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Survivorship: Pain Version 1.2014:

Clinical Practice Guidelines in Oncology

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Pain in Survivors

More than one-third of posttreatment cancer survivors experience chronic pain, which often leads to psychological distress; decreased activity, motivation, and personal interactions; and an overall poor quality of life.[1-5] Pain in survivors is often ineffectively managed. Barriers to optimal pain management in cancer survivors include health care providers' lack of training, fear of side effects and addiction, and reimbursement issues.[6]

Pain has 2 predominant mechanisms: nociceptive and neuropathic.[7,8] Injury to somatic and visceral structures and the resulting activation of nociceptors present in skin, viscera,

NCCN Categories of Evidence and Consensus

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Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.
All recommendations are category 2A unless otherwise noted.
Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Please Note

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Disclosures for the NCCN Survivorship Panel

At the beginning of each NCCN Guidelines panel meeting, panel members review all potential conflicts of interest. NCCN, in keeping with its commitment to public transparency, publishes these disclosures for panel members, staff, and NCCN itself.
Individual disclosures for the NCCN Survivorship Panel members can be found on page 500. (The most recent version of these guidelines and accompanying disclosures are available on the NCCN Web site at NCCN.org.)

These guidelines are also available on the Internet. For the latest update, visit NCCN.org.

muscles, and connective tissues cause nociceptive pain. Somatic nociceptive pain is often described as sharp, throbbing, or pressure-like, and often occurs after surgical procedures. Visceral nociceptive pain is often diffuse and described as aching or cramping. Neuropathic pain is caused by injury to the peripheral or central nervous system and might be described as burning, sharp, or shooting. Neuropathic pain often occurs as a side effect of chemotherapy or radiation therapy or is caused by surgical injury to the nerves.

Screening for and Assessment of Pain

All cancer survivors should be screened for pain at regular intervals. If pain is present, the intensity should be quantified by the survivor. Because pain is inherently subjective, self-report of pain is the current standard of care for assessment. Intensity of pain should be quantified using a 0 to 10 numeric rating scale, a categoric scale, or a pictorial scale (eg, Wong-Baker FACES Pain Rating Scale).[9-12] In addition, the survivor should be asked to describe the characteristics of the pain (eg, aching, burning). Severe uncontrolled pain is a medical emergency and should be responded to promptly. An oncologic emergency also should be ruled out in these cases.

A comprehensive evaluation, as outlined in the NCCN Guidelines for Adult Cancer Pain (available at NCCN.org), is essential to ensure proper pain management. The cause and pathophysiology of the pain should be identified to determine the optimal therapeutic strategy. In addition, the survivor's goals for comfort and function should be determined.

Management of Pain

The goals of pain management are to increase comfort, maximize function, and improve quality of life. A multidisciplinary approach is recommended, with a combination of pharmacologic treatments, psychosocial and behavioral interventions, physical therapy and exercise, and interventional procedures.[2,13,14]

The NCCN Survivorship Panel made recommendations for the management of 8 categories of cancer pain syndromes: neuropathic pain, chronic postoperative pain (ie, pain syndromes after amputation, neck dissection, mastectomy), myalgias/arthralgias, skeletal pain, myofascial pain, gastrointestinal/urinary/pelvic pain, lymphedema, and postradiation pain. Neuropathic pain commonly results from some systemic anticancer agents.[1] The incidence of chronic pain after surgical treatment varies with the type of procedure and is as high as 60% in patients treated with breast surgery and 50% in those treated with lung surgery.[1] Arthralgias, characterized by joint pain and stiffness, occur in roughly half of women taking aromatase inhibitors as adjuvant therapy for breast cancer.[15] Pelvic pain often occurs after pelvic radiation, resulting from fractures, fistulae, proctitis, cystitis, dyspareunia, or enteritis.[1]

Pharmacologic interventions, local therapies, psychosocial support and behavioral treatments, physical therapy and exercise, and interventional procedures are discussed. For more information about the management of cancer-related pain, please see the NCCN Guidelines for Adult Cancer Pain (to view the most recent version of these guidelines, visit NCCN.org). These guidelines include information on opioid use and pain treatment

agreements for patients at risk for medication misuse or diversion; adjuvant analgesics; and psychosocial support and behavioral interventions that may be modified to fit the individual survivor's circumstances.

Pharmacologic Interventions

Pharmacologic measures are the foundation of treatment of many of the common pain syndromes in survivors. Pharmacologic recommendations in these guidelines vary depending on the pain syndrome and include opioids, adjuvant analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), and muscle relaxants.[2,16-18] Topical medications are discussed in "Local Therapies" (see page 497).

