1990-2009; chemotherapy only 1965-2009, reported search terms but not results -Assessment, follow principles of cancer pain management, opioids + adjunct analgesia, palliative RT,	52

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<b>Pancreatic</b>				
ASCO	Sohal, 2016 [192]	Pancreatic cancer, metastatic	Treatment. Includes questions on pain -Systematic review: PubMed, Cochrane Jan 2000-June 2015 -Opiate medication; adjuvant medications such as gabapentin, pregabalin, nortriptyline, duloxetine for neuropathic pain; palliative RT or chemotherapy; interruption of neural pathways in the celiac plexus	88
ASCO	Balaban, 2016 [193]	Pancreatic cancer, locally advanced unresectable	Treatment. Includes questions on pain -Systematic review: MEDLINE and Cochrane Jan 2000-June 2015 -Aggressive treatment of pain; palliative RT; opiate medication; adjuvant medications such as gabapentin, pregabalin, nortriptyline, duloxetine for neuropathic pain; neurolytic celiac block	88
ASCO	Khorana, 2016 [194]	Pancreatic cancer, potentially curable	Potentially curative therapy (paragraph on aggressive pain management) -Systematic review: MEDLINE and Cochrane, Jan 2002-June 2015 -Opiate medication; adjuvant medications such as gabapentin, pregabalin, nortriptyline, duloxetine for neuropathic pain; neurolytic celiac block	90
<b>Prostate</b>				
EAU - ESTRO - ESUR - SIOG	Mottet, 2017 [196]	Prostate cancer	Diagnosis, management, follow-up -Comprehensive literature search: systematic reviews to update specific questions, other systematic reviews ongoing for next revision -MEDLINE (1946-March 2015), Embase (1974-2015), Cochrane (2005-April 2015). 2017 version online only; 2016 version [195] can be downloaded -Painful bone metastases: external beam RT, radionuclides, analgesics -High-dose corticosteroids, surgery, RT for spinal cord compression - <sup>223</sup> Ra, bisphosphonates, denosumab for pain from bone metastasis	65
PEBC/CCO	Alibhai, 2016 [132]	Prostate cancer: bone health	Bone health and bone-targeted therapies Systematic review: MEDLINE, Embase to Jan 2016 + Cochrane reviews -Radiopharmaceuticals: <sup>223</sup> Ra for survival and pain; <sup>89</sup> Sr, <sup>153</sup> Sm, <sup>186</sup> Re for bone pain (no guidance on which to use, though) -Bisphosphonates or denosumab for bone pain	88



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American Urological Association (AUA)	Lowrance, 2016 [197]; Cookson, 2015 [198]	Prostate cancer: castration resistant	Systematic review: MEDLINE, Embase, Cochrane, Scopus original 1996-2013, updated 2013-Feb 2015 -Radionuclide therapy with <sup>153</sup> Sm, <sup>89</sup> Sr, <sup>223</sup> Ra for pain due to bone metastasis -Docetaxel as first line therapy and palliative benefit for bone pain -Mitoxantrone	71
ASCO/CCO	Basch, 2014 [199]	Prostate cancer: metastatic + castration-resistant	Systemic therapy -Based on systematic review by CCO (MEDLINE and Embase 2003-June 2012) and updated on MEDLINE June 2012-June 2013 - <sup>223</sup> Ra for bone pain	90
NICE	NICE, 2014 [200]	Prostate cancer	Diagnosis and management -Systematic review [201]: MEDLINE, Embase, Web of Science, Cochrane, SSCI, SIGLE, Biomed Central until May 2013 -Bisphosphonates, <sup>89</sup> Sr for bone pain	85
Cancer Council Australia	Cancer Council Australia, 2010 [202]	Prostate cancer: locally advanced or metastatic	Management -Systematic review: MEDLINE, Embase, CINAHL, Cochrane, Clinical Evidence, PsycINFO until April 2006 -Note: while the document was published in 2010, the evidence is 4 years older	63

Abbreviations: AI, aromatase inhibitor; ASCO, American Society of Clinical Oncology; CCO, Cancer Care Ontario; EAU, European Association of Urology; ESTRO, European Society for Radiotherapy & Oncology; NICE, National Institute for Health and Care Excellence; NSAIDs, non-steroidal anti-inflammatory drugs; NSCLC, non-small cell lung cancer; PEB, Program in Evidence-Based Care; RT, radiation therapy; SIGN, Scottish Intercollegiate Guidelines Network; SIOG, International Society of Geriatric Oncology

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Table 5. Guidelines on Diseases Requiring Palliative Care

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Organization	Citation	Topic	Notes	AGREE RoD <sup>7</sup>
<b>Cardiovascular/CHF</b>				
American Heart Association/American College of Cardiology (AHA/ACC)	Amsterdam, 2014 [212]	Non-ST-elevation acute coronary syndromes	<p>Management</p> <ul style="list-style-type: none"> <li>-Systematic review (see [213] for methodology): MEDLINE, Embase, Cochrane, AHRQ reports until October 2012 and some select references until Apr 2014; some search terms reported</li> <li>-Focused mostly on diagnosis and treatment</li> <li>-Sublingual nitroglycerin for patients with NSTEMI-ACS with continuing ischemic pain, IV nitroglycerin for persistent ischemia, HF, hypertension</li> <li>-IV morphine sulphate for continued ischemic chest pain despite maximally tolerated anti-ischemic medication</li> </ul> <p>After discharge</p> <ul style="list-style-type: none"> <li>-For musculoskeletal discomfort: a) acetaminophen, non-acetylated salicylates, tramadol, small doses of narcotics; b) if not effective then use nonselective NSAIDs such as naproxen; c) NSAIDs with increasing degrees of relative COX-2 selectivity at lowest effective dose for shortest possible time if still intolerable discomfort</li> </ul>	67
NICE	NICE, 2011 [214]	Stable angina	<p>Management</p> <ul style="list-style-type: none"> <li>-Systematic review [215]: MEDLINE, Embase, Cochrane, CINAHL until 22 Oct 2010; PsycINFO, AMED for some questions, search strategies reported</li> <li>-Short-acting nitrate for preventing and treating episodes of angina; call emergency/ambulance if pain persists</li> </ul>	81
<b>Diabetes</b>				
American Diabetes Association	American Diabetes Association, 2017 [216]	Standards of care	<p>Systematic review (indicates that the ADA adheres to the Institute of Medicine Standards for Developing Trustworthy Clinical Practice Guidelines): MEDLINE, articles published since Jan 1 2016 (this is a yearly update; older material in previous versions)</p> <ul style="list-style-type: none"> <li>-Chapter 10 includes neuropathy</li> </ul>	56

<sup>7</sup> AGREE II Rigor of Development sub-scale score (see Methods section and Appendix G)

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American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation	Bril, 2011 [217]	Painful diabetic neuropathy	Systematic review: MEDLINE, Embase until August 2008; search terms and results reported	50
NICE	NICE, 2015 [218]	Type 1 diabetes	Diagnosis and management -Systematic review [219]: MEDLINE, Embase, Cochrane until 28 Aug 2014, full search strategy reported -Recommendations on managing acute painful neuropathy associated with rapid blood glucose control -Refers to neuropathic pain guideline NICE, 2013 [42]	83
SIGN	Healthcare Improvement Scotland, 2013 [220]	Diabetes	Management -Systematic review: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2003-2009; search strategy online <a href="http://www.sign.ac.uk/pdf/sign116strategy.pdf">www.sign.ac.uk/pdf/sign116strategy.pdf</a> -Is a 2010 document with minor revisions (not on pain) in 2013 -Focus on neuropathy related to foot disease (neuropathy only small portion of guideline, and therefore not as thorough as some of the others)	69
(Based on Dutch/Belgium guidelines and then revised with additional pain specialist from USA)	Pluijms, 2011 [221]	Painful diabetic neuropathy	Chapter in book "Evidence-Based Interventional Pain Medicine according to Clinical Diagnoses". Methodology in the introduction [222] -Systematic reviews: PubMed, literature update to 2010 -Pharmacological discussion based on non-current versions of guidelines -Recommends spinal cord stimulation as part of a study for patients with pain resistant to pharmacological management	54
<b>Multiple Sclerosis</b>				
American Academy of Neurology	Yadav, 2014 [52]	Complementary and alternative medicine (CAM)	Systematic review (see methods manual [258]): MEDLINE, Web of Science, Embase, Cochrane, Allied and Complementary Medicine 1970 - March 2011. -Pragmatic (non-systematic) MEDLINE search March 2011 - Sept 2013; details in online data supplement <a href="http://www.neurology.org/content/82/12/1083/suppl/DC1">http://www.neurology.org/content/82/12/1083/suppl/DC1</a> . Search strategy for MEDLINE reported, relies heavily on index/MESH terms; main search only until 2009, does not	54

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			include separate terms for cannabinoids; search results reported -Oral cannabis extract, tetrahydrocannabinol, Sativex or mucosal cannabinoid spray for spasticity and pain -Letter by Wright et al. [223] states Sativex is a prescription product evaluated in RCTs and not CAM	
NICE	NICE, 2014 [224]	Management	Systematic review [225]: MEDLINE, Embase, Cochrane until Feb 2014; search strategy reported -Refer to NICE CG173 [42] for neuropathic pain; no other pain recommendations -Spasticity: baclofen and/or gabapentin (first line), tizanidine or dantrolene (2 <sup>nd</sup> line), benzodiazepines (3 <sup>rd</sup> line)	83
<b>Neurodegenerative Diseases (Parkinson's disease, ALS, dementia)</b>				
NICE	NICE, 2016 [226]	Motor neurone disease	Assessment and management -Has recommendations on treatment of muscle problems (cramps, stiffness, spasticity) though not specifically pain -Systematic review [227]: MEDLINE, Embase, Cochrane, CINAHL, PsycINFO until May 2015; search strategy reported	83
<b>Rheumatoid Arthritis</b>				
3e (Evidence, Expertise, Exchange) Initiative. Expert rheumatologists from Australasia, Canada, Europe, South America	Whittle, 2012 [228]; New Zealand/ Australian recommendations in Richards, 2014 [229]	Pain management in inflammatory arthritis by pharmacotherapy	Systematic reviews: MEDLINE, Embase, Cochrane until April 2010; plus 2008-09 EULAR/ American College of Rheumatology abstracts -Systematic reviews for each question published separately [230-241]; search terms available online at <a href="http://www.3epain.com/">http://www.3epain.com/</a>	56
The Ottawa Methods Group	Brosseau, 2012 [242]	Educational interventions in rehabilitative care	Systematic review: MEDLINE, Embase, Current Contents, CINAHL, SUMSearch, Cochrane trials until June 2010; inclusion/exclusion criteria and search results reported -Patient education, cognitive behavioural programmes recommended	56
SIGN	SIGN, 2011 [243]	Management of early RA	Systematic review: MEDLINE, Embase, Cochrane 2003-Jan 2009; additional search to May 2010 for some questions; search strategy reported online <a href="http://www.sign.ac.uk/pdf/sign123narrative.pdf">www.sign.ac.uk/pdf/sign123narrative.pdf</a>	69
Turkish League Against Rheumatism (TLAR)	Ataman, 2011 [244]	Management	Systematic review: MEDLINE, Cochrane, Embase, Turkish Medical Index 2009-2010 (pharmacological) or 2007-2010 (non-pharmacological); used EULAR 2010 recommendations for earlier pharmacological publications	54

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NICE	NICE, 2009 [245]	Management	Systematic review [246]: MEDLINE, Embase, Cochrane, CINAHL until 2008	69
Haute Autorité de Santé (HAS), France	Forestier, 2009 [247]	Non-drug treatment	Systematic review: MEDLINE, Embase, CINAHL, Pascal, Cochrane, HTA, PEDRO 1985-2006; search terms and results reported	65
Asia Pacific League of Associations for Rheumatology (APLAR)	Lau, 2015 [248]	Treatment	Adaptation of international RA guidelines for use in the Asia-Pacific region -Systematic review of guidelines: Embase, MEDLINE, Google Scholar, SCOPUS Jan 2000-Dec 2013; search terms and results reported	69
<b>Stroke</b>				
Heart and Stroke Foundation Canadian Stroke Best Practice Committees	Hebert, 2016 [249]	Stroke rehabilitation	Systematic review (see methodology manual [259]): 2012-2015 (older literature in previous versions) -Literature review done by affiliated organization (EBSR); databases may include Embase, CINAHL, PubMed, ProQuest, PsycINFO, AMED, and Scopus (actual databases used depend on topic) <a href="http://www.ebsr.com/evidence-review/1-introduction-and-methods">http://www.ebsr.com/evidence-review/1-introduction-and-methods</a> ; search terms and results not reported -Methodology manual at <a href="http://www.strokebestpractices.ca/wp-content/uploads/2014/08/CSBPR2014_Overview_Methodology_ENG.pdf">http://www.strokebestpractices.ca/wp-content/uploads/2014/08/CSBPR2014_Overview_Methodology_ENG.pdf</a> -Guideline also on website <a href="http://www.strokebestpractices.ca/index.php/stroke-rehabilitation/">http://www.strokebestpractices.ca/index.php/stroke-rehabilitation/</a> -Recommendations regarding spasticity, hemiplegic shoulder pain, central post-stroke pain (CPSP)	60
Stroke Foundation (Australia)	Stroke Foundation, 2017 [250]	Stroke management	-Systematic review: Methodology in accompanying Technical Report -MEDLINE, Embase, Cochrane, CINAHL, EBM Review, PsycInfo, Web of Science until Nov 2015/January 2016, with final searches June/July 2016; inclusion/exclusion criteria, search terms and strategy reported - central post-stroke pain, hemiplegic shoulder pain, painful spasticity -2010 version used in draft document [298]; 2017 version added after copyediting	79 (2010 version)
Stroke Foundation of New Zealand; New Zealand	Stroke Foundation of New Zealand,	Stroke management	Systematic review: MEDLINE, Embase, Cochrane for all questions; CINAHL, PsycINFO, PEDro for some. Searched until	79

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Guidelines Group	2010 [251]		<p>sometime in the period May-August 2009, with update 19 Feb 2010 in MEDLINE and Embase</p> <ul style="list-style-type: none"> <li>-Indicates search terms available from NSF (Australian National Stroke Foundation); results reported</li> <li>-Recommendations on shoulder pain, central post-stroke pain, spasticity</li> <li>-Note that evidence and most recommendations are the same as in the 2010 Australian guideline [251]; not updated to 2017</li> </ul>	
SIGN	SIGN, 2010 [252]	Management	<p>Management including rehabilitation, prevention and management of complications, discharge planning</p> <ul style="list-style-type: none"> <li>-Systematic review: MEDLINE, Embase, CINAHL, PsycINFO, PEDro, Cochrane 2002-2009</li> <li>-Includes shoulder pain, spasticity, central post-stroke pain</li> </ul>	60
<b>Other: Pressure Ulcers</b>				
National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, Pan Pacific Pressure Injury Alliance	National Pressure Ulcer Advisory Panel et al, 2015 [253]	Pressure ulcers	<p>Systematic review: PubMed, CINAHL, MEDLINE, Embase, Scopus, Biomedical Reference Collection, Health Business Elite, Cochrane, HTA, AMED until July 1 2013; search strategy and inclusion/exclusion criteria reported in Methodology Addendum</p> <ul style="list-style-type: none"> <li>-Includes pain assessment and treatment</li> </ul>	67
<b>Other: Restless Leg Syndrome</b>				
American Academy of Neurology	Winkelman, 2016 [254]	Restless legs syndrome	<p>Systematic review: MEDLINE, Embase, and Science Citation Index to July 2015; search strategy included</p> <ul style="list-style-type: none"> <li>-Doesn't make specific pain recommendations</li> <li>-Pramipexole, rotigotine, gabapentin enacarbil (level A); ropinirole, pregabalin, IV ferric carboxymaltose (level B)</li> <li>-Oxycodone/naloxone for patients failing other treatment</li> </ul>	56
International Restless Legs Syndrome Study Group (IRLSSG)	Garcia-Borreguero, 2013 [255]	Restless legs syndrome/Willis-Ekbom disease: long-term treatment	<p>Pharmacologic agents for long-term treatment</p> <ul style="list-style-type: none"> <li>-Systematic review: MEDLINE, CINAHL, clinicaltrials.gov; search terms, inclusion/exclusion criteria, results reported; period of search not reported but estimated to be to 2012 based on included RCTs</li> <li>-Doesn't deal with any specific disease</li> <li>-Level A evidence for pregabalin (up to 1 year); pramipexole, ropinirole, and rotigotine (up to 6 months; probably effective)</li> <li>-Level B evidence for 1 to 5 years: gabapentin enacarbil, pramipexole, and ropinirole (1 year); levodopa (2 years); and rotigotine (5 years)</li> <li>-First line either dopamine-receptor agonists or <math>\alpha 2\delta</math> ligands, with the latter considered for patients with comorbid pain</li> </ul>	65



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			<p>syndrome or painful restless legs</p> <ul style="list-style-type: none"> <li>-Indicates <math>\alpha 2\delta</math> ligands somewhat likely and opioids very likely to have pain reduction benefit</li> <li>-Evidence for opioids lower but can be considered for patients with RLS refractory to other treatments</li> </ul>	
European Federation of Neurological Societies (EFNS), the European Neurological Society and the European Sleep Research Society	Garcia-Borreguero, 2012 [256]	Restless legs syndrome (Willis-Ekbom disease)	<p>Systematic review: MEDLINE, Embase, CINAHL Jan 2005 -Dec 31 2011; Cochrane; search terms and results reported</p> <ul style="list-style-type: none"> <li>-Does not deal with any specific disease</li> <li>-Level A evidence for short-term treatment: rotigotine, ropinirole, pramipexole, gabapentin enacarbil, gabapentin, pregabalin</li> <li>-Less evidence for long-term treatment: rotigotine is considered effective, gabapentin enacarbil is probably effective, and ropinirole, pramipexole and gabapentin are considered possibly effective</li> </ul>	60
American Academy of Sleep Medicine	Aurora, 2012 [257]	Restless legs syndrome and periodic limb movement disorder	<p>Systematic review and meta-analyses: MEDLINE to June 29, 2011 using Cochrane Highly Sensitive Search Strategy to identify RCTs; search terms and results reported</p> <ul style="list-style-type: none"> <li>-Pramipexole or ropinirole (highest evidence); levodopa, opioids; gabapentin enacarbil; gabapentin or pregabalin</li> <li>-Gabapentin for patients with both RLS and pain</li> <li>-Relative ranking appears slightly outdated compared to recent reviews</li> </ul>	69