Opioids—Opioids may be recommended for the treatment of neuropathic, postoperative, and skeletal pain. Data on the long-term use of opioids in survivors are lacking.[14,17,19]

The NCCN Guidelines for Adult Cancer Pain (available at NCCN.org) recommend screening survivors for risk factors of aberrant opioid use or diversion of pain medication, using a detailed patient evaluation or tools such as the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) or Opioid Risk Tool (ORT), before prescribing.[20-24] In addition, if opioids are deemed necessary for any survivor (regardless of aberrant use risk level), the NCCN Survivorship Panel recommends using the lowest dose possible and reevaluating the effectiveness and necessity of opioids on a regular basis. Pain treatment agreements can also be considered.[25]

Adjuvant Analgesics—Adjuvant analgesics include antidepressants (eg, serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants), anticonvulsants (eg, gabapentin, pregabalin), and corticosteroids. These are recommended for the treatment of neuropathic and postoperative pain in survivors. The term *adjuvant* refers to the fact that they are often coadministered with an opioid to enhance analgesia or reduce the opioid requirement, but they may also be used as sole pain treatment. A recent systematic review found that antidepressants, anticonvulsants, other adjuvant analgesics, and opioids were all effective at reducing neuropathic pain in patients with cancer.[17] Another review found that antidepressants and antiepileptics provide additional neuropathic pain relief when added to opioids in patients with cancer.[26]

Tricyclic antidepressants have been shown to relieve neuropathic pain in the noncancer setting.[27,28] In addition, the SNRI duloxetine was recently shown to effectively reduce pain in a multiinstitutional, randomized, double-blind, placebo-controlled crossover trial of 231 patients with painful chemotherapy-induced neuropathy.[29]

The most commonly used anticonvulsant drugs for the treatment of cancer-related pain, gabapentin and pregabalin, have primarily been studied in noncancer neuropathy syndromes.[30,31] Only limited data support the effectiveness of corticosteroids for cancer-related pain, and these may also have anti-inflammatory effects.[32-34]

NSAIDs—NSAIDs are recommended for the treatment of myofascial and skeletal pain and for myalgias and arthralgias. NSAIDs are nonopioid analgesics that block the biosynthesis

of prostaglandins, which are inflammatory mediators that initiate, cause, intensify, or maintain pain. A recent systematic review found that data supporting the use of NSAIDs for control of pain in patients with advanced cancer are limited and weak, but suggest some efficacy at reducing pain and opioid dose requirement.[35]

A discussion of contraindications and safety precautions that should be considered before prescribing NSAIDs is provided in the NCCN Guidelines for Adult Cancer Pain (to view the most recent version of these guidelines, visit NCCN.org).

Muscle Relaxants—Muscle relaxants (eg, diazepam, lorazepam, metaxalone) reduce muscle spasm and are recommended for the treatment of skeletal pain, myalgias, and arthralgias. Evidence for their efficacy in providing pain relief in the noncancer settings is limited.[36,37] No data could be found in the setting of cancer-related pain.

Psychosocial Support and Behavioral Interventions

Cognitive interventions are aimed at enhancing a sense of control over the pain or its underlying cause. Breathing exercises, relaxation, imagery or hypnosis, and other behavioral therapies can be very useful.[3,38-43] Psychosocial support and education should also be provided.[44] Some studies in patients with cancer suggest that psychosocial and behavioral interventions such as skills training, education, relaxation training, supportive–expressive therapy, and cognitive behavioral therapy may be effective at reducing pain.[40,45] Hypnosis can also be considered for treatment of neuropathic pain. Overall, data support the benefit of hypnosis for controlling pain in cancer and other settings, but are lacking in the survivorship population.[46]

In general, studies regarding psychosocial support and behavioral interventions for reducing pain in survivors are limited. A recent systematic review and meta-analysis assessed the efficacy of psychosocial interventions for treating pain in patients with breast cancer and survivors.[47] Although results suggest an effect, more studies are clearly needed in the survivorship population.