Abbreviations: AHRQ, Agency for Healthcare Research & Quality; CAM, Complementary and alternative medicine; COX-2, cyclo-oxygenase-2; HF, heart failure; IV, intravenous; NICE, National Institute for Health and Care Excellence; NSAIDs, non-steroidal anti-inflammatory drugs; NSTEMI-ACS, non-ST-segment elevation acute coronary syndrome; RCT, randomized controlled trial; RLS, restless legs syndrome; SIGN, Scottish Intercollegiate Guidelines Network

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Table 6. Guidelines on Pain Assessment

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Organization	Citation	Topic	Notes	AGREE RoD <sup>8</sup>
Breast Cancer EDGE Task Force - part of The American Physical Therapy Association's (APTA) Evaluation Database to Guide Effectiveness (EDGE) Task Force	Harrington, 2014 [285]	Clinical measures of pain in breast cancer	Identification of evidence-based pain assessment tools in breast cancer survivors -Systematic search: PubMed, CINAHL, PsycINFO Apr 2012 to June 1 2013 (plus updates during review process); search strategy and results reported -Recommends eight measures for pain	63
Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain (IASP)	Haanpaa, 2011 [286]	Assessment of neuropathic pain	Systematic review of MEDLINE and Cochrane: 1950-2008 for topics not in EFNS guideline; 2002-2008 for topics in EFNS guideline [288]; search strategy reported (online only) -Note: issues of assessment in primary care are described in an earlier (non-systematic) review by the same group [287]	73
European Federation of Neurological Societies (EFNS)	Cruccu, 2010 [288]	Assessment of neuropathic pain	Systematic review (based on EFNS methodology [289] and earlier version [290]): MEDLINE, Cochrane, 2004-2009, search terms and results not reported	60
Nursing Home Pain Collaborative funded by The MayDay Fund and composed of representatives from five Hartford Centers of Geriatric Nursing Excellence.	Herr, 2010 [291]	Pain-behavioural assessment tools in nursing homes	Assessment of pain in nonverbal older adults in nursing homes using behavior pain assessment tools -Review of literature in PubMed, CINAHL, PsycINFO Apr 2004 to July 2008; search terms and results reported -Recommend use of PAINAD and PACSLAC	56
Oncology Section Head and Neck EDGE Task Force of the American Physical Therapy Association	Spinelli, 2014 [292]	Head and neck cancer	Neck dysfunction; assessment using patient-reported outcomes -Systematic review: PubMed, PEDro, EBSCO Host, MEDLINE, PsycINFO, Cochrane to Dec 2013	58
Oncology Section Head and Neck EDGE Task Force of the American Physical Therapy Association	Eden, 2014 [293]	Head and neck cancer	Shoulder dysfunction; assessment using patient-reported outcomes -Systematic review: PubMed, PEDro, EBSCO Host, MEDLINE, PsycINFO, Cochrane to June 2013	58

Abbreviations: EFNS, European Federation of Neurological Societies

<sup>8</sup> AGREE II Rigor of Development sub-scale score (see Methods section and Appendix G)[Back to Results](#)

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## APPENDICES

**Appendix A: Members of the Working Group and their COI declarations**  
(see the PEBC Conflict of Interest (COI) Policy)

Name	Affiliation	COI declaration
Mona Sawhney RN(EC), MN, PhD	Faculty of Health Sciences, School of Nursing, Queens University Nurse Practitioner, Acute Pain Service North York General Hospital Toronto, Ontario	Thesis involved studying the implementation of the RAO Best practice guideline on pain assessment and management in an ambulatory surgery setting
Jill Rice MD, CCFP(PC)	Champlain Regional Palliative Consultation Team (RPCT) Champlain Regional Palliative Care Lead	None
Judy Watt-Watson RN, MSc, PhD	Professor Emeritus The Lawrence S. Bloomberg Faculty of Nursing, University of Toronto Senior Fellow, Massey College, University of Toronto, Toronto, Ontario Past-President, Canadian Pain Society	None
Trish Rawn RN, MN, CHPCN (C)	Clinical Nurse Specialist /Nurse Educator; Pain and Symptom Management Consultant, North Simcoe Muskoka Hospice Palliative Care Network (NSMHPCN)	None
Glenn Fletcher, MSc	Health Research Methodologist, Program in Evidence-Based Care, McMaster University	None

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## Appendix B: Literature Search Strategy

Database(s): AMED (Allied and Complementary Medicine) 1985 to October 2016, Embase 1996 to 2016 November 07, OVID MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches	Results
1	exp practice guideline/ or exp consensus development conference/ or guideline.pt. or practice guideline\$.mp. or (guideline: or recommend: or consensus).ti. or (guideline: or recommend: or consensus).kw.	653129
2	exp pain/ or exp pain clinic/ or exp pain measurement/ or exp analgesia/ or exp analgesic agent/ or exp narcotic analgesic agent/ or exp narcotic agent/ or exp "analgesic, antiinflammatory, antirheumatic and antigout agents"/ or exp tricyclic antidepressant agent/ or exp medical cannabis/ or exp cannabinoid/ or exp Transcutaneous Electric Nerve Stimulation/ or exp opiate alkaloids/ or exp Opium/ or exp narcotics/ or analgesics, opioid/ or exp analgesics/ or exp Anti-Inflammatory Agents/ or exp Antidepressive Agents, Tricyclic/ or exp medical marijuana/ or exp Cannabinoids/	3272995
3	(tricyclics or tricyclics or Amitriptyline or Amoxapine or Clomipramine or Desipramine or Doxepin or Imipramine or Nortriptyline or pain or analgesi* or opioid* or morphine* or hydromorphone or methadone or narcotic* or pain* or oxycodone* or fentanyl or acetaminophen or antiinflammator* or anti-inflammator* or NSAIDS or COX-2 inhibitors or cannabinoid* or marijuana or marijuana or cannabinol* or tetrahydrocannabinol* or THC* or cannabis or dronabinol or Sativex or Transcutaneous Electric Nerve Stimulation or nociceptive or neuropathic).mp. or TENS.ti. or TENS.kw.	2367928
4	exp neoplasm/ or exp oncology/ or exp oncology nursing/ or exp cancer patient/ or exp cancer survivor/ or exp chronic obstructive lung disease/ or exp kidney failure/ or exp diabetes mellitus/ or exp Human Immunodeficiency Virus/ or exp rheumatoid arthritis/ or exp multiple sclerosis/ or exp cerebrovascular disease/ or exp dementia/ or exp Parkinson disease/ or exp amyotrophic lateral sclerosis/ or exp demyelinating disease/ or exp degenerative disease/ or exp Neurodegenerative Diseases/ or exp hospice care/ or exp hospice/ or exp hospice nursing/ or exp hospice patient/ or exp palliative care/ or exp palliative medicine/ or exp "Hospice and Palliative Care Nursing"/ or exp palliative therapy/ or exp terminal care/ or exp terminally ill patient/ or exp terminally ill/	9189174
5	(neoplasm* or tumour* or tumor* or cancer* or carcin* or neoplas* or metasta* or oncolog* or malignan* or lymphoma* or melanoma* or melanotic or (non small adj2 cell) or (nonsmall adj2 cell) or nsccl or adenocarcin* or osteosarcom* or phyllodes or cystosarcom* or fibroadenom* or hepatoma* or hepatoblastom* or plasmacytoma* or myeloma* or blastoma* or lymphangioma* or lymphangiomyoma* or lymphangiosarcoma* or lymphoblastoma* or lymphocyoma* or lymphosarcoma* or lymphoma? or immunocyoma* or angiosarcoma* or astrocytoma? or neuroma? or cytoma? or gist or neurocytoma? or squamous cell? or cytosarcoma* or hodgkin* or non-hodgkin* or nonhodgkin* or incidentaloma* or retinoblastoma* or plasmacytoma* or cholangiocarcinoma* or leiomyoblastoma* or leiomyocarcinoma* or leiomyosarcoma* or melanosis or melanoameloblastom* or melanoblastom* or melanocarcin* or	11196736

	melanomalign* or naevocarcin* or nevocarcin* or adamantinom* or ameloblastom* or adenosquam* or teratoma* or leukemia* or metaplas* or (COPD or (chronic adj3 pulmonary disease) or (chronic adj3 lung disease) or cardiovascular disease or congestive heart failure or CHF or kidney failure or renal insufficiency or end-stage renal disease or diabetes or aids or acquired immune deficiency or hiv or Human Immunodeficiency or (rheumatoid adj2 arthritis) or multiple sclerosis* or stroke or dementia or alzheimer* or Parkinson* disease or ALS or amyotrophic lateral sclerosis or sclerosis amyotrophic lateral or lateral sclerosis amyotrophic or neurodegenerative disease or palliat* or end of life or terminal care or terminally ill or hospice*).mp.	
6	1 and (2 or 3) and (4 or 5)	37455
7	limit 6 to yr="2009 -Current"	20379
8	7 not (abstract or editorial or comment or letter or historical or note).pt.	17314
9	limit 8 to yr="2015 -Current"	4730
10	remove duplicates from 9	3813
11	limit 8 to yr="2013 - 2014"	4588
12	remove duplicates from 11	4088
13	limit 8 to yr="2010 - 2012"	5929
14	remove duplicates from 13	5466
15	8 not (9 or 11 or 13)	2067
16	remove duplicates from 15	1927
17	10 or 12 or 14 or 16	15294

**CINAHL, searched November 7, 2016**

S1	MH Neoplasms+ or MW neoplasm* or MH Oncology+ or MH "Cancer Patients" or MH "Cancer Survivors" or (neoplasm* or tumour* or tumor* or cancer* or carcin* or neoplas* or metasta* or oncolog* or malignan*) or lymphoma* or melanoma* or melanotic or non small n2 cell or nonsmall n2 cell or nslc or adenocarcin* or osteosarcom* or phyllodes or cystosarcom* or fibroadenom* or hepatoma* or hepatoblastom* or plasmacytoma* or myeloma* or blastoma* or lymphangioma* or lymphangiomyoma* or lymphangiosarcoma* or lymphoblastoma* or lymphocytoma* or lymphosarcoma* or lymphoma? or immunocytoma* or angiosarcoma* or astrocytoma? or neuroma? or cytoma? or gist or neurocytoma? or squamous cell? or cytosarcoma* or hodgkin* or non-hodgkin* or nonhodgkin* or incidentaloma* or retinoblastoma* or plasmacytoma* or cholangiocarcinoma* or leiomyoblastoma* or leiomyocarcinoma* or leiomyosarcoma* or melanosis or melanoameloblastom* or melanoblastom* or melanocarcin* or melanomalign* or naevocarcin* or nevocarcin* or adamantinom* or ameloblastom* or adenosquam* or teratoma* or leukemia* or metaplas* or (MH "Hospice and Palliative Nursing") OR (MH "Palliative Care") OR (MH "Terminal Care+") or (MH "Terminally Ill Patients+") or palliat* or end of life or terminal care or terminally ill or hospice* or (MH "Cardiovascular Diseases+") or congestive heart failure or CHF or cardiovascular disease* or (MH "Pulmonary Disease, Chronic Obstructive+") or COPD or chronic n3 pulmonary disease or chronic n3 lung disease or (MH "Renal Insufficiency+") or	823,183
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	kidney failure or renal insufficiency or end-stage renal disease or (MH "Diabetes Mellitus+") or diabetes or (MH "Human Immunodeficiency Virus+") or (MH "HIV Infections+") or aids or acquired immune deficiency or hiv or Human Immunodeficiency or (MH "Arthritis, Rheumatoid+") or rheumatoid n2 arthritis or (MH "Multiple Sclerosis+") or multiple sclerosis* or (MH "Stroke+") OR (MH "Cerebrovascular Disorders+") or (MH "Dementia+") or dementia or alzheimer* or (MH "Parkinson Disease") or Parkinson* disease or (MH "Amyotrophic Lateral Sclerosis") or ALS or amyotrophic lateral sclerosis or sclerosis amyotrophic lateral or lateral sclerosis amyotrophic or (MH "Heredodegenerative Disorders, Nervous System") OR (MH "Neurodegenerative Diseases+") OR "neurodegenerative disease"	
S2	(MH "Practice Guidelines") or (MH "Professional Practice, Evidence-Based+") OR (MH "Nursing Practice, Evidence-Based+") OR (MH "Medical Practice, Evidence-Based") OR (MH "Physical Therapy Practice, Evidence-Based") OR (MH "Occupational Therapy Practice, Evidence-Based") OR "evidence based practice" or practice guideline* or TI guideline* or TI recommend* or TI consensus or TI standards	113,822
S3	MH Pain+ or MW pain or MH pain clinics or MH pain measurement or MH analgesia+ or MH analgesics+ or (MH "Antiinflammatory Agents, Antirheumatic Agents, and Inflammation Mediators+") or (MH "Antidepressive Agents, Tricyclic+") OR tricyclics OR tricyclics OR Amitriptyline OR Amoxapine OR Clomipramine OR Desipramine OR Doxepin OR Imipramine OR Nortriptyline OR MH "Medical Marijuana" or MH Cannabis or pain or analgesi* or opiod* or morphine* or hydromorphone or methadone or narcotic* or pain* or oxycodone* or fentanyl or acetaminophen or antiinflammator* or anti-inflammator* or NSAIDS or COX-2 inhibitors or cannabinoid* or marihuana or marijuana or cannabinol* or tetrahydrocannabinol* or THC* or cannabis or dronabinol or Sativex or Transcutaneous Electric Nerve Stimulation or TI TENS or nociceptive or neuropathic	226,547
S4	S1 AND S2 AND S3  Limiters - Published Date: 20090101-  Search modes - Boolean/Phrase	1,318

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## Appendix C: Websites Searched

- **National Guideline Clearing House:** <http://www.guideline.gov/> Dec 9, 2016
- **National Institute for Health and Clinical Excellence (NICE):** <https://www.nice.org.uk/guidance> Dec 12, 2016
- **SIGN (UK) -** <http://www.sign.ac.uk> Dec 12, 2016
- **National Cancer Institute (NCI):** <https://www.cancer.gov/publications> Dec 12, 2016
- **NCCN** [www.nccn.org](http://www.nccn.org) [only for symptom management guidelines] Dec 20 2016
- **Inventory of Cancer Guidelines (SAGE):** <http://www.cancerview.ca/sage> Dec 20, 2016
- **Canadian Medical Association CPG Infobase:** <https://www.cma.ca/En/Pages/clinical-practice-guidelines.aspx> Jan 6, 2017
- **CancerIndex:** [www.cancerindex.org](http://www.cancerindex.org). Jan 9, 2017. Search for “pain”, “guideline” ; review “cancer pain and palliative care” links
- **WHO:** Jan 9, 2017
- **ASCO (US) - ASCO Guidelines** Jan 16, 2017
- **Alberta Health Services:** <http://www.albertahealthservices.ca/info/cancerguidelines.aspx> Jan 16, 2017
- **British Columbia Cancer Agency:** [www.bccancer.bc.ca](http://www.bccancer.bc.ca) Jan 17, 2017  
<http://www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines>; these have no mention of systematic reviews; refer also to  
<http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines>  
<http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management> Note: these are not based on systematic reviews; only the palliative care pain and symptom management may be of interest  
<http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management>
- **Cancer Care Nova Scotia:** [www.cancercare.ns.ca](http://www.cancercare.ns.ca) Jan 18, 2017  
Guidelines on cancer care, pain, and supportive care are from around 2006 and no longer listed on website; emergencies and thyroid ones are based on documents from other organizations that have since been revised
- **Cancer Care Ontario:** [www.cancercare.on.ca](http://www.cancercare.on.ca) Jan 18, 2017
- **Saskatchewan Cancer Agency:** <http://www.saskcancer.ca/> Jan 18, 2017  
No mention of methodology or systematic review; only breast, prostate, hepatocellular cancer mention pain: exclude all
- **National Health and Medical Research Council (Australia):** <https://www.nhmrc.gov.au/guidelines-publications> Jan 18, 2017
- **Cancer Australia:** <https://canceraustralia.gov.au/publications-and-resources/clinical-practice-guidelines> Jan 18, 2017
- **The Cancer Council of Australia:** [www.cancer.org.au](http://www.cancer.org.au) Jan 19, 2017
- **New Zealand-MOH:** <http://www.health.govt.nz/publications> Jan 19, 2017

Organizations: (project or disease specific):

- Fraser Health Hospice Palliative care Program <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/> Jan 19 2017  
Opioid principles 2006 but Fentanyl Transdermal section 2014 (section revised Jan 2016)  
Refractory Symptoms and Palliative Sedation Therapy search 2009, document 2011
- Canadian Association of Psychosocial Oncology: [www.capo.ca](http://www.capo.ca) Jan 19, 2017
- Oncology Nursing Society: [www.ons.org](http://www.ons.org) Jan 20, 2017
- American Society for Therapeutic Radiology and Oncology: [www.astro.org](http://www.astro.org) Jan 20, 2017
- RNAO: [www.rnao.org](http://www.rnao.org) Jan 20, 2017
- International Society of Nurses in Cancer Care:  
[http://www.isncc.org/?page=Position\\_Statements](http://www.isncc.org/?page=Position_Statements) Jan 20, 2017
- European Oncology Nursing Society: <http://www.cancernurse.eu/education/guidelines-recommendations.html> Jan 20, 2017
- American Association of Pain Management Nursing: [www.aspmn.org/](http://www.aspmn.org/) Jan 20, 2017