Physical Therapy and Exercise

Physical therapy and general exercise may also be effective for the treatment of pain in survivors, with the main goal of increasing mobility.[3,13,48,49] Several randomized controlled trials have reported a reduction of neck and shoulder pain associated with exercise or therapy programs.[50-52] In one study, 52 survivors of head and neck cancer were randomized to a progressive-resistance exercise training (PRET) program or standard therapeutic exercise for 12 weeks.[52] Pain scores decreased more dramatically in the PRET group (P=.001). In another study of 66 survivors of breast cancer, those randomized to an 8-week water exercise program experienced a greater reduction of neck and shoulder pain than those randomized to usual care.[50] In addition, group exercise in the community, with trainers specifically trained to work with cancer survivors, has been shown to reduce pain and other symptoms.[53]

Local Therapies

Local therapies, including heat, cold packs, massage, medicated creams, ointments, and patches, are recommended for the treatment of myalgias, arthralgias, and neuropathic and myofascial pain.[3] Specifically, topical lidocaine, capsaicin, ketamine, and amitriptyline are recommended for treatment of some of the various cancer pain syndromes. Data are limited on the effectiveness of ketamine and amitriptyline,[54-59] but the evidence for the effectiveness of lidocaine and capsaicin is stronger.[54,56-58] In a randomized trial of 35 patients with non–cancer-related postherpetic, postoperative, or diabetes-related neuropathic pain, pain intensity was reduced with topical lidocaine but not with topical amitriptyline when compared with placebo.[57] A larger trial with a similar population of 92 patients found no effect of topical amitriptyline, ketamine, or a combination of the two.[60] Another study found that a higher dose of amitriptyline had some efficacy in reducing peripheral neuropathy, but also showed systemic effects.[61] Lidocaine has been shown to reduce the severity of postherpetic neuropathy and cancer-related pain.[62,63]

Interventional Procedures

Referral to pain management services for interventional procedures, including transcutaneous electrical nerve stimulation (TENS), intercostal nerve blocks, and dorsal column stimulation, is recommended for refractory pain in survivors. Data on the efficacy of these interventions are mainly from patients with active cancer or the noncancer setting.[3,64] TENS is a noninvasive procedure with electrodes placed in or around the painful area.[3] A recent systematic review found that data supporting the efficacy of TENS for reducing cancer-related pain are inconclusive.[65]

The goal of invasive interventions, such as an intercostal nerve block, is to interrupt nerve conduction by either destroying nerves or interfering with their function.[3] The data on these interventions are also limited.[3]

Acupuncture

Acupuncture is recommended as an option for the treatment of myofascial pain in survivors. Evidence supporting the efficacy of this technique for reducing cancer-related pain is extremely limited.[66,67]

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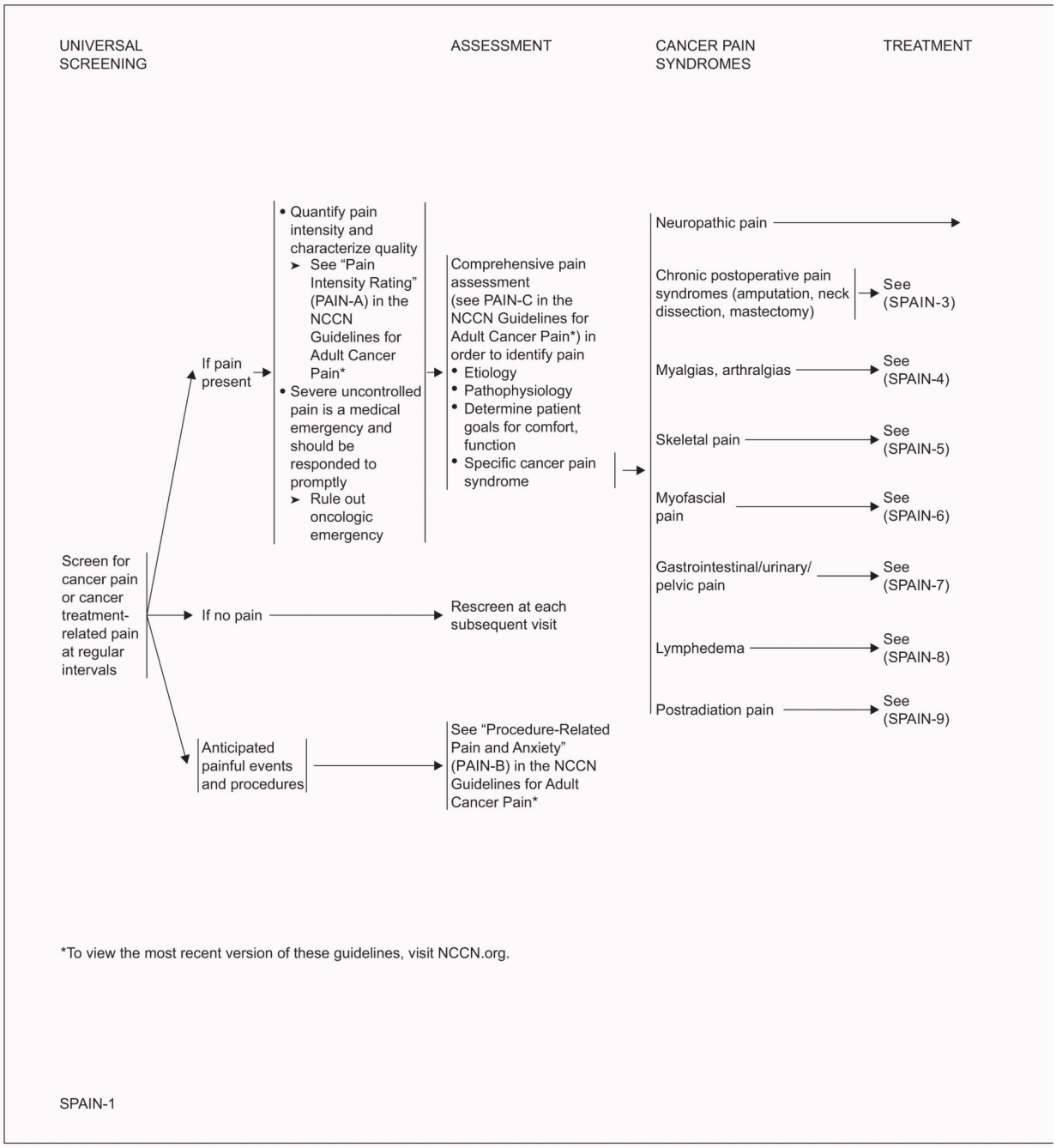

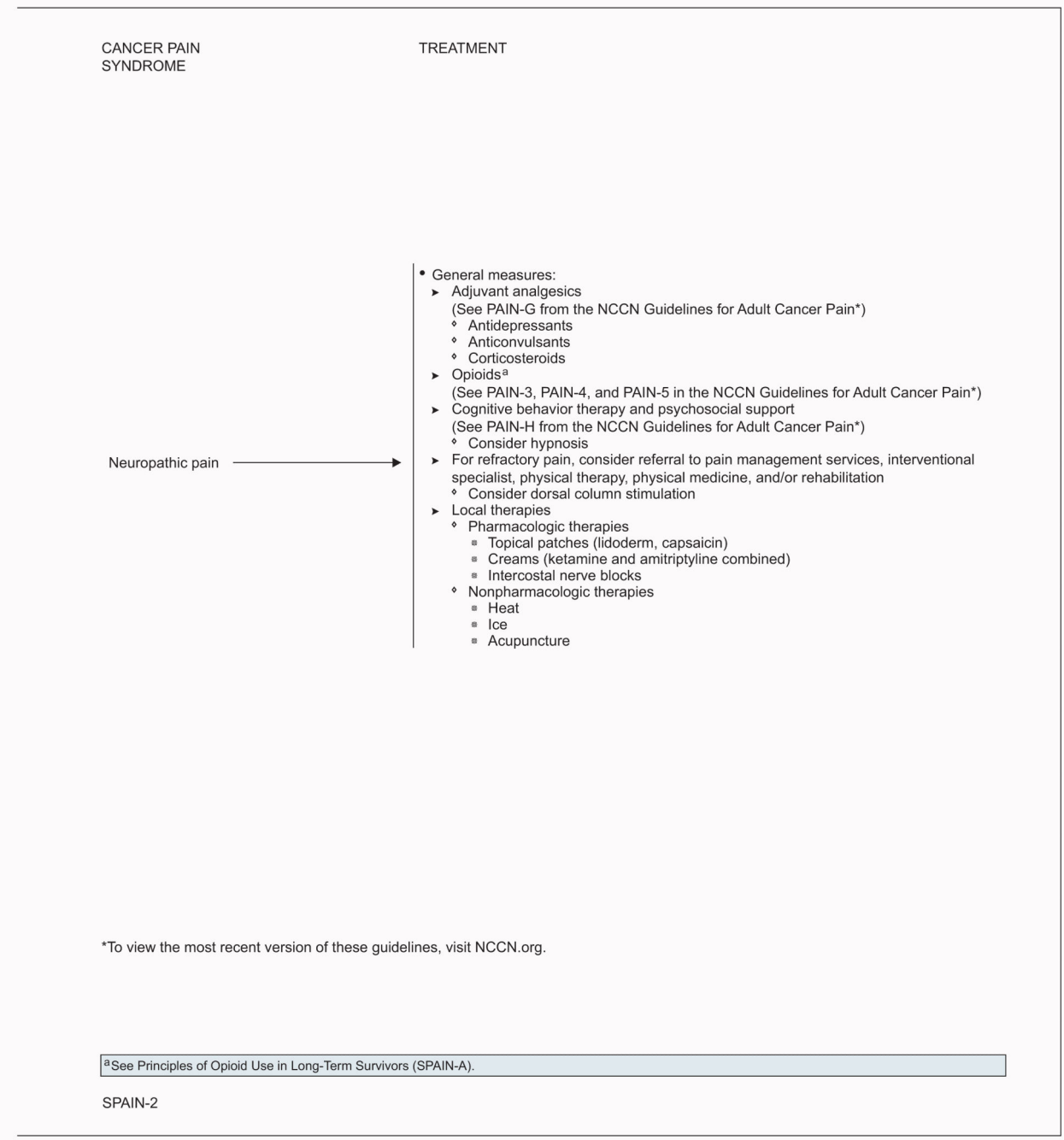