Guidelines/organizations referred to in other documents (searched for latest versions)

American geriatric society

[http://www.american geriatics.org/health\\_care\\_professionals/clinical\\_practice/clinical\\_guidelines\\_recommendations/](http://www.american geriatics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/)

<http://www.healthquality.va.gov/> (US VA/DoD, evidence based guidelines)

<http://www.iasp-pain.org/Guidelines?navItemNumber=648>. International Association for the Study of Pain

Michael G DeGroote National Pain Centre, McMaster University:

<http://nationalpaincentre.mcmaster.ca/guidelines.html>

Scottish Palliative Care Guidelines: <http://www.palliativecareguidelines.scot.nhs.uk/>

Canadian Diabetes Association <http://www.diabetes.ca/clinical-practice-education/clinical-practice-guidelines/>

American Diabetes Association <http://www.diabetes.org/>

European Association for the Study of Diabetes <http://www.easd.org/>

American Association of Clinical Endocrinologists (AACE)

<https://www.aace.com/publications/guidelines>

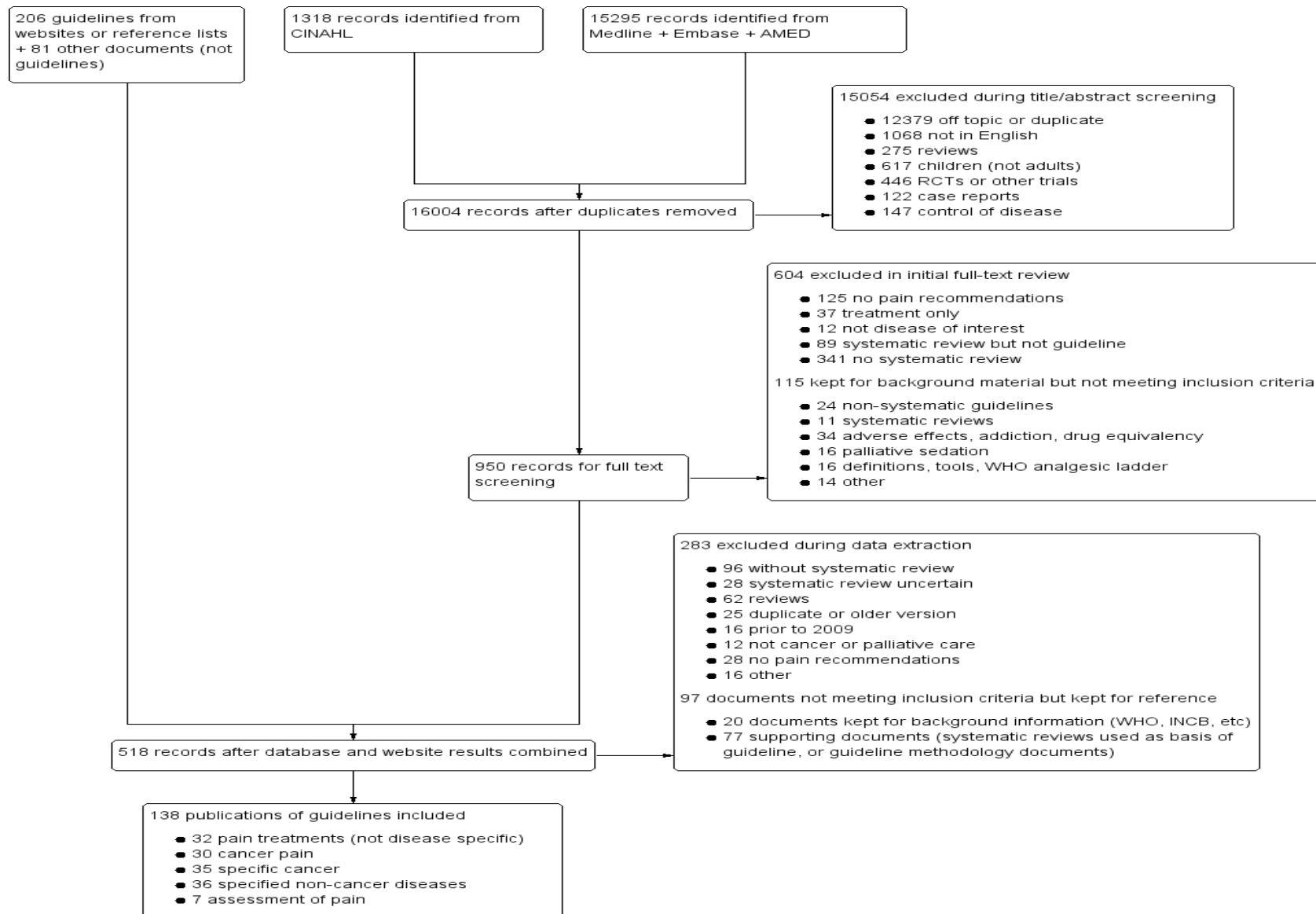
American College of Physicians (ACP) <https://www.acponline.org/clinical-information/guidelines>

American Academy of Neurology <https://www.aan.com/Guidelines/>

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## Appendix D: PRISMA Flow Diagram

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## Appendix E: Guidelines with AGREE II Rigour of Development Scores Less than 50

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Organization	Citation	Topic	Notes	AGREE RoD <sup>9</sup>
<b>Guidelines on Pain (Not Disease-Specific) [see Table 2]</b>				
(Based on Dutch/Belgium guidelines and then revised with additional pain specialist from USA)	Wolff, 2011 [48]	Phantom pain	Part of the series: Evidence-based interventional pain medicine: According to clinical diagnosis. Methodology in the introduction [222]. -Systematic review: PubMed until Sept 2010	42
Group of 33 European experts	Lefaucheur, 2014 [62]	Repetitive transcranial magnetic stimulation	Chronic pain (neuropathic or non-neuropathic) -Systematic review: separate searches for each question, used PubMed; reported search terms and results -Sufficient evidence only for neuropathic pain; possible analgesic effect for complex regional pain syndrome (CRPS)	48
Italian Consensus Conference on Pain in Neurorehabilitation (ICCPN)	Castelnuovo, 2016 [63]	Psychological treatment	Psychological Treatments and Psychotherapies in the Neurorehabilitation of Pain -Systematic review using PubMed, Embase, Cochrane with update until Jan 2015; search terms and results reported	48
<b>Guidelines that Focus on Cancer Pain [see Table 3]</b>				
(Based on Dutch/Belgium guidelines and then revised with additional pain specialist from USA)	Visser, 2011 [154]	Cancer pain - interventional	Interventional techniques (intrathecal/epidural, nerve blocks, spinal cord or nerve stimulation). Part of the series: Evidence-based interventional pain medicine: According to clinical diagnosis. Methodology in the introduction [222]. -Systematic reviews: PubMed, literature update to 2010	44
[Consensus panel of internationally recognized experts in focused ultrasound] Under auspices of the Focused Ultrasound Foundation	Huisman, 2015 [163]	Bone metastasis	Focused ultrasound for painful bone metastases -Systematic review: MEDLINE, Embase, Web of Science, Cochrane 1980-June 2014; search terms and strategy reported;	46

<sup>9</sup> AGREE II Rigor of Development sub-scale score

<b>Guidelines on Specific Cancers which Include Pain Recommendations [see Table 4]</b>				
European Association of Urology	Witjes, 2017 [204,205]	Bladder cancer, metastatic and muscle-invasive	Diagnosis, treatment, follow-up -Systematic review: MEDLINE, Embase, Cochrane, Apr 1 2014-July 21 2015; reported search strategy. It appears systematic reviews are done as new topics are added, and then yearly searches for new evidence -Limited update on website reports search until Apr 5 2016, search strategy given -RT or radical cystectomy as a palliative treatment; extremely minor component of guideline	44
UK and Ireland Neuroendocrine Tumour Society; endorsed by British Society of Gastroenterology, the Society for Endocrinology, the Association of Surgeons of Great Britain and Ireland (and its Surgical Specialty Associations), the British Society of Gastrointestinal and Abdominal Radiology and others	Ramage, 2012 [210]	Gastroentero-pancreatic neuroendocrine (including carcinoid) tumours (NETs)	Management -Systematic review: no details given -External beam RT for bone pain from metastasis	38
<b>Guidelines on Diseases Requiring Palliative Care [see Table 5]</b>				
(Based on Dutch/Belgium guidelines and then revised with additional pain specialist from USA)	Van Kleef, 2011 [260]	Chronic refractory angina pectoris	Part of the series: Evidence-based interventional pain medicine: According to clinical diagnosis. Methodology in the introduction [222] -Systematic reviews: PubMed, literature update to Sep 2010 -Spinal cord or nerve stimulation	48
American Academy of Neurology	Dubinsky, 2010 [266]	Pain in neurologic disorders	Use of transcutaneous electric nerve stimulation (TENS) -Recommends TENS be considered for painful diabetic neuropathy -Systematic review: MEDLINE, Cochrane to Apr 2009, search terms and results reported	48
Italian Consensus Conference on Pain in Neurorehabilitation	Paolucci, 2016 [268]	Stroke, MS, cerebral palsy, spinal cord injury, and other conditions associated with spasticity:	-Systematic review (see [299] for details): PubMed and Embase 1983-2013 and updated to 2015; search terms reported, level of evidence evaluated -Covers type of pain, assessment, impact, pharmacological and non-pharmacological treatment;	42

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		assessing and treating pain	these are subdivided by disease	
Italian Consensus Conference on Pain in Neurorehabilitation	Bartolo, 2016 [273]	Movement disorders, ALS, severe acquired brain injury, disorders of consciousness, dementia, oncology, neuroinfectiology: assessing and treating pain	-Systematic review (see [299] for details): PubMed, Embase, 1983 to 2015; Cochrane reviews, guidelines from websites; search terms reported	42
EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis	EFNS, 2012 [272]	ALS	Systematic review: MEDLINE, Embase, Science citation Index, Cochrane trials, and others, 2008-Feb 2011 -Recommendations for cramps, spasticity, intractable pain	46
German Cooperative Group on Radiotherapy for Benign Diseases (GCG-BD); German Society of Radiation Therapy and Oncology (DEGRO): DEGRO S2e guidelines	Seegenschmiedt, 2015 [275]; Reichl, 2015 [276]; Ott, 2015 [277]	RT for non-malignant disorders	Painful arthrosis including rheumatoid arthritis -Systematic review as per method document [35]; MEDLINE, PubMed, Cochrane + pertinent clinical information (dates not stated, but appears to cover to 2014 based on included references)	44
	Hennessy, 2016 [300]	Foot and ankle guidelines	Systematic review of guidelines on management of foot and ankle in rheumatoid arthritis -MEDLINE, Embase, CINAHL, AMED, PEDro, Cochrane until Aug 2015; search strategy reported -Latest guideline meeting our criteria is from 2011	44
<b>Guidelines on Pain Assessment [see Table 6]</b>				
European Palliative Care Research Collaborative (EPCRC) and the European Association for Palliative Care Research Network (EAPC RN)	Kaasa, 2011 [294]	Cancer pain	Consensus conference, with presentations based on series of published systematic reviews and ongoing work -Propose use of Cancer Pain Assessment and Classification System (CPACS)	44

Abbreviations: ALS, amyotrophic lateral sclerosis; RT, radiation therapy

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Appendix F: Guidelines with Uncertainty about the Literature Review Process<sup>10</sup>

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Organization	Citation	Topic	Notes	AGREE RoD <sup>11</sup>
<b>Guidelines on Pain (Not Disease-Specific) [see Table 2]</b>				
Hospice Palliative Care Program of Fraser Health (BC)	Fraser Health, 2015 [301]	Transdermal fentanyl in palliative care (rest of document outdated)	Transdermal fentanyl (Appendix A) updated 2015: Ovid (MEDLINE), Embase, PubMed, International Pharmaceutical Abstracts, CINAHL (via Ebsco), All Evidence-Based Medicine Reviews (OVID) for Jan 1 2006 - May 14 2014; rest of document search only to 2006; search terms (MeSH headings only) reported but no results (systematic review not included or referenced) -Did not include professionals outside Fraser Health	31
Pain Association of Singapore	Ho, 2013 [302]	Chronic non-cancer pain	PubMed, Scopus, Cochrane reviews until March 2012; search terms and results not specified. -Persistent postsurgical pain, diabetic peripheral neuropathic; other causes off topic	50
Neurostimulation Appropriateness Consensus Committee (NACC) of The International Neuromodulation Society (INS)	Deer, 2014 [56-58]; Deer 2017 [59-61]	Neurostimulation for chronic pain	Neurostimulation of spinal cord and peripheral nervous system for chronic pain and ischemic diseases; neurostimulation of intracranial and extracranial space and head for chronic pain; complications -PubMed, Embase, PubMed, Google Scholar until 2013; MEDLINE, PubMed and Google Scholar for complications in 2014 article -MEDLINE, Embase, Cochrane, PubMed, Scopus, Current Contents Connect, BioMed Central, Web of Science for update of risk mitigation and safety (until July 2016 for infection; not stated from bleeding or neurological injury publications) -Comment: These are detailed consensus guidelines supported by a literature search but not a strict systematic review	71

<sup>10</sup> A literature search was conducted, but the reporting is such that it is unclear whether or not it meets the criteria of a systematic review.

<sup>11</sup> AGREE II Rigor of Development sub-scale score

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American Society of Regional Anesthesia and Pain Medicine (ASRA) <sup>12</sup>	Narouze, 2015 [303]	Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medication	Extensive database search strategies; recommendations were evidence-based when available and pharmacology-driven otherwise	27
Polyanalgesic Consensus Conference (PACC) of the International Neuromodulation Society	Deer, 2017 [304-306]	Intrathecal	PubMed, Embase, MEDLINE, Biomed Central, Google Scholar, Current Contents Connect, and International Pharmaceutical Abstracts; January 2011 to October 9, 2016 for safety; Jan 2007-Nov 2015 for best practices; included key words -Comment: These are detailed consensus guidelines supported by a literature search but unclear whether there is a systematic review	69
European Association of Urology	Paez Borda, 2014 [307]	Pain management and palliative care in urology practice	Systematic literature searches using Embase, MEDLINE and Cochrane trials, plus PsycINFO and Eur-Lex for psychological therapies and legal regulations, respectively; search terms and results not reported	42
<b>Guidelines that Focus on Cancer Pain [see Table 3]</b>				
NCCN	Swarm, 2017 [164]	Adult cancer pain	Evidence-based but without systematic review. -Yearly update using PubMed to obtain key literature Oct 2014-Sept 2015 -Included here as current and widely used	58
National Cancer Institute (USA)	National Cancer Institute, 2016 [165]	Cancer pain	Evidence-based but without systematic review -Included here as current and widely used	42
Society for Integrative Oncology (SIO)	Deng, 2009 [308]	Complementary therapies	Massage, acupuncture, mind-body modalities (hypnosis, relaxation training, music therapy) -Review of MEDLINE + textbooks; unclear if meets systematic review criteria, though there were explicit systematic reviews in later guidelines for lung cancer [127] and breast cancer [128]. -Evaluation: this is the main guideline on the topic, however the methodology (or at least its reporting) is not as rigorous as was used in the more recent documents by	48

<sup>12</sup> Committee endorsed by the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain

# Evidence Summary 18-4

			the same organization on lung and breast cancer; these more specific documents should be looked at first	
DEGRO (and AGO rating)	Souchon, 2009 [309]; Souchon, 2010 [310]	Breast cancer, metastatic	Palliative radiotherapy: bone metastases and metastatic spinal cord compression -Comprehensive survey of literature PubMed +GIN 1995-2008; search terms reported -Pain medication according to WHO scheme; surgery (immediate depending on symptoms/diagnosis) + RT	35
National Cancer Institute (USA)	National Cancer Institute, 2016 [168]	Last Days of Life PDQ	Not explicit systematic review, but is evidence-based -Included here as current and widely used	38
NCCN	Denlinger, 2017 [167]	Survivorship	Not explicit systematic review, but is evidence-based -Included here as current and widely used	60
NCCN	Dans, 2017 [166]	Palliative care	Not explicit systematic review, but is evidence-based -Included here as current and widely used	58
<b>Guidelines on Specific Cancers which Include Pain Recommendations [see Table 4]</b>				
Japanese Urological Association	Akaza, 2010 [311]	Bladder cancer	English summary of Japanese guideline -RT for pain due to local progression or due to bone, lymph node, cerebral metastasis -PubMed and Japana Centra Revuo Medicina for 10 years (to about 2008) -guideline formulated in accordance with the 'Japan Society of Clinical Oncology - Guidelines for Developing Cancer Treatment Guidelines Ver. 4'; this document could not be located	33
Menopause and Osteoporosis Working Group, Society of Obstetricians and Gynaecologists of Canada	Reid, 2014 [206]	Menopause	Managing menopause. Chapter 3: Menopausal Hormone Therapy and Breast Cancer; Chapter 8: Sexuality and Menopause -PubMed and Cochrane to 2009-Jan 5 2013, some search terms reported -vulvovaginal atrophy	54
DEGRO (and AGO rating)	Feyer, 2010 [207]; Souchon, 2010 [310]	Breast cancer	Palliative radiotherapy: brain metastases and leptomeningeal carcinomatosis -Comprehensive survey of literature: PubMed + GIN 1995-2008 -Dexamethasone, RT; pain medication and sedative treatment as supportive care if not otherwise treatable	38
Society of Obstetricians and Gynaecologists of Canada	Lamont, 2012 [209]	Female sexual health	Includes subsections on gynaecologic cancers, breast cancer -PubMed, CINAHL, Cochrane to Dec 2010 + grey literature	44



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			<p>[312]</p> <ul style="list-style-type: none"> <li>-Need to address both physical and psychological components of cancer and pain</li> <li>-Vaginal stenosis/fibrosis after RT</li> <li>-Surgically/chemically induced menopause (breast and gynecologic cancers): atrophic vaginitis/dryness.</li> </ul>	
World Health Organization	WHO, 2014 [208]	Cervical cancer	<p>Chemotherapy or radiotherapy may be used in advanced cancer as palliative treatment; pain control is discussed in Chapter 7: Palliative care; also see practice sheets 7.1 and 7.2</p> <ul style="list-style-type: none"> <li>-Recommendations come from 1996 publication “Cancer pain relief: with a guide to opioid availability” [80]; new documents on palliative care [2,3,79] are available; a new guideline on adult cancer pain [155] is being developed</li> <li>-Systematic Review (?): Methodology in WHO handbook [313], but no details for this specific guideline</li> <li>-RT as palliative therapy in very advanced/metastatic cancer</li> <li>-Use national pain and palliative care guidelines</li> <li>-Opioids often essential; NSAIDs alone for mild pain, or in addition to opioids; non-pharmacological methods (emotional support, massage, distraction, music, relaxation, meditation, acupuncture) may be added but not instead of pain-relieving medicines</li> </ul>	44
European Association of Urology	Bader, 2012 [314]	Prostate cancer	<p>Pain management</p> <ul style="list-style-type: none"> <li>-Structured search: MEDLINE, Embase, Cochrane reviews 2000-2010; excerpted from original pain guideline (now discontinued) which was based on a systematic literature search up until 2009</li> <li>-Surgery</li> <li>-RT, radionuclides (<sup>89</sup>Sr, <sup>153</sup>Sm), surgery, bisphosphonates, corticosteroids, chemotherapy, systemic analgesics for bone metastasis</li> </ul>	46
<b>Guidelines on Diseases Requiring Palliative Care (see Table 5)</b>				
American Diabetes Association	Pop-Busui, 2017 [315]	Diabetic neuropathy	<p>Position statement</p> <ul style="list-style-type: none"> <li>-Based on several reviews including those by the Toronto Consensus Panel in 2010-2011(may be non-systematic) and NeuPSIG systematic review/guideline from 2015 [41] (see Table 2)</li> </ul>	58

#### Evidence Summary 18-4

Guidelines on Pain Assessment [see Table 6]				
American College of Radiology (ACR)	Douglas, 2014 [65]	Headache	Imaging assessment of headache -Extensive analysis of current literature; no details of search given -Update in progress with expected completion early 2018 -ACR methodology starting 2015 requires search summary to be reported, so will be in update	52

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; RT, radiation therapy

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## Appendix G: AGREE II Rigour of Development Scores

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Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
<b>General Pain (Table 2)</b>									
<b>Pain (general)</b>									
British Pain Society, 2013 [10]	7	7	6	2	7	6	3	5	43
	PubMed and CINAHL 1997-2009, AMED, PsycINFO. Search terms and search strategy given	Inclusion criteria: English only, types of study, patient population, interventions and comparisons	Graded according to system by Harbour and Miller. Grade for individual studies given in table. Study design and methodology	It is just said that the papers that were considered acceptable were included in the commentary. No information on consensus or process of how final statements were reached	Balanced discussion on harms/benefits	Clearly linked	Peer/consensus review. Member names given	These guidelines will be updated in 3 to 5 years	73
Wolff, 2011 [48]	5	2	6	2	5	6	1	1	28
	Systematic review PubMed until 2010. Search strategy given. Hard to find this information, not in the actual text	Selected abstracts that reported on injection therapy, epidural steroid injection, radiofrequency, ... etc.	Used grading strength of recommendations and quality of evidence in clinical guidelines by Guyatt (ref 2) table 1. little discussion throughout	No info on consensus/ process of development	Not much discussion of harms	Can see how it is linked	No info	No info	42
<b>Pain (general, not including cancer pain)</b>									
Makris, 2014 [11]	6	6	4	2	7	6	1	1	33
	Systematic review MEDLINE Cochrane Jan 1990-May 2014, search terms given. Search strategy given in appendix	English only, study designs, mean sample age of 60 or greater	Graded evidence using a standard approach (ref 17) level of evidence given in tables. Grading based on study design. Little discussion throughout	No info on reaching consensus	Safety data in table 1	Linked, but would have organized it so it is more clear	No info	No info	52
Healthcare Improvement Scotland, 2013 [12]	7	3	6	2	7	7	5	7	44
	Systematic review MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2007-2012 search strategies in supporting material	Excludes interventions delivered in secondary care, headache, children, treatment of underlying conditions	Levels of evidence, grade recommendations. Study design, bias, applicability, consistency	From SIGN handbook: usually use informal consensus	Balanced discussion	Clearly linked	Section 13.3 consultation and peer review. Number of reviewers. Comment on comprehensiveness and accuracy. Address every comment and justify	Considered for review in 3 years. Method for updating in is SIGN handbook	75

<sup>13</sup> The first number for each guideline is the total score (i.e., the sum of scores for questions 7 to 14), while the second number is the Domain Score, which is a type of percentage taking into consideration the minimum and maximum values possible (see Methods section).

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
							disagreements. Quality control check		
<b>Opioids</b>									
NICE, 2012 [13,14]	7 Cochrane reviews and RCTs, DARE, HTA, CINAHL, Embase, MEDLINE, PsycINFO, web of science 1950-2011. search strategy given	6 Inclusion/exclusion criteria under review protocols	4 Guidelines manual: section 9. concept of strength is reflected in the wording of the recommendation	2 Guidelines manual: formal consensus techniques may be used, no particular approach recommended	7 Balanced discussion	7 Clear link	4 Guidelines manual says they have stakeholders comment on guideline, and they respond to them. Quality assurance and peer review	5 In the guidelines manual: The formal process for updating begins 3 years after publication. In exceptional circumstances, and only if significant changes to the process of clinical guideline development are anticipated, this interval will be reduced to 2 years	42 71
Fraser Health, 2015 [301]	4 Databases and dates search terms given for Transdermal Fentanyl Systematic search. Search strategy not given for others	2 English, human	2 No info	2 No info	7 Balanced discussion	4 Recommendations are linked to references. But no discussion of the evidence	1 No info	1 No info	23 31
Jarzyna, 2011 [15]	6 MEDLINE 2009. Figures show the search strategy. Search terms given	6 Study design (RCTs, clinical trials etc.), >19, English	5 ASA evidence categories. Table 1. strength of recommendation also evaluated	2 Reached consensus. No methods for ho/extent it was reached	7 Balanced discussion	6 Clearly linked	4 External peer review to ensure accuracy, completeness, relevance. Names given	1 No info	37 60
Chou, 2014 [16]	7 MEDLINE, Cochrane, PsycINFO until Jul 2012 (ref 17 full report- gives search strategy in Appendix C)	6 Inclusion: patients, outcomes, study design, English	7 GRADE to rate recommendations. Quality ratings given in appendix of ref 17	6 Multi stage Delphi - steps explained. unanimous or near unanimous consensus was achieved for all recommendations	7 Balanced discussion	7 Clearly linked	4 More than 20 external peer reviewers gave comments. Another round of revisions	5 Update by 2018 or earlier if critical new evidence becomes available	49 85
Muller-Lissner, 2016 [19]	7 MEDLINE 1946-Sept 2014, Embase, and Embase classic	6 Inclusion: adults receiving opioids confirmed diagnosis	6 Strength of recommendation taxonomy, corresponds	6 Statements labeled with the degree of agreement. Independent electronic	6 Balanced discussion	6 Clearly linked	1 No info	1 No info	39 65

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	1947-Spet 2014, Cochrane. Terms listed in appendix	of OIBD, comparison, study design, English	to GRADE	voting. Agreement level in appendix					
The Opioid Therapy for Chronic Pain Working Group, 2017 [20]	7 MEDLINE, CINAHL, Embase, PsycINFO, DARE, HT, Cochrane reviews and RCTs 2009-2015, search terms/strategy in appendix J	6 English only, study design, number of patients, reported on outcome of interest	6 Used GRADE grading recommendations	2 Talks about the face to face meeting where they developed recommendations, no other info	7 Balanced discussion	7 VIII discussion of recommendations. Clearly linked	4 Peer review process, named external organizations involved, all feedback was discussed and considered, modifications made in accordance with evidence	3 Medical practice evolutions require continuous updating based on published info.	42 71
Dowell, 2016 [21]	6 Based on 2014 AHRQ report which included SR on MEDLINE, Cochrane, PsycINFO, CINAHL Jan 2008 Aug 2014. search information found in MMWR and online appendices (ref 11) search terms <a href="https://stacks.cdc.gov/view/cdc/38026">https://stacks.cdc.gov/view/cdc/38026</a>	7 English language, study design, patient characteristics, comparison <a href="https://stacks.cdc.gov/view/cdc/38026">https://stacks.cdc.gov/view/cdc/38026</a>	7 Assessed using GRADE. GRADE table- table 1. quality assessment table in supplement	2 Sought perspectives on draft recommendations. No other info. In MMQR: experts did not vote on recommendations or seek to come to a consensus	7 Balanced discussion	5 Would have liked to see explicit paragraphs of evidence for recommendations	4 CDC obtained input from peer reviewers. OGW reviewed the guideline. Had unanimous or majority support. CDC further considered recommendations that had mixed opinions. CDC reviewed and carefully considered comments. Names of reviewers in 'additional contributions'	4 Will revisit the guideline to determine if evidence gaps warrant an update	42 71
Washington State Agency, 2015 [22]	6 March 2014 or later using PubMed and also MEDLINE. Search terms given	4 Limited to English, humans, study design	4 Workgroups did not summarize overall strength of recommendations, but do discuss limitations of studies	2 Large proportion based on consensus of expert opinion. Work groups made recommendations. No other info	7 Balanced discussion	6 Clearly linked	5 Guideline was posted for public comment, comments were reviewed- available on AMDG website	6 The guideline is updated every 5 years or if there is substantial new evidence. Methods given	40 67
<b>Opioids: non-cancer pain</b>									
National Opioid use Guideline Group, 2010 [23,24], Kahan,	7 Systematic review: Cochrane RCTs, MEDLINE, and	7 Section 10.1.2 Inclusion/Exclusion	6 Jadad, study scores in Appendix B-13. recommendations were	7 10.3.1 Modified Delphi technique with the NAP. Consensus was defined at	7 Balanced discussion	7 Clearly linked	2 NAP experts provided consultation.	4 Update as new evidence becomes	47 81

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
2011 [25,26]. Furlan, 2010 [27]	Embase to 2009. strategies listed in appendix		also graded (10.3.2)	80% support. If not reached, was revised. Results in tables			Revising with NAP input in section 11.4. However, unsure if they would be considered "external reviewers" because were involved in development process	available	
Chou, 2009 [28]	7 Evidence review is ref 19. Cochrane, MEDLINE, Embase until Oct 2008. Appendix 3 is search strategies	7 Inclusion: patient pop, outcomes, study design, language	6 Used GRADE. Quality ratings given in Appendix tables of Ref 19	6 Multistage Delphi, steps explained. Unanimous agreement achieved on all but 2 recommendations	7 Balanced discussion	7 Clearly linked	4 Over 20 external reviewers solicited for comments, then another round of revisions	5 Updated by 2012 or earlier if new evidence available	49 85
Manchikanti, 2012 [32,33]	2 They used several reviews. Not sure how they were picked. No other info	5 Outcomes, study design, patients with CNCP	6 USP-STF criteria (Table 1) overall strength of evidence assessed	4 Consensus through electronic communications, final recommendations approved by at least 2/3 of the majority	7 Balanced discussion	6 Clearly linked	2 Peer review	5 Provided expected revision date. Important new evidence warrants modification	37 60
Hauser, 2014 [34]	5 Systematic search Central, MEDLINE, Scopus, Oct 2008-Oct 2013. no search terms of full search strategy	6 RCTS at least 4 weeks in duration, compared with placebo or other analgesics for the treatment of CNCP. Long term efficacy and risks	4 Assess using agree. Methodological quality assessed with GRADE. Recommendation strength determined. Evidence level using Oxford scheme. Some discussion of study design and limitations	5 14 Delphi rounds. Consensus strength in Tables	7 Balanced discussion	4 Recommendations not clearly linked with evidence	4 Wider public given opportunity to comment, in response to comments, modified in further 4 Delphi rounds. Also had external assessment	2 Is itself an update, no other info	37 60
Ho, 2013 [302]	5 PubMed, Scopus, Cochrane reviews until March 2012. combination of terms related to CNCP and opioid treatment	6 English, CNCP, opioid. Study designs, conditions included, opioids included	3 Some of discussion of study quality in text	2 Says it is consensus based, but no other info	7 Balanced discussion	7 Clearly linked	1 No info	1 No info	32 50
Busse, 2017 [36]	7 Embase, MEDLINE, search strategies available, search until 2016	2 Including randomized trials and observational studies (excluding case	7 Used GRADE. Used Cochrane risk of bias. Quality of evidence given in tables	5 Voted on recommendations. Anonymous online voting software. At least 80%	7 Balanced discussion	7 Clearly linked	5 External review committee given a checklist. Names provided. Posted	5 If we are unable to implement the dynamic updating process,	45 77

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
		reports)		endorsement			for public consultation. Encouraged participation from 429 stakeholders. Explains what changes were made	we plan to update this guideline at minimum within 5 years	
<b>Cannabinoids</b>									
National Academies of Sciences Engineering and Medicine, 2017 [37]	7 MEDLINE, Embase, Cochrane reviewed 1999-June 2016. search strategy in appendix B	6 Limit to those published in English, study design, cannabis exposure and health endpoints	6 Weight of evidence categories. Systematic reviews were assessed by the committee. Primary research - Cochrane and Newcastle Ontario	2 Evidence based consensus. No other info	7 Balanced discussion	7 Clearly linked	3 Reports are peer reviewed. Purpose of the review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible. Reviewers listed	1 No info	39 65
Koppel, 2014 [38]	7 MEDLINE, Embase, PsycINFO, web of science, Scopus 1948-Nov 2013, search strategy reported (appendix e-3)	4 Excluded non-neurologic pain, study designs	7 Graded according to the American academy of neurology classification. Classification scheme appendix e-4. rating of class given in evidence tables	2 No info	6 Balanced discussion	7 Evidence tables given. Clearly linked	2 There were peer reviewers	1 No info	36 58
<b>Cranial or neuro-stimulation</b>									
Crucchi, 2016 [39]	6 PubMed/MEDLINE, Embase, Cochrane, 2006-Dec 2014	6 Interventions, outcomes, study design	7 Used GRADE, risk of bias using Cochrane. Grade tables in supplement	2 Used GRADE. No info on consensus	7 Balanced discussion	7 Clearly linked	1 No info	5 Formally updated in 5 years	41 69
Lefaucheur, 2014 [62]	5 PubMed searches for each question. Up until March 2014. Keywords given.	1 No info	7 Class of study given in tables. Criteria derived from the European federation of neurological societies. Also gave a level of evidence	2 Experts compared their respective classifications until they reached a consensus. No info on reaching consensus	7 Balanced discussion	7 Clearly linked	1 No info	1 No info	31 48
Deer, 2014 [56-58]; Deer, 2017 [59-61]	6 Databases, dates and key words given	2 English	6 Evaluated by the authors, levels and	6 Recommendations show strength of consensus	7 Balanced discussion	7 Clearly linked	3 Peer reviewed through Wiley.	5 It is a "living document".	42 71



## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
			grades of evidence				Provide methods for peer review	Continued refreshment and evidence synthesis	
<b>Intraspinal/ intrathecal analgesia</b>									
Narouze, 2015 [303]	2 "Extensive database search strategies and the recommendations were evidence based when available and pharmacology driven otherwise"	1 No info	1 "We could not provide strength and grading of these recommendation"	1 No info	6 Balanced discussion	7 Clearly linked	1 No info	2 Mentions an update	21 27
Deer, 2017 [304-306]	6 PubMed, Embase, MEDLINE, Biomed Central, Google Scholar, Current Contents Connect, and International Pharmaceutical Abstracts Jan 2011-Oct 9 2016 for safety; Jan 2007-Nov 2015 for best practices. Key search words given	1 No info	6 Evidence level rated by US preventive Services Task Force, and degree of recommendation	6 Recommendations show strength of consensus	7 Balanced discussion	7 Clearly linked	3 Peer reviewed through Wiley. Provide methods for peer review	5 Is itself an update. It is a "living document". Continued refreshment and evidence synthesis	41 69
<b>Cognitive behavioural, psychological</b>									
Castelnuovo, 2016 [63]	7 PubMed, Embase, Cochrane with Update until Jan 2015, searches strategy given	4 Intervention, outcomes, the presence of an evaluation of at least one neurological condition was also used as the inclusion criterion	6 Rated strength of recommendations using SIGN. Checklist to assess risk of bias	1 Recommendations formulated according to evidence. No other info	4 Lack discussion of harms	7 Clearly linked	1 No info	1 No info	31 48
<b>Neuropathic pain</b>									
Finnerup, 2015 [41]	7 MEDLINE, PubMed, Cochrane trials, Embase 1966 until Apr 2013. search strategy in appendix	7 Study design, exclude certain interventions, outcome. Appendix 2 details criteria for considering studies for this review	7 Assessed methodological quality using Oxford Quality Scale. GRADE used to assess recommendations. Grade tables provided	2 The final recommendations were agreed on by consensus of the authors. No other info on methods for reaching consensus	7 Calculated NNT and NNH. Balanced discussion	5 Sometimes will mention studies without referencing them	2 In the contributors section it says there were some authors who were external advisors who reviewed the recommendations	2 Is itself an update. No other info	39 65