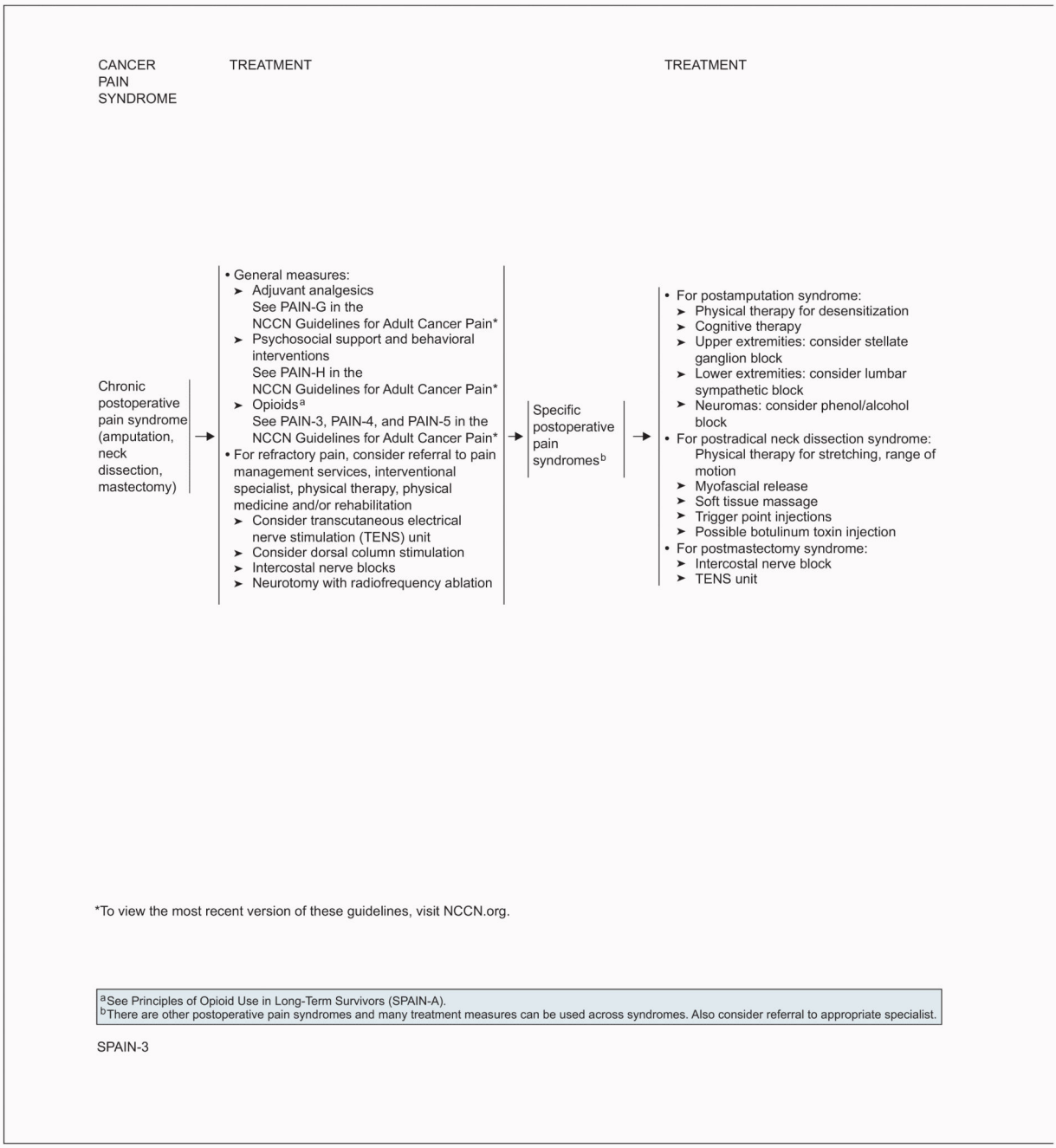