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
NICE, 2013 [42]	7	7	7	3	7	7	7	6	51
	CINAHL, Cochrane, DARE, Embase, HEED, HTA, MEDLINE, NHS Economic Evaluations until July 2012. search strategy provided	In appendix D, all the inclusion/exclusion criteria are listed	Used GRADE. Grade profiles in appendices G and J	Guidelines manual: in most cases, committee reaches decisions through informal consensus	Balanced discussion. Trade-off between benefits and harms section	Clearly linked	Names of stakeholders given. Comments and responses in History tab. More details in guideline manual	Is itself an update. Methods for update in guidelines manual. Check for currency of guideline 2 years post publication	90
Attal, 2010 [44]	5	7	7	1	7	7	1	2	37
	Cochrane, MEDLINE, Jan 2005-2009. No search terms of full search strategy	Inclusion/exclusion criteria reported: study design, study population, outcome, setting, English	Classification of evidence and recommendation grading adhered to the EFNS standards. Classifications in evidence tables	No info	Balanced discussion	Clearly linked	No info	Is itself an update. No other info	60
<b>Palliative Care</b>									
NICE, 2015 [45]	7	7	7	3	7	7	6	5	49
	MEDLINE, Embase, Cochrane to Jan 2015, full search strategies reported (appendix G)	English. Appendix C has inclusion/exclusion criteria	Critically appraised using the checklist in the NICE guidelines manual. GRADE tables	Recommendations were drafted on the basis of the committee's interpretation of the available evidence. Done informally. Consensus recommendations agreed through discussion	Balanced discussion	Evidence tables in appendix H. clearly linked	Consultation by stakeholder. 6 week public consultation and feedback. Comments were responded and posted on NICE website	When progressed significantly. Methods in guidelines manual	85
Paez Borda, 2014 [307]	3	1	6	1	7	7	1	2	28
	Embase, MEDLINE, Cochrane, PsycINFO, Eur-Lex. No dates, no search strategy	No info	Level of evidence and grading of recommendations	No info	Balanced discussion	Clearly linked	No info	Have had previous updates	42
McCusker, 2013 [47]	3	1	6	3	5	7	6	6	37
	Search terms are given. Dates given.	No info	Used GRADE. Quality of evidence and strength of recommendation given	Use evidence to write recommendations. All decisions are done using a consensus process. Don't know how consensus is reached	Lack discussion of harms	Clearly linked	Document available for review during the revision process by member medical groups and sponsors. Specific reviewer comments available. Names of reviewers in acknowledgements. Feedback used by and responded	Document available for review during the revision process by member medical groups and sponsors. Provides info for issues such as content update. Next revision will be no later than Dec 2018	60

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
							to by the work group		
<b>Cancer Pain (Table 3)</b>									
<b>Cancer Pain</b>									
National Clinical Effectiveness Committee, 2015 [93]	5 Searched for guidelines published Nov 2008- Nov 2011. Literature search June 2007- Nov 2011. Databases: Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, CINAHL, MEDLINE, and PsycINFO. Updated Jan 2015. No full search strategy or search terms	5 Appendix VII- Inclusion and Exclusion criteria for each health question	6 Grade quality of evidence based on CEBM method (based on study design). Considered judgement-inconsistencies and generalizability. Guidelines were graded using AGREE II tool. A table detailing methodology limitations would have been nice	3 Consensus reached informally. ADAPTE process	7 Balanced discussion on benefits and adverse events	7 Evidence is placed next to recommendation. It is clear how they are connected	7 Section 1.9- provided description of reviewers. Comments were received. Summary of the external review and amendments in Appendix VII	5 Section 1.13- will be reviewed in 3 yr, based on formal evidence search (methodology provided)	45 77
Paice, 2016 [53]	6 Lit search PubMed 1995-Nov 5, 2014. Listed full search strategy (data supplement 2). Only used PubMed, so it is not an exhaustive search	7 Criteria listed in Methods section of guideline. Included info on population, interventions, outcomes, English, specific study designs. Articles considering acute pain or with certain study design excluded	7 SRs were assessed using AMSTAR. Assessed methodology of RCTs, used Newcastle-Ottawa for other study designs. Strength of evidence takes into account magnitude and direction of effect. Ratings in Data Supplement	5 Informal consensus. Used Bridge-wiz steps	7 Balanced discussion on benefits and adverse events	7 Evidence is placed next to recommendation. It is clear how they are connected. Clear what is evidence based and what is informal consensus based	7 Circulated for external review, editorial review by JCO. 2 external reviewers. Rated on quality and usefulness. Feedback on Table 5	7 On basis of formal review, determine need to update. Will use SIGNALs approach to update	53 94
Visser, 2011 [154]	6 PubMed, literature update to 2010. Search strategy given	2 Articles selected based on relevant intervention	3 Gave evidence scores based on study design, quality, benefit v harm, direction. Could be more explicit and detailed	2 Recommendations formulated based on "grading strength of recommendation and quality of evidence in clinical guideline"	7 Balanced discussion on benefits and adverse events	7 Evidence is placed next to recommendation. It is clear how they are connected	1 No info	1 No info	29 44
Health Quality Ontario, 2016 [94]	7 MEDLINE, Embase, Cochrane 1994-Apr 2014; full search strategy reported	7 Inclusion/exclusion criteria provided: English, populations, intervention, comparison, study design	7 Assessed risk of bias for primary studies using the Cochrane tool for randomized controlled trials; for observational studies	1 No info	6 Balanced discussion	6 Clearly linked	2 Reviewer comments were obtained	1 No info	37 60

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
			using a generic assessment. Used GRADE, GRADE tables in appendix 2						
Mercadante, 2015 [95]	7	6	7	2	7	7	1	1	38
	MEDLINE, Embase, Cochrane RCTS until Feb 3 2014 Search terms and search strategy in table 1	Inclusion criteria: comparisons, patients, "relevant outcomes", English	Table 2 Studies graded by quality of evidence. Data analyzed using GRADE. Study design. Looked at quality, consistency, directness, imprecision, bias	No explicit detail on development process	Balanced discussion on benefits and adverse events	Evidence is placed next to recommendation. It is clear how they are connected	No info	This work is an update. No other info	63
Gaertner, 2016 [96]	6	7	3	6	7	7	1	1	38
	MEDLINE, Embase, Cochrane 1948- Sept 27 2012. Updated Sept 12 2013. Search strategy given (not full search strategy, only MEDLINE)	Inclusion and exclusion criteria in box 1	Level of evidence graded according to SIGN. No further detail provided	Agreed upon in a formal structured consensus process. Consensus if >75% agree	Balanced discussion on benefits and adverse events	Evidence is placed next to recommendation. It is clear how they are connected	No info	No info	63
van den Beuken-van Everdingen, 2017 [68]	6	7	6	2	7	6	1	1	36
	MEDLINE, Embase, Cochrane trials Jan 2005-May 2014, search terms reported. No full search strategy	Inclusion criteria: study design, language, patient pop, intervention, comparison, outcomes	Data S1 table of quality assessment for systematic reviews of RCTs and observational studies. Based on AMSTAR. Grading of recommendations takes into account benefit vs. risk, consistency, imprecision etc.	Recommendations formulated considering rated evidence and practical considerations	Balanced discussion on benefits and adverse events	It is clear how evidence is connected with recommendations. Would have preferred if they were placed next to each other in text	No info	This work is an update. No other info	58
Hershman, 2014 [98]	7	7	6	2	7	6	4	4	43
	MEDLINE, Embase, AMED to April 2013. search strategy and search results in Appendix table A3 and Appendix figure A1	Criteria: population, outcome, study designs, language	Table 1 quality assessment, study design, rating recommendations takes into account benefits vs. harms, consistency	Does not really explain the consensus process at all	Data supplement for table 5 data on adverse events. Table 3 compares benefits and harms	It is clear how evidence is connected with recommendations. Would have preferred if they were placed next to each other in text	Circulated for external review. Description of external reviewers. Comment and feedback, and agreement with recommendations. Clarity and implementation	Need for revision based on periodic review of the literature	73
Yamaguchi, 2012, 2013 [99,100]	6	2	5	4	6	7	3	1	34
	Search PubMed Jan 2000-July 2008, search PaPaS	Only studies that evaluated the drugs available in Japan	Follow concept from GRADE. Strength of recommendation takes	3 sequential sessions of discussions using the Delphi method. Modified	Balanced discussion on benefits and	Evidence is placed next to recommendation.	12 external reviewers	No info	54

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	category of Cochrane (search strategy apparently in full Japanese guideline)		into account benefit v harms. LoE takes into account quality, design, consistency	Delphi. Explains steps	adverse events	It is clear how they are connected			
Ali, 2017 [155]	<b>Guideline in development</b>								N/A
Swarm, 2017 [164]	5 PubMed Oct 2014-Sept 2015, provided search terms	3 Inclusion: humans, English, study design	2 Benefits and harms described. Nothing else about quality	6 Info for development is on NCCN website. Based on high level evidence. Consensus when there is no high level evidence. Degree of consensus is shown by category number. Steps in consensus not explained	6 Balanced discussion on benefits and adverse events	6 Could have been formatted in table or next to each other for greater ease	1 No info	7 Update methodology on NCCN website	36 58
National Cancer Institute, 2016 [165]	1 Not an explicit literature search	1 Not an explicit literature search	6 Evaluate strength of the evidence. Used formal evidence ranking system. Discussion of quality through out	2 Changes in the summary are made through a consensus process. No other info	7 Balanced discussion on benefits and adverse events	5 Does not provide formal guidelines or recommendations. But does provide evidence followed by suggestions of what to do	2 Says this document is peer reviewed. No other info	4 Reviewed regularly and updated as necessary, monthly	28 42
<b>Opioids for Cancer Pain</b>									
Carmona-Bayonas, 2017 [103]	6 PubMed, Embase, Cochrane, google scholar 1980-2015, include search terms. No full search strategy	6 English language. Selection criteria: clinical or biological information of use for the physicians having to make decisions, contributed to enhance the existing conceptual and theoretical framework regarding this particular patient population. References on preclinical or in vitro accepted if triggered development of new treatment strategies. Excluded pediatric population, so	5 there was no formal quality assessment, but did discuss study design, limitations throughout	3 Based on review and agreed upon by all authors. No other info	7 Balanced discussion on benefits and adverse events	6 A section for each aspect is given	1 No info	1 No info	35 56

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
		assessment of opiate therapy or not applicable to cancer survivors. Excluded certain study designs							
Caraceni, 2012 [104]	5 Lit search up to 2009-2010 MEDLINE, Embase, CINAHL, Cochrane. Appendix has more details. No search terms used or full search strategy	7 Included if carried out in adult pts with chronic cancer pain, data on efficacy or side effects, English, RCT or non-randomized	6 Followed GRADE, balance between desirable and undesirable effects. Quality assessment based on study design and quality of studies.	3 Expert consensus process, formalised, step wise, referenced a modified 2 round Delphi,	7 Balanced discussion on benefits and adverse events	7 Clearly linked, recommendations placed next to summaries	1 No info	4 Potential clinical effects of new pharmacology need further research and continuous updating of the guidelines is required	40 67
Handsaker, 2013 [126]	5 2011 review by Zepptella. MEDLINE, search terms given, to Jul 2009. No full search strategy	7 All RCTs blinded and non-blinded, assessed management of breakthrough pain. Adult patients with cancer and breakthrough pain, any setting. Comparators. Outcomes	6 GRADE approach. Would have liked to see individual assessments of the study	2 Methods of development were just agreement with Zeppetella, authors rate the guideline. This section is a little irrelevant	7 Taking into consideration the benefits, risks, and side effects	7 Summary accompanies recommendation	1 No info	1 No info	36 58
<b>Complementary Techniques</b>									
Deng, 2009 [308]	4 MEDLINE and textbook chapters. Key words given	2 No explicit criteria	5 recommendations are graded based on strength of evidence	2 Made recommendations based on strength of evidence and risk/benefit ratio. No info about consensus	7 Balanced discussion on benefits and adverse events	7 Evidence placed next to recommendations	1 No info	3 Guidelines are a work in progress, they will be updated as needed	31 48
Deng, 2013 [127]	7 Ovid, MEDLINE, PubMed, web of science (2000-2011), keywords given Search strategies described, full descriptions available on request	7 Searches limited to meta-analyses, SR, and RCTs. Narrative reviews and single arm studies were excluded. Studies exclusively involving adult patients with cancer that provided subjects with mind body interventions. Intervention included. English	7 (ref 1) SRs and meta-analyses assessed using DART. GRADE assessed risk of bias, precision, consistency, directness. Supplementary material	5 The overall process for the development of these guidelines... described in the methodology article (ref 1) anonymous voting to achieve consensus. he voting procedure used the GRADE grid, at least 67% consensus	7 Balanced discussion on benefits and adverse events	7 Evidence placed next to recommendations	4 (ref 1)	6 (Ref 1) guidelines must be updated and kept current. Use a new living guidelines model	50 88
Greenlee, 2014 [128]	7 9 databases Jan 1990-	7 Table 2 interventions	6 Recommendations	4 Not much information	7 Balanced	6 Recommendations	4 Externally	5 Plans to updates	46 79

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	Dec 2013, search terms in appendix	and outcomes of interest, women receiving standard BC treatment. Selected for inclusion RCT, English, at least 50% BC pts, outcome of interest	graded with US preventive services task force grading system. Quality was assessed using Jada and Delphi scoring. Study quality score given for each study	about recommendation development. Based on strength of evidence using accepted standards	discussion on benefits and adverse events	linked to evidence in tables (supplementary)	reviewed. Names of reviewers given	these specific guidelines every 3 years	
<b>RT; bone-modifying agents</b>									
Shibata, 2016 [129]	7	2	5	4	6	7	2	2	35
	PubMed, Cochrane, CINAHL, Japan Medical Abstracts Society 2003-2013, search strategy on website	Meta-analyses or RCT	Evaluated critically and rated. Criteria for rating given here: <a href="http://minds4.jcqh.c.or.jp/minds/guideline/pdf/MindsHB2014.pdf">http://minds4.jcqh.c.or.jp/minds/guideline/pdf/MindsHB2014.pdf</a>	Majority voting >70% of the conference. Delphi	Balanced discussion	Clearly linked	Externally peer reviewed	Says it is desirable to revise within 5 years: <a href="http://minds4.jcqh.c.or.jp/minds/guideline/pdf/MindsHB2014.pdf">http://minds4.jcqh.c.or.jp/minds/guideline/pdf/MindsHB2014.pdf</a>	56
Lutz, 2017 [130]	6	7	4	7	6	7	3	6	46
	PubMed Dec 2009 to Jan 2015 search terms given	English, outcomes of interest. Inclusion: age >18, bone metastases previously unirradiated, treatment with external beam RT. Exclude study designs	Rate strength of evidence, but does not give criteria	Formulated based on lit review. 2 rounds of modified Delphi, steps explained. % agreement shown	Toxicity. One question addresses long term adverse events	Evidence placed next to recommendations	Manuscript reviewed by 5 expert reviewers, and posted for public comment	ASTRO has established a formal process for reviewing guidelines more than 2 yr post publication for novel high quality evidence. New data potentially impacting practice	79
Alberta Health Services, 2016 [131]	6	5	4	4	7	7	1	5	39
	PubMed Jan 2012-Dec 2014. search strategy given in appendix A-I60	Excluded if not English, case studies, pediatric patients.	Does not use formal rating schemes, but describes the type and quality if research	Development process can be found in guideline resource unit handbook. General agreement can use informal consensus. More formalized process may be required in some situations- Delphi process	Balanced discussion	Clearly linked	No info	Reviewed annually for required updates	65
Souchon, 2009 ; Souchon, 2010 [309,310]	6	2	3	2	4	6	1	1	25
	survey of literature PubMed + GIN 1995-2008, search terms given	No info	Rate level of evidence, but does not say what criteria forms the LoE	Recommendations formulated based on panel's interpretation of level of evidence	Lack discussion of harms	Clearly linked	No info	No info	35
PEBC, 2004	7	7	2	3	6	6	7	5	43
	Databases and dates search terms given.	Inclusion criteria: study design,	No explicit assessment	There is a DSG consensus process	Adverse effects listed, section 5	Clearly linked	External review section, number	Updated lit search put this	73



## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	Lit search strategy given at the end	comparison, patients, outcomes, language		section, but does not really explain the methods for consensus			and expertise of reviewers, survey items listed. Comments and response described	doc into education and information	
NICE, 2009 [133]	7 MEDLINE, Embase, Cochrane, CINAHL, AMED, until June 30 2008. Appendix A Search strategy	4 Systematic reviews and RCTs, foreign language papers were not requested. Can't find an explicit statement of the inclusion/exclusion criteria	6 Assessed quality by referring to the SIGN criteria. Guideline development manual- says they use a methodology checklist	3 Developed during meetings. Sub groups made draft recommendations. Where evidence is weak, used informal consensus	7 Balanced discussion	7 Clearly linked	4 List of stakeholders. Format of comment form given. They were asked to comment and GDG responded. Can't find the document for comments and response	7 <a href="https://www.nice.org.uk/process/pmg17/chapter/purpose">https://www.nice.org.uk/process/pmg17/chapter/purpose</a> Method for updating Criteria for updating	45 77
Van Poznak, 2011 [135]	6 MEDLINE and Cochrane 2003 to July 15 2009. search strategy in data supplement	6 Inclusion criteria: had metastatic breast cancer and were randomly assigned to receive bone modifying agent or placebo or an alternative intervention. Outcomes, study design.	4 Study quality: definition of SRE was not uniform across all studies, difference efficacy end points used in different trials. Study design. Mention other limitations	3 In absence of definitive data expert consensus. Met via three teleconferences. No other info on how they reached consensus	7 Balanced discussion	7 Clearly linked	3 JCO for peer review. Named other expert reviewers in the acknowledgement section	6 Uses signals approach to facilitate guideline updating. Normally updated every 3 yrs. Annual intervals, will determine need for revisions based on examination of literature	42 71
Porta-Sales, 2016 [137]	6 MEDLINE, Embase, Cochrane until Jan 31, reported search terms, search strategy	7 Inclusion: adult patients, RCT or meta-analyses, outcomes, comparisons, English	7 GRADE assessment, table 2, comments risk of bias in table 3	2 Had conclusions, not really recommendations that needed to be formulated	7 Balanced discussion on benefits and adverse events	6 Clearly linked	1 No info	1 No info	37 60
Cancer Australia, 2011 [138]	7 Cochrane review and separate review for more recent literature until April 2010. ref 2 and 3	7 Ref 2 and 3. Criteria based on PICO	5 Level of evidence (NHMRC level of evidence- which takes into account consistency, generalizability, etc.). Strengths and weakness of evidence section	2 No info on methods of development of how consensus was reached	7 Balanced discussion	7 Clearly linked	2 Acknowledges those who gave their time to provide comment on the draft guideline recommendations as part of external review. Reviewed externally by key	2 No info, but is itself an update	39 65

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
							stakeholders and the wider community		
Mercadante, 2016 [139]	6	7	6	2	6	6	1	1	35
	MEDLINE, Embase, Cochrane trials searched to Feb 2015, search strategy in Table 1	Inclusion: comparison, adult pts with cancer pain, outcome, English, study design	Assessed using GRADE	Did not provide methods for how it was formulated	Balanced discussion on benefits and adverse events	Clearly linked	No info	No info	56
Huisman, 2015 [163]	6	4	2	2	7	7	1	1	30
	MEDLINE, Embase, web of science, Cochrane, 1980-June 2014. search terms given, but they seem a little limited	criteria: study design, patients	No explicit assessment	Developed consensus statements, did not explain how/ or extent that consensus was reached	Balanced discussion on benefits and adverse events	Clearly linked	No info	No info	46
<b>Metastatic Spinal Cord Compression</b>									
l'Esperance, 2012 [67]	5	4	5	2	7	7	3	1	34
	PubMed until Feb 2011. key words given	Phase II and III trials that included assessment of neurologic function. Prospective studies, English or French	Used ASCO grading system	No info	Balanced discussion	Clearly linked	Reviewed by independent external experts. Names of external reviewers are mentioned in acknowledgements	No info	54
NICE, 2008 [140]	7	4	6	3	7	7	6	6	46
	MEDLINE, Embase, Cochrane, CINAHL, BNI, PsycINFO, SIGLE, Web of Science, ISI proceedings, biomed central search strategy in appendix	Systematic reviews and RCTs, foreign language papers were not requested. Can't find an explicit statement of the inclusion/exclusion criteria	Assessed quality by referring to the SIGN criteria. Guideline development manual- says they use a methodology checklist	Developed during meetings. Sub groups made draft recommendations. Where evidence is weak, used informal consensus	Balanced discussion	Clearly linked	Stakeholders provide comments. Names of reviewers given. Comments given in a table under history tab	Two years after publication NICE will commission NCC to determine whether evidence base has progressed to alter guideline recommendations for an early update. If not, will be updated in 4 years	79
Cancer Australia, 2014 [142]	7	7	7	2	7	7	2	1	40
	MEDLINE, Embase, PubMed, Jan 2001-April 2012, appendix C search strategy	Humans and English language. Section 2.1 Inclusion criteria. Exclude based on study design, inappropriate outcomes,	NHMRC methodology was used to grade recommendations Appendix 2, strengths and weakness of the evidence section	NHMRC methodology used to formulate recommendations. No info on consensus	Balanced discussion	Clearly linked	Reviewed externally by key stakeholders and the wider community	No info	67

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
		inappropriate population, inappropriate interventions							
<b>Mucositis</b>									
Lalla, 2014 [144]	7 OVID before December 2010 keywords were not stated explicitly. No full search strategy	7 English reporting intervention for mucositis, exclude if did not report effects of an intervention, study design, include all age groups	7 Quality was assessed by identifying major and minor flaws as per Hadorn et al., specify methodology. Body of evidence assigned a level based on Somerfield et al- type of study and if well designed. Consistency	5 Guidelines discussed and finalized in a meeting. No info on extent/how consensus was reached	6 Doesn't really talk about the risks. Will say that the evidence is against the use of certain treatment, but does not explain why	6 Clearly linked	3 No info	5 This is itself an update to newly published lit, no other info	46 79 <sup>14</sup>
<b>Palliative or Survivorship</b>									
Alberta Health Services, 2016 [153]	6 PubMed Jan 2012- Sept 2014. Full details in appendix A	5 Excluded: not in English, case studies, pediatric patients	2 No formal assessment.	4 <a href="http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-utilization-handbook.pdf">http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-utilization-handbook.pdf</a> informal consensus process can be used , a more formalized Delphi method can also be used and will update guideline	6 Balanced discussion (toxicities, complications, benefits etc.)	7 Clearly linked	1 No info	7 Reviewed annually or earlier. More info about methods in the handbook	38 63
National Cancer Institute, 2016 [168]	1 No systematic review	1 No systematic review	4 Says there are: reference citations accompanied by a level of evidence designation but can't find. Mostly details methodology. There is some discussion of quality throughout	2 Changes in the summary are made through a consensus process. No other info	6 Balanced discussion on benefits and adverse events	5 Does not provide formal guidelines or recommendations. But does provide evidence followed by suggestions of what to do	1 No info	6 Reviewed regularly (each month) and updated as necessary. Changes made through consensus process	26 38
Denlinger, 2017 [167]	5 PubMed Sept 2014 - Oct 2015, provided search terms	3 Inclusion: humans, English, study design	3 Benefits and harms described. Nothing else about quality.	6 Info for development is on NCCN website. Based on high level evidence.	6 Balanced discussion on benefits and	6 Could have been formatted in table or next to each	1 No info	7 Update methodology on NCCN website	37 60

<sup>14</sup> Original rating was 48, however this was revised to 79 by a second rater. The original score may not have taken into account additional information in accompanying methods documents and systematic reviews which were the foundation for the guideline.

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
			Categories of evidence given	Consensus when there is no high level evidence. Degree of consensus is shown by category number. Steps in consensus not explained	adverse events	other for greater ease			
Dans, 2017 [166]	5 PubMed Oct 2014-June 2015, provided search terms	3 Inclusion: humans, English, study design	2 Benefits and harms described. Nothing else about quality. Categories of evidence given	6 Info for development is on NCCN website. Based on high level evidence. Consensus when there is no high level evidence. Degree of consensus is shown by category number. Steps in consensus not explained	6 Balanced discussion on benefits and adverse events	6 Could have been formatted in table or next to each other for greater ease	1 No info	7 update methodology on NCCN website	36 58
<b>Specific Cancers (Table 4)</b>									
<b>Bladder/Kidney</b>									
Witjes, 2017 [204,205]	4 Missing search terms and full strategy	1 No inclusion criteria	4 Used Oxford Centre for Evidence-based Medicine - Levels of Medicine	2 Mentioned the use of consensus panel but did not explain the process	5 Considered benefits and risks and encourages clinicians to advise patients of both but did not report trade off in details	4 Recommendations follow summary of evidence but no explicit link	4 Mentioned single expert external reviewer but did not go into details about process	5 Noted that guidelines are updated annually but did not further explain methods	29 44
NICE. 2015 [169]	7 All criteria met	6 Inclusion criteria in the PICO	7 Used GRADE, provided GRADE tables	4 Formulated in meetings. Discussed and agreed upon. Where evidence was weak, used informal consensus	7 Balanced discussion	7 LETR statements. evidence summaries prepared	7 Stakeholders comment on draft. List of stakeholders in appendix f. consultation comments table in History tab	7 NICE guideline manual- review in 3 years. Methodology provided	52 92
Akaza, 2010 [311]	5 Missing key terms and full search strategy	1 Did not explicitly state what papers would be considered relevant	3 Only considered study designs and balance between magnitude of benefit vs. harm	2 Consensus was used but did not describe in detail about how the process was	5 Described benefits and harms. Briefly mentioned need for consideration of	6 Yes, answer (recommendation) precedes explanation	1 No mention of external review	1 No updating procedures	24 33
Lujungberg, 2016 [171,172]	7 MEDLINE, Embase, Cochrane library 1 Jan 2013- 30 July 2015. search strategy on line	3 Study design and English	6 Assessed according to their level of evidence and given grade of recommendation	1 No description of consensus or development process	6 Balanced discussion	7 Clearly linked	2 Sections were peer reviewed	2 Is itself an update	34 54

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
<b>Breast</b>									
Cancer Australia, 2016 [173]	7 PubMed, MEDLINE, Embase, psych INFO, CINAHL, and Cochrane 2001-Nov 2015. appendix B search strategy	7 Inclusion criteria in systematic review	7 Grade recommendation using FORM methodology. Level of study and risk of bias provided for each study. Provided recommendation matrices	2 Recommendations are based on evidence statements. When evidence is lacking, use expert opinion	7 Balanced discussion	7 Clearly linked. Evidence summaries are provided for	3 Commented on guideline as external review process. By key stakeholders and the wider community	1 No info	41 69
Runowicz, 2016 [175]	6 PubMed through April 2015. give search terms	6 Studies on childhood cancers, qualitative studies and non-English publications were excluded	6 Consider LOE criteria and consistency across studies, dose-response, race difference, second primary cancers. In discussion section, talks about limitations	4 In ASCO guidelines wiki- evidence based consensus approach. Modified Delphi when lacking evidence	6 Balanced discussion	7 Clearly linked	3 External review. Review comments were reviewed and integrated into the final article	7 On basis of formal review will determine need to update. At minimum, updated every 5 years. Methods for updating in wiki	45 77
Alberta Health Services, 2015 [176]	6 MEDLINE, Embase 2001-Sept 2011. search terms given	6 Limited to clinical trials an meta-analyses published in English during the previous 10 yrs. Present data on delivery of follow-up or investigations for follow-up	2 No formal assessment. Talks about study design a little	4 <a href="http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-utilization-handbook.pdf">http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-utilization-handbook.pdf</a> informal consensus process can be used , a more formalized Delphi method can also be used and will update guideline	7 Balanced discussion	6 Clearly linked	1 No info	7 Formal review will be conducted at the annual provincial meeting in 2016. Will revise earlier if evidence is brought before that time. More info about methods in handbook	39 65
Reid, 2014 [206]	6 PubMed and Cochrane to 2009-Jan 5 2013, gives examples of key words	4 Study design, English or French	6 Quality of evidence evaluated based on criteria by Canadian task force on Preventive Health Care "the number, size and quality of RCTs are still too low to permit firm conclusions"	2 No info	7 Balanced discussion	7 Clearly linked	1 No info	1 No info	34 54
<b>Brain</b>									
Alberta Health Services, 2014 [66]	6 MEDLINE, PubMed, CINAHL to Nov	5 The patient population was limited to adolescents	2 No info	4 <a href="http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-">http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-</a>	7 Balanced discussion	7 Clearly linked	3 Distributed this document for review and	7 Formal review will be conducted at the	41 69

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	2012, search terms given	and adults, there were no limitations by date, publication type or study design		guide-utilization-handbook.pdf informal consensus process can be used , a more formalized Delphi method can also be used and will update guideline			comment to members of the Alberta Provincial CNS Tumour Team (n=30) via an anonymous electronic survey	annual provincial meeting in 2013. Will revise earlier if evidence is brought before that time. More info about methods in the handbook	
Feyer, 2010 [207]	4 PubMed and GIN 1995-2008	2 Study design	5 Level of evidence provided. Not too sure how they determine level of evidence	2 No info	5 Lack discussion of harms	6 Clearly linked	1 No info	1 No info	26 38
<b>Gastric, Hepatic</b>									
Park, 2015 [177]	4 MEDLINE up to 2014, search terms related to clinical questions (but not directly given)	2 English or Korean	6 Used GRADE. Rating is given but would be nice to see GRADE tables	3 Committee reviewed the evidence and suggested recommendations through intra and interdepartmental discussion	7 Balanced discussion	7 Clearly linked	4 External review board meeting and an open symposium. 8 specialists	4 Updates when new evidence accumulates	37 60
Lee, 2014 [178]	5 PubMed, MEDLINE, Cochrane, KoreaMed 1980-2011. search terms and full search strategy not provided	3 English or Korean. Says inclusion/ exclusion criteria were determined for each key question, but is not provided	6 Rated according to GRADE, QUADAS, new Ottawa evaluation. Rating is given but would be nice to see GRADE tables	2 No info	6 Balanced discussion	7 Clearly linked	4 Public hearing. Revisions that reflected the opinions expressed in the public hearing were made	5 Renewed in 3 to 5 years based on the accumulated clinical evidence	38 63
<b>Gynecologic</b>									
Alberta Health Services, 2009 [179]	6 MEDLINE, Embase, Cochrane 1965-June 25, 2009. search terms given	3 English only	4 Levels of evidence are provided. Unsure what the levels of evidence mean	2 No info	7 Balanced discussion	6 Clearly linked	1 No info	5 A formal review will be conducted in 2010, however if new evidence is brought forward before, guideline will be changed accordingly	34 54
Healthcare Improvement Scotland, 2013 [180]	7 MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2003-2012. search strategies given	1 No info	7 Graded levels of evidence, and grading for recommendations	3 From manual: usually the GDG forms recommendations through informal consensus	6 Balanced discussion	7 Clearly linked	6 Public consultation. Also reviewed by expert referees, comment on	5 Will be considered for review in 3 years	42 71

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	(separate document on website)						comprehensiveness and accuracy of interpretation. Addresses every comment made by an external reviewer and must justify any disagreement. Names of reviewers given		
Lamont, 2012 [209]	5	3	6	2	5	6	1	1	29
	PubMed, CINAHL, Cochrane to Dec 2010. examples of search terms given	Inclusion: study design, no language restriction	Quality of evidence evaluated based on criteria by Canadian task force on Preventive Health Care	No info	Some discussion of harms	Clearly linked. list of evidence available online	No info	No info	44
WHO, 2014 [208]	2	2	4	3	7	2	4	5	29
	This guideline refers to other WHO guidelines. Perhaps systematic reviews were performed individually for the guidelines, but it is difficult to assess it as a whole	This guideline refers to other WHO guidelines. Perhaps systematic reviews were performed individually for the guidelines, but it is difficult to assess it as a whole	Use GRADE, but does not give GRADE tables	WHO or GRADE process for development of recommendations. Discussed in the manual. No info about reaching consensus	Balanced discussion	This guideline specifically does not refer directly to the evidence. It refers to other WHO guidelines, which probably will reference evidence more directly.	External review group (names in Annex 1). Info on purpose in the guideline development manual	Evidence published will be monitored so that updates to the guidance and recommendations can be promptly considered. Approximately 5 years after publication	44
<b>Head &amp; Neck</b>									
Cohen, 2016 [181]	6	6	6	3	6	7	5	5	44
	PubMed 2004 to April 2015, search terms given. Only used one database	Exclude childhood cancers, qualitative studies and non-English, entirely non-North American	LOE criteria, consistency, dose-response	Internal review. Recommendations are based on current evidence in the literature and expert consensus opinion. Don't know how consensus was reached	Balanced discussion	Clearly linked. list of evidence available online	External experts for review. Comments were reviewed and integrated. Acknowledgements thank reviewers.	On the basis of formal review of the emerging literature, ACS will determine the need to update. Minimum 5 years	75
Mirabile, 2016 [182]	5	4	2	5	6	6	3	1	32
	MEDLINE 1994-March 2013, search terms given. No full search strategy only used one database.	inclusion: English, study design	No info	Delphi appropriateness method used for consensus. 2 round process, steps explained	Balanced discussion	Clearly linked	External expert reviewers evaluated the final statements. Specialists in MO and supportive cancer	No info	50



## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
<b>Hematologic</b>									
NICE, 2016 [183]	7 MEDLINE, Cochrane, Embase, web of science, CINAHL, PsycINFO, AMED until June 8 2015. search strategies in evidence review	6 English language, specified study designs. The scope sets the inclusion/exclusion criteria	7 Quality of evidence sections in evidence review. evaluated using GRADE	4 Held meetings where recommendations were formulated. Where evidence is weak, use informal consensus	7 Balanced discussion	7 LETR statement	6 Stakeholders comment. in History tab. List of stakeholders in appendix F	7 NICE guideline manual- review in 3 years. Methodology provided	51 90
<b>Lung</b>									
Simoff, 2013 [185]	5 MEDLINE, CINAHL, PsycINFO, Cochrane, Embase, web of science, google scholar, until 2012	3 Original research. No limiters of language or article type	6 Assessed for quality. Documentation and appraisal review tool. Used GRADEpro	5 Recommendations were developed with supporting evidence and the consensus of the writing committees. Controversial recommendations were identified for further consultation by the entire panel, anonymous voting used GRADE grid, at least 80% in favour to be approved	7 Balanced discussion	6 Clearly linked	5 Provided external review. Authors were required to respond to all mandatory issues. Included nearly 30 individual reviewers	6 Embarking on a new living guidelines model for revising existing recommendation s, continual assessment of the currency of these recommendation s, will begin 1 year after publication	43 73
Healthcare Improvement Scotland, 2014 [187]	7 MEDLINE, Embase, CINAHL, PsycINFO and Cochrane Library 2005-2012. search strategy: <a href="http://www.sign.ac.uk/pdf/SIGN137_search%20narrative.pdf">http://www.sign.ac.uk/pdf/SIGN137_search%20narrative.pdf</a>	2 No info	6 Evaluated using the standard SIGN methodological checklist. Use GRADE methodology (this information is from the methodology handbook)	4 evidence to decision tool, usually formed through informal consensus	7 Balanced discussion	7 Clearly linked	6 Section 16.4 consultation and peer review. Comment on comprehensiveness and accuracy. Every comment is addresses. Names of expert reviewers given	5 considered for review in three years	44 75
Deng, 2013 [127]	6 MEDLINE, PubMed, web of science 2000-2011. Provided key words. Full descriptions of search strategies are available upon request	6 Searches were limited to meta-analyses, systematic reviews and RCTs. Adult patients with cancer with mind body interventions. English	5 Assessment of quality given in the supplementary data tables	2 No info	7 Balanced discussion	7 Clearly linked	1 No info	1 No info	35 56
Cancer Council Australia, 2012 [188]	7 Databases and dates provided. Search strategy provided in	7 Limited to the highest level of evidence available,	7 NHMRC grading system for recommendations.	3 Internal review of recommendations. Consensus for practice	6 Balanced discussion	7 Clearly linked	5 Public consultation. Comments are	7 Annual WP meeting to review all	49 85

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	the Wiki	English. Section 3.4. Exclusion criteria: study design, treatment, and comparator. More info on wiki	Grade recommendations are made using the body of evidence assessment matrix. Use wiki critical appraisal form	points			reviewed and content is updated. External reviewers complete a brief feedback survey. Insight into guideline usage and evaluate dissemination. Engage stakeholders on a long term basis	changes made by authors. Updating guideline content section	
NICE, 2011 [189]	7 Databases and dates provided. Search strategy in appendix 1	4 Search filters such as those to identify systematic reviews and randomised controlled trials were applied to the search strategies when necessary. No language restrictions, but foreign language papers not requested or reviewed.	5 Discusses bias	4 Derived recommendations from clinical evidence. When evidence was weak, agreed through informal consensus	7 Balanced discussion	7 Clearly linked	6 Comments from stakeholders. List of stakeholders in Appendix 9.2. History has comments and responses	7 Will be reviewed and updated as considered necessary. Criteria for deciding the update status is defined in the guidelines manual. Methodology given. Three years after publication	47 81
Rodrigues, 2011 [190]	6 PubMed 1966-March 2010. key words given	3 RCTs or other prospective clinical trial evaluations	2 No formal assessment. Some discussion, e.g.: there are several limitations regarding the data available. Majority are early phase I studies	2 Formulated through conference calls and emails	7 Balanced discussion	7 Clearly linked	5 Reviewed by 3 expert reviewers (acknowledgement) and public comment. Integrated feedback	3 Will monitor guideline and initiate an update when appropriate	35 56
Scherpereel, 2010 [191]	6 MEDLINE, Embase, chorine, national guideline clearinghouse, HTA database 1990-2009. Search terms given. No full search strategy	2 No info	6 Each recommendation graded using criteria from American College of Chest Physicians	5 Each recommendation was voted by all experts. If <85% in agreement, recommendation was modified	6 Balanced discussion	6 Clearly linked	1 No info	1 No info	33 52
<b>Pancreatic</b>									
Sohal, 2016 [192]	7 PubMed, Cochrane Jan 2000-June 2015. search strategy in	6 Inclusion: population, study design, comparison,	6 Type and strength of recommendation, evidence and potential	5 On basis of the consideration of the evidence, authors	7 Balanced discussion	7 Clearly linked	5 Circulated for external review and submitted to	7 Work to keep abreast of any newly published	50 88

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	data supplement 3	English	bias provided	contribute to the development of the guideline. Crafted using BRIDGE wiz. Evidence lacking- informal consensus			JCO for editorial review. 2 external reviewers. Rated as high quality. Comment were reviewed and integrated	data that signal an update to this guideline, methodology supplement provides info about the signals update approach	
Balaban, 2016 [193]	7	6	6	5	7	7	5	7	50
	MEDLINE and Cochrane Jan 2000-June 2015. search strategy in data supplement 3	Inclusion: population, study design, comparison, English	Type and strength of recommendation, evidence and potential bias provided	On basis of the consideration of the evidence, authors contribute to the development of the guideline. Crafted using BRIDGE wiz. Evidence lacking- informal consensus	Balanced discussion	Clearly linked	Circulated for external review and submitted to JCO for editorial review. 2 external reviewers. Rated as high quality. Comment were reviewed and integrated	Work to keep abreast of any newly published data that signal an update to this guideline, methodology supplement provides info about the signals update approach	88
Khorana, 2016 [194]	7	6	7	5	7	7	5	7	51
	MEDLINE and Cochrane, Jan 2002-June 2015. full search strategy found in data supplement 3	Inclusion: population, study design, comparison, English	Type and strength of recommendation, evidence and potential bias provided. Study quality assessment in data supplement	On basis of the consideration of the evidence, authors contribute to the development of the guideline. Crafted using BRIDGE wiz. Evidence lacking- informal consensus	Balanced discussion	Clearly linked	Circulated for external review and submitted to JCO for editorial review. 2 external reviewers. Rated as high quality. Comment were reviewed and integrated	Work to keep abreast of any newly published data that signal an update to this guideline, methodology supplement provides info about the signals update approach	90
Ramage, 2012 [210]	1	1	6	1	6	7	2	2	26
	No details given.	No info	Oxford Centre for Evidence Based Medicine's level of evidence and grading of recommendation	No info	Balanced discussion	Clearly linked	Externally peer reviewed	Is itself an update	38
<b>Prostate</b>									
Mottet, 2016 [196]	7	3	6	2	7	7	2	5	39
	MEDLINE (1946-March 2015), Embase (1974-2015), Cochrane (2205-April 2015)	Study designs representing high levels of evidence, English	Level of evidence and grading of recommendation given. Classification system modified from oxford centre for evidence based medicine levels of evidence	No info	Balanced discussion	Clearly linked	Peer review	Ongoing systematic reviews	65

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
Alibhai, 2016 [132]	7 MEDLINE, Embase to Jan 2016 and Cochrane reviews. Literature search strategy appendix 2	6 Study design, population, intervention	7 AMSTAR rating (appendix 4), appendix 1 methodological quality assessment of RCTs. Appendix 8 consider inconsistency, indirectness, imprecision (GRADE)	4 Internal review, vote 75%. Use agree II to develop recommendations	7 Balanced discussion	7 Clearly linked	7 From content expert and target users, provide feedback through online survey. Intended to facilitate dissemination of final guidance to Ontario practitioners. Section 5 gives comments and responses	5 Currency of each document is ensured through periodic review of the scientific literature. Methods in PEBC document assessment and review protocol	50 88
Lowrance, 2016 [197]; Cookson, 2015 [198]	6 <a href="http://www.auanet.org/guidelines/castration-resistant-prostate-cancer-(2013-amended-2015)">http://www.auanet.org/guidelines/castration-resistant-prostate-cancer-(2013-amended-2015)</a> --> there is an unabridged version of this guideline. MEDLINE, Embase, Cochrane, Scopus original 1996-2013. search strategy given	3 English describes outcomes and treatments of interest. No other info	6 Limitations of the literature section, rated methodological quality and provided overall judgement of the whole body of evidence. Used GRADE framework	4 Use evidence to formulate recommendations, if gap in evidence, will achieve consensus with modified Delphi	7 Balanced discussion. Have trade-off between clinical benefits and harms section	7 Clearly linked	4 Extensive peer review- 56 peer reviewers. Comments given, panel reviewed and discussed, and revised as needed	5 This document will continue to be periodically updated to reflect the growing body of literature. AUA amendment process - newly published literatures is reviewed and integrated into previously published guidelines	42 71
Basch, 2014 [199]	7 Systematic review by CCO (MEDLINE and Embase 2003-June 2012). Search strategy in data supplement	7 Eligible if they were RCTs with at least 50 pts per study, compared systemic therapy with placebo or other drug regimens in men with mCRPC. Outcomes of interest	6 Appendix of systematic review- methodological quality. Rated strength of recommendations	6 Methodology supplement: GLIDES methodology to formulate recommendations	7 Balanced discussion. Have trade-off between clinical benefits and harms section	6 Clearly linked	7 Disseminated for external review. In acknowledgement section: 14 US and Canadian external reviewers. External review section, asked a structured questionnaire	5 <a href="http://www.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/2014-mcrpc-ms.pdf">http://www.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/2014-mcrpc-ms.pdf</a> revision dates: annual intervals, examine current literature	51 90
NICE, 2014 [200]	7 MEDLINE, Embase, Web of Science, Cochrane, SSCI,	6 Search filters such as those to identify systematic reviews	7 Used GRADE	4 Had meetings to formulate recommendations.	7 Balanced discussion. Have trade-off between	7 Linking evidence to recommendations	6 Stakeholders comment on draft scope. Stakeholder	5 Updates are made in accordance with	49 85

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	SIGLE, Biomed Central until May 2013. search strategy in appendix	and randomised controlled trials were applied to the search strategies when necessary. No language restrictions, but foreign language papers not requested or reviewed. The scope sets the inclusion/exclusion criteria		Recommendations were discussed and agreed by the GDG. Where evidence was weak, GDG agreed through informal consensus	clinical benefits and harms section	statements	comments in History tab	NICE guideline development process. Updated as considered necessary	
Bader, 2012 [314]	6 MEDLINE, Embase, Cochrane 2000-2010. no full search strategy	2 No info	5 Assessed quality and level of evidence assigned. Recommendations graded. Used system modified from the oxford Centre for Evidence based Medicine	1 No info	7 Balanced discussion	6 Clearly linked	1 No info	2 No info	30 46
Cancer Council Australia, 2010 [202]	6 MEDLINE, Embase, CINAHL, Cochrane, Clinical Evidence, PsycINFO, until April 2006. search terms are available on request from the Australian Cancer Network		7 Assessed methodology. Also performed critical appraisal, produce levels of evidence	2 Formulate based on summarized body of evidence. No info on reaching consensus	7 Balanced discussion	7 Clearly linked	4 Public consultation. Feedback was reviewed, changes agreed by consensus. A final independent review of experts was conducted before submission	5 Review the guideline after a period not exceeding five years	38 63
<b>Palliative Care (Table 5)</b>									
<b>Cardiovascular/CHF</b>									
Amsterdam, 2014 [212]	6 MEDLINE, Embase, Cochrane, AHRQ reports until Oct 2012, some search terms reported	4 Study designs that were included, human subjects, English	7 Weight strength and quality of evidence. Study limitations in data supplement tables	2 No info	7 Balanced discussion	7 Clearly linked	2 Reviewed by two official reviewers each nominated by the ACC and AHA. Lists more reviewers.	5 To ensure that CPGs remain current, new data are reviewed biannually. A target cycle of 5 years is planned for full revisions	40 67
Van Kleef, 2011 [260]	5 PubMed, literature update to Sep 2010, search strategy given	2 Interventions listed. No other info	5 Ratings provided	2 No info	4 Lack discussion of harms	6 Clearly linked	4 Submitted for review and comments to the entire Dutch	3 Careful attention to this evolution is warranted and when necessary,	31 48

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
							speaking anesthesiologists pain physicians community. Questions and remarks were discussed and broad consensus was reached. Peer review in two stages. Submitted to the members of the associations of anesthesiologists with special interest for pain management from the Netherlands	an update of the guideline should be made	
NICE, 2011 [214]	7 MEDLINE, Embase, Cochrane, CINAHL, until 22 Oct 2010, search strategies reported, appendix D	7 English. Inclusion and exclusion criteria in appendix c	7 Appraised studies using the appropriate checklist. Study's methods in evidence tables (appendix e2). Grade profiles	2 No info	7 Section for trade off of benefits and harms	7 Clearly linked	7 Appendix b: stakeholder consultation comments table. For quality assurance	3 NICE will conduct an evidence review and consult with stakeholders to assess whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update	47 81
<b>Diabetes</b>									
Pop-Busui, 2017 [315]	7 Based on several technical reviews. Methods are given in these reviews	6 Criteria given in the technical reviews referenced	5 Recommendations are graded. Does not provide criteria for the grading. Evidence levels are assigned based on the strength of the published clinical evidence for the efficacy and safety of the agents for the treatment of DSPN pain	1 No info	7 Balanced discussion	7 Clearly linked	2 Reviewed by the American Diabetes Association Professional Practice committee but unsure if this group is external	1 No info	36 58
American Diabetes	3 Using MEDLINE,	2 Human studies	6 ADA evidence grading	2 No info	7 Balanced	7 A table linking the	3 ADA standards of	5 PPV performs an	35 56

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
Association, 2017 [216]	articles published since Jan 1 2016		system (Table 1). Recommendations are rated depending on the quality of evidence		discussion	changes in the recommendations to new evidence can be reviewed at <a href="http://professional.diabetes.org/SOC">http://professional.diabetes.org/SOC</a> .	care, position statements, and scientific statements undergo a formal review process by ADA's professional practice committee and the Board of directors. Readers who wish to comment on the 2017 Standards of Care are invited to do so.	extensive literature search and updates the standards of care annually	
Bril, 2011 [217]	5	4	6	2	5	7	2	1	32
	MEDLINE, Embase 1960-aug 2008, search terms reported. Appendix e-1	Treatment of PDN, defined the outcome measures clearly. Side effects of treatment and measures of function and QOL. Case reports and review articles were excluded	Classified according to the American Academy of Neurology classification of evidence scheme. In tables	No info	Lack discussion of harms	Clearly linked	Drafts have been reviewed by at least three AAN committees, a network or neurologists, neurology peer reviewers and representatives from related fields	No info	50
NICE, 2015 [218]	7	7	7	2	7	7	6	5	48
	MEDLINE, Embase and Cochrane. Searches updated on Aug 2014. Searches were undertaken according to the parameters stipulated within the guidelines manual 2012. Search strategy in Appendix F	English only. Appendix C	Appraised using the appropriate checklist as specified in the guidelines manual. Info reported in GRADE tables	Done informally. Formally for economic model. Agreed through discussion	Section for trade off of benefits and harms	Clearly linked	In history there are stakeholder's comments and developer's response	2 years' time when NICE next considers updating this guideline. Considering setting up a standing committee for diabetes	83
Health Improvement Scotland, 2013 [220]	7	1	6	3	7	7	5	5	41
	MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, 2003-2009; search strategy online	No info	Graded levels of evidence, and grading for recommendations	From manual: usually the GDG forms recommendations through informal consensus	Balanced discussion	Clearly linked	Specialist review group (independent expert referees) comment on comprehensiveness and accuracy guideline group addressed every	Considered for review in three years	69



## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
							comment, sign editorial group reviews guideline		
Pluijms, 2011 [221]	5 PubMed Nov 2008-oct 2010, search strategy given	2 Interventions listed. No other info	6 Ratings and discussion in the text	2 No info	6 Balanced discussion	6 Clearly linked	4 Submitted for review and comments to the entire Dutch speaking anesthesiologists pain physicians community. Questions and remarks were discussed and broad consensus was reached. Peer review in two stages. Submitted to the members of the associations of anesthesiologists with special interest for pain management from the Netherlands	3 Careful attention to this evolution is warranted and when necessary, an update of the guideline should be made	34 54
Dubinsky, 2010 [266]	5 MEDLINE, Cochrane to Apr 2009, search terms	5 Inclusion criteria were clinical trials of TENS compared to placebo or to another therapy for well-defined painful neurologic disorders with more than 10 subjects	6 Classified evidence and recommendations	2 No info	3 Lack discussion of harms	7 Clearly linked	2 Drafts have been reviewed by at least three AAN committees, a network of neurologists, neurology peer reviewers and representatives from related fields	1 No info	31 48
<b>Multiple Sclerosis</b>									
Paolucci, 2016 [268]	6 PubMed, Embase, Cochrane library. 1983-2013 and updated to 2015. Keywords given. Example Search strategy given	1 No info	5 Strength of recommendations was scored according to a scale ranging from A to GPP. Evidence was scored according to the Oxford 2011 levels of evidence	1 No info	6 Balanced discussion	7 Clearly linked	1 No info	1 No info	28 42
Yadav, 2014 [52]	7 MEDLINE, web of	2 No info	7 Classified articles	2 No info	6 Balanced	7 Clearly linked	2 Drafts have been	1 No info	34 54

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	science, Embase, Cochrane, allied and complementary medicine 1970-2011. search strategy for MEDLINE reported, relies heavily on index/MESH terms/ search strategies in appendix e-3 and e-4		according to American Academy of Neurology therapeutic scheme. Discussed in text		discussion		reviewed by at least three AAN committees, a network or neurologists, neurology peer reviewers and representatives from related fields		
NICE, 2014 [224]	7 MEDLINE, Embase, Cochrane until Feb 2014, search strategy reported in appendix F	7 English. Inclusion and exclusion criteria in appendix c	7 Used GRADE, provided GRADE tables	3 Informal consensus. Consensus recommendations were done through discussions in the GDG	7 section for trade off of benefits and harms	7 Clearly linked	7 In history section, there is document for stakeholder consultation comments and responses. For quality assurance	3 Nice will conduct an evidence review and consult with stakeholders to assess whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update	48 83
<b>Neurodegenerative Diseases (Parkinson, ALS, dementia)</b>									
NICE, 2016 [226]	7 MEDLINE, Embase, Cochrane, CINAHL, PsycINFO until May 2015, search strategy reported in appendix f	7 English. Inclusion and exclusion criteria in appendix c	7 Used GRADE, provided GRADE tables	3 Consensus recommendations were done through discussions in the GDG. Informal	7 Section for trade off of benefits and harms	7 Clearly linked	7 In history section, there is document for stakeholder consultation comments and responses. For quality assurance	3 NICE will conduct an evidence review and consult with stakeholders to assess whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update	48 83
Bartolo, 2016 [273]	6 PubMed, Embase, Cochrane library. 1983-2013 and updated to 2015. Keywords given. Example Search strategy given	1 No info	5 Strength of recommendations was scored according to a scale ranging from A to GPP. Evidence was scored according to the Oxford 2011 levels of	2 There was unanimous consensus regarding the utility of multidisciplinary approach. No other info	5 Lack discussion of harms	7 Clearly linked	1 No info	1 No info	28 42

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
EFNS, 2012 [272]	4 MEDLINE, Embase, science citation index, Cochrane trials and others, 2008-Feb 2011. no search terms or full search strategy	2 No constraints based on language or publication status	5 Recommendations rated from A to GCPP. Evidence class also rated	5 Consensus of an expert panel. All recommendations had to be agreed to by all members of the task force unanimously	6 Balanced discussion	6 Clearly linked	1 No info	1 No info	30 46
<b>Rheumatoid Arthritis</b>									
Whittle, 2012 [228]	4 MEDLINE, Embase, Cochrane until April 2016; plus 2008-09 EULAR/ACR abstracts. No search terms of full search strategy	3 Predetermined inclusion and exclusion criteria. Restricted to those published in languages in which at least one member of the bibliographic group was fluent	6 Oxford levels of evidence. Trials assessed for risk of bias according to Cochrane collaboration.	6 Used discussion and formal voting system (modified Delphi). Level of agreement found in table 1	7 Balanced discussion	7 Clearly linked	1 No info	1 No info	35 56
Brosseau, 2012 [242]	4 MEDLINE, Embase, current contents, CINAHL, SUMSearch, Cochrane trials until June 2010. no search terms or full search strategy	7 Inclusion/exclusion criteria table 1	6 Methodological quality assessed using Jadad scale, and reported in the results section. Recommendation grade also given	2 Consensus meeting. No other info	3 Lack discussion of harms	7 Clearly linked	5 Externally reviewed to assess clinical usefulness and ensure relevance of findings. Five practitioners. Asked to comment on four questions	1 No info	35 56
SIGN, 2011 [243]	7 MEDLINE, Embase, Cochrane 2003-jan 2009; search strategy reported online	1 No info	6 Graded levels of evidence, and grading for recommendations	3 From manual: usually the GDG forms recommendations through informal consensus	7 Balanced discussion	7 Clearly linked	5 Draft was available for public consultation and specialist review. Specialists were asked to comment on comprehensiveness and accuracy. The guideline group addresses every comment made by the external reviewer	5 Considered for review in three years	41 69
Ataman, 2011 [244]	4 MEDLINE, Cochrane, Embase, Turkish medical	2 Included study designs	6 Levels of evidence were determined. Oxford centre for	5 Delphi. A consensus was reached for all recommendations and	7 Balanced discussion	7 Clearly linked	1 No info	2 Recommendation s....should be regularly updated	34 54

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	index 2009-2010 (pharmacological) or 2007-2010 (non-pharmacological)		evidence based medicine was used to assess the strength of recommendations and level of evidence	their strength levels were voted upon. Description of Delphi rounds given.					
NICE, 2009 [245]	4 MEDLINE, Embase, Cochrane, CINAHL until 2008. no search terms or full search strategy	4 Conference paper abstract and non-English papers were excluded. Exclusion criteria: non UK related population.	7 Evidence was appraised. Grade levels given. Discussion in text	3 Formal consensus: at the end of the guideline development process the GDG met to review and agree the guideline recommendations. No other information about how consensus was reached, or extent of consensus	7 Balanced discussion	7 Clearly linked	6 Submitted for formal public and stakeholder consultation. In history section, there is a document for stakeholder comments and responses.	3 NICE will ask a National Collaborating Centre to determine whether the evidence base has progressed significantly enough to alter the guideline recommendations and warrant an update	41 69
Forestier, 2009 [247]	6 MEDLINE, Embase, CINAHL, Pascal, Cochrane, HTA, PEDRO 1985-2006, search terms and results reported	6 Inclusion criteria. Had to be RCT, in French or English, refer to adult RA patients, endpoints given	6 Each study was allocated an evidence level. Grade of guideline depended on the evidence level	4 Consensus voting (at least 15 out of 18 members in agreement)	4 Lack discussion of harms	7 Clearly linked	5 Submitted to external peer review. 60 peer reviewers. Recommendations allocated scores between 7 and 9 by fewer than 85% of the peer reviewers were revised by the working group	1 No info	39 65
Seegenschmiedt, 2015 [275]; Reichl, 2015 [276]; Ott, 2015 [277]	3 MEDLINE, PubMed, Cochrane + pertinent clinical information. No other info	2 "Presentation of the selection criteria for the evidence, in particular exclusion grounds" no other info	6 "Determine strength of evidence and strength of the recommendation" discussion of limitations in text	3 First consensus draft was opened to propositions and comments from all participating institutions according to the established Delphi process	5 Lack discussion of harms	6 Clearly linked	2 No info	2 No info	29 44
Hennessy, 2016 [300]	6 MEDLINE, Embase, CINAHL, AMED, PEDRO, Cochrane until Aug 2015; search strategy reported for MEDLINE	7 Selection criteria reported	6 Critical appraisal with AGREE II	2 Determination of whether a guideline was high or low quality was informed by the overall quality score and made at the discretion of the reviewers following	3 There is not really evidence for benefits and harms	3 Recommendations based on existing guidelines... not really directly linked to the "evidence"	1 No info	1 No info	29 44

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
Lau, 2015 [248]	6 Embase, MEDLINE, google scholar, Scopus Jan 2000-dec 2013; search terms reported	6 Clinical practice guidelines or consensus statements for adult RA populations, published in English, AP region,	6 AGREE, translated each guideline's grading system into a systems suggested by SIGN	5 Consensus was achieved using Delphi, statements were included as recommendations provided more than 80% of members participated in voting and more than 50% voted in favour of the outcome. Setting the acceptance margin to 70% resulted in exclusion of many questions considered important during meeting discussions	7 Balanced discussion	7 Summarizes both the source guidelines and original evidence presented in source guidelines	3 2 reviewers for comments. Feedback from the respondents was used to finalize recommendations	1 No info	41 69
<b>Stroke</b>									
Hebert, 2016 [249]	3 2012-2015. Databases may include Embase, CINAHL, PubMed, ProQuest, PsycINFO, AMED and Scopus. No other info	2 No info	6 Recommendations were assigned a level of evidence	2 Consensus. No other info	7 Balanced discussion (online)	7 Summary of evidence found online	3 External review by 20 Canadian and international experts, all feedback was reviewed and addressed by the writing group members	7 Undergo a thorough formal review and update of each chapter every two years. Details about update cycle and process given	37 60
Paolucci, 2016 [268]	6 PubMed, Embase, Cochrane library. 1983-2013 and updated to 2015. Keywords given. Example Search strategy given	1 No info	5 Strength of recommendations was scored according to a scale ranging from A to GPP. Evidence was scored according to the Oxford 2011 levels of evidence	1 No info	6 Balanced discussion	7 Clearly linked	1 No info	1 No info	28 42
Stroke Foundation of New Zealand, 2010 [251]	6 MEDLINE, Embase, Cochrane for all questions; CINAHL, PsycINFO, PEDro for some. Searched until sometime in the period May-Aug 2009 with update 19 Feb 2010 in MEDLINE and Embase. Indicates	6 Inclusion criteria in appendix 2: type of study, type of participant, language	6 Based on forms adapted from GIN and SIGN. Developed draft recommendations based on NHMRC matrix. NHMRC draft grade of recommendation matrix	3 Final decisions were made by informal group processes	7 Balanced discussion	7 Clearly linked	6 Acknowledgement s section- individuals who gave formal responses in the public and professional consultation, peer review. A specific feedback form was circulated.	5 Aims to update the guidelines every three to 5 years	46 79

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	search strategies are available from NSF						Responses were developed. Summary of some of the comments		
National Stroke Foundation, 2010 [298]	6 MEDLINE, Embase, Cochrane for all questions; CINAHL, PsycINFO, PEDro for some. Searched until sometime in the period May-Aug 2009 with update 19 Feb 2010 in MEDLINE and Embase. Indicates search strategies are available from NSF	6 Inclusion criteria in appendix 2: type of study, type of participant, language	6 Based on forms adapted from GIN and SIGN. Developed draft recommendations based on NHMRC matrix. NHMRC draft grade of recommendation matrix	3 Final decisions were made by informal group processes	7 Balanced discussion	7 Clearly linked	6 Acknowledgement s section- individuals who gave formal responses in the public and professional consultation, peer review. A specific feedback form was circulated. Responses were developed. Summary of some of the comments	5 Aims to update the guidelines every three to 5 years	46 79
SIGN, 2010 [252]	6 MEDLINE, Embase, CINAHL, PsycINFO, PEDro, Cochrane 2002-2009. search strategy should be available online	1 No info	6 Graded levels of evidence, and grading for recommendations	3 From manual: usually the GDG forms recommendations through informal consensus	7 Balanced discussion	7 Clearly linked	5 Draft was available for public consultation and specialist review. Specialists were asked to comment on comprehensiveness and accuracy. The guideline group addresses every comment made by the external reviewer	2 Is itself and update, no other info	37 60
<b>Other: Pressure Ulcers</b>									
National Pressure Ulcer Advisory Panel et al, 2015 [253]	7 PubMed, CINAHL, MEDLINE, Embase, Scopus, biomedical reference collection, health business elit, Cochrane, HTA, AMED until July 1 2013, search strategy	7 Inclusion and exclusion criteria reported	7 Methodological quality assessed using SIGN tool. Level of evidence reported and strength of evidence ratings. Critical appraisals given in separate document	3 Consensus voting process (GRADE). No other info about steps of consensus or extent of consensus reached	4 Adverse events reported in the included research have been reported in the evidence summaries and caution statements. Evidence not reported in quick reference guide	2 The quick reference guide does not link evidence to recommendations. Perhaps it is available in the full guideline but that one needs to be paid for	5 Ensures that all relevant evidence had been included and comment on the draft guideline. Number of stakeholders reported. GDG reviewed all stakeholder comments	5 GDG will continue to monitor the pressure ulcer literature after the 2014 guideline has been published. Another revision is planned for 2019	40 67
<b>Other: Restless Leg Syndrome</b>									

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
Winkelman, 2016 [254]	7	6	6	1	6	6	2	1	35
	MEDLINE, Embase, and Science Citation Index to July 2015, search strategy included	Inclusion/exclusion criteria in data supplement	Evidence level and recommendation strength reported	No info	Balanced discussion	Clearly linked	Drafts of the guidelines have been reviewed by at least 3 AAN committees, a network of neurologists, neurology peer reviewers and representatives from related fields	No info	56
Garcia-Borreguero, 2013 [255]	4	6	6	5	7	7	3	1	39
	MEDLINE, CINAHL, clinicaltrials.gov; search terms reported. Estimated period of search to 2012. Some search terms given	Inclusion/exclusion criteria reported: any pharmacological treatment of RLS, any language, study duration minimum 6 months	Studies categorized according to evidence level of the AHCRC and EFNS grading systems. Rated recommendations as well	Reached consensus on each recommendation. Defined by at least 80% of the members of the task force agreeing on a clinical recommendation	Additional tables were developed for adverse events. Balanced discussion	Clearly linked	Members of the IRLSSG were given an opportunity to comment on the recommendations	No info	65
Garcia-Borreguero, 2012 [256]	6	6	6	2	7	7	1	2	37
	MEDLINE, Embase, CINAHL Jan 2005-dec 31 2011. search terms reported	Only studies that clearly diagnosed RLS according to the essential criteria were included, study designs, English, types of outcome measures	Risk of bias was assessed. Studies were classified according to type of study design. Rating of recommendation	No info	Balanced discussion	Clearly linked	No info	Is itself an update. No other info	60
Aurora, 2012 [257]	6	6	7	2	7	7	3	3	41
	MEDLINE to Aug 2010, updated June 29, 2011. Keywords given	Limits of the search were: humans, English, all adults, study design, benefit/efficacy or harm data	Grade system used. Level of recommendations also rated. Presented in tables	No info about decision making process	Benefit vs. harm analysis conducted	Clearly linked	Recommendations were critically reviewed by and outside expert and the concerns that were raised were addressed by the spc	Will be reviewed, updated, and revised as new information becomes available	69
<b>Assessment (Table 6)</b>									
Kaasa, 2011 [294]	6	6	3	5	2	2	2	3	29
	Consensus conference with presentations based upon published systematic reviews. The systematic reviews have info about databases,	Criteria in the SRs referenced	Some evaluation of methodology in the SR papers	Consensus. Describes some steps for arriving at the recommendations. But don't know the consensus method. Says the present position paper was unanimously acknowledged by all as	Lack discussion of harms. As for benefits: "improve patient care by facilitating communication between clinicians, aid in	I don't think it is clear how the evidence supports the use of these assessments	Externally peer reviewed. No other info	We anticipate that revisions will be needed, based on clinical experience and ongoing, planned empirical studies	44



## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	search dates, search terms			the product of the expert consensus	the evaluation of treatment outcomes and compare the patient cohorts with samples from research reports". But this is not really supporting data				
Harrington, 2014 [285]	7 PubMed, CINAHL, PsycINFO Apr 2012 to June 1 2013; search strategy reported	6 Breast cancer population. Studies of assessment methodology, pain prevalence and epidemiology were included. Excluded articles that only measured acute surgical procedure pain and also references where pain was not a primary end point. Limited to English	7 Primary reviews of the assessment tools were completed using the Cancer EDGE Task Force Outcome Measure Rating Form. Reliability, validity, availability of normal values, MCID, MDC, clinical utility. Give EDGE rating	4 Based on established criteria, researchers came to consensus on a list of pain outcome measures. No other info about methods/degree of consensus. But consensus only had to be reached between 3 people	6 Discussion of benefits and drawbacks of certain assessment methods	6 Clearly linked	1 No info	1 No info	38 63
Haanpaa, 2011 [286]	6 MEDLINE and Cochrane: 1950-2008 for topics not in EFNS guideline; 2002-2008 for topics in EFNS guideline. There is a search strategy in appendix 1	6 Searches were limited to original articles published in English. Only full original communications were included. Only studies with definite and probable neuropathic pain conditions were included. Included study design depends on if the topic had high quality publications or not. Appendix 1 has more details and inclusion/exclusion for epidemiological papers.	7 Class of the study given in the evidence table. Classification of evidence and recommendation grading adhered to the EFNS standards. Criteria used to evaluate outcome measures: specificity, sensitivity and reliability in neuropathic pain and availability in different cultures and languages	2 Prepared guidelines according to the EFNS guidance (ref 55). No info on reaching consensus	6 Discussion of benefits and drawbacks of certain assessment methods	7 Clearly linked	4 Ref 55- the scientific committee will have the guideline reviewed by its members, the president of the EFNS and the chairpersons of any Scientist Panels which might be affected by the guidelines but where not involved in the preparation	5 Ref 55- the validity of published guidelines will be reviewed by the chairpersons of the Task Force and the relevant Scientist Panel at least every 2 years. Is itself an update	43 73
Crucchi, 2010	5	1	7	2	6	7	4	5	37

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[288]	MEDLINE, Cochrane, 2004-2009. Search methods adhered to those used in previous guidelines. Can't find full search strategy	No info	Rated according to the EFNS method of classification for diagnostic procedures. Give evidence levels. Rating of recommendations	Prepared guidelines according to the EFNS guidance (ref 2). No info on reaching consensus	Discussion of benefits and drawbacks of certain assessment methods	Clearly linked	Ref 2- the scientific committee will have the guideline reviewed by its members, the president of the EFNS and the chairpersons of any Scientist Panels which might be affected by the guidelines but were not involved in the preparation of them.	Ref 2- the validity of published guidelines will be reviewed by the chairpersons of the Task Force and the relevant Scientist Panel at least every 2 years. Is itself an update	60
Herr, 2010 [291]	6 PubMed, CINAHL, PsycINFO Apr 2004 to July 2008, search terms reported. No full search strategy	2 Exclusion: did not use reproducible pain assessment tools	7 Table 1: created criteria for rating tools for assessing pain. Table 3 scores for relevance, reliability, validity, utility	4 Ratings were given. The collaboration decided that more than 50% of the 10 reviewers had to recommend the instrument to be included in the final review. consensus of experts	7 Discussed strength and limitation of tools.	6 Clearly linked	1 There were "expert consultants" but I don't think they were external because they were involved in developing the criteria and rating the tools	2 Is itself an update. No other info	35 56
Douglas, 2014 [65]	3 No details of search given. But would have used ACR methodology: PubMed, MEDLINE, general classes of keyword are related to the condition and describe the diagnostic or therapeutic intervention	3 ACR methodology: humans, may restrict to adults/pediatrics only, exclude if only summaries or case reports	5 Study quality rating given in evidence tables. Categories for rating are given in ACR methodology	4 Modified Delphi, (ACR methodology) consensus is defined as 80% agreement, a maximum of 3 rounds may be conducted	5 Lack discussion of harms	7 Clearly linked	1 No info	5 Reviewed every 2 years by a multidisciplinary panel	33 52
Spinelli, 2014 [292]	7 PubMed, PEDro, EBSCOhost, MEDLINE, PsycINFO, Cochrane to Dec 2013. Search terms given. Search strategy given in	6 Inclusion/exclusion criteria: outcomes, English, include all study designs	5 Outcome measure rating form (appendix 1). Not done at the study level	3 2 investigators rated. Disagreements were brought for discussion, agreed upon as a group. No information on consensus	6 I don't think this section is actually very relevant to the guideline	7 Clearly linked	1 No info	1 No info	36 58

## Evidence Summary 18-4

Agree II item Reference	7. Systematic methods for evidence search.	8. Clearly described evidence selection criteria	9. The strengths and limitations of the body of evidence are clearly described.	10. The methods for formulating the recommendations are clearly described.	11. Considered health risks and benefits in recommendations	12. Explicit link between recommendations and evidence.	13. Externally reviewed by experts	14. Updating procedure provided.	Total; Domain score <sup>13</sup>
	figure 1								
Eden, 2014 [293]	7	6	5	3	6	7	1	1	36
	PubMed, PEDro, EBSCOhost, MEDLINE, PsycINFO, Cochrane to June 2013. Search terms given. Search strategy given in figure 1	Inclusion/exclusion criteria: outcomes, English, include all study designs	Outcome measure rating form (appendix 1). Not done at the study level	2 investigators rated. Disagreements were brought for discussion, agreed upon as a group. No information on consensus	I don't think this section is actually very relevant to the guideline	Clearly linked	No info	No info	58

Abbreviations: AAN, American Academy of Neurology; ACC, American College of Cardiology; ACS, acute coronary syndrome; ADA, American Diabetes Association; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; ASCO, American Society of Clinical Oncology; CDC, Centers for Disease Control and Prevention; CNCP, chronic non-cancer pain; DSG, Disease Site Group; EFNS, European Federation of the Neurological Societies; GDG, Guideline Development Group; GIN, Guidelines International Network; JCO, Journal of Clinical Oncology; LOE, level of evidence; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence; NNH, number needed to harm; NNT, number needed to treat; OIBD, opioid-induced bowel dysfunction; PDN, painful diabetic neuropathy; RCT, randomized controlled trial; RT, radiation therapy; SIGN, Scottish Intercollegiate Guidelines Network; SR, systematic review; SRE, skeletal-related events; USP-STF, U.S. Preventive Services Task Force

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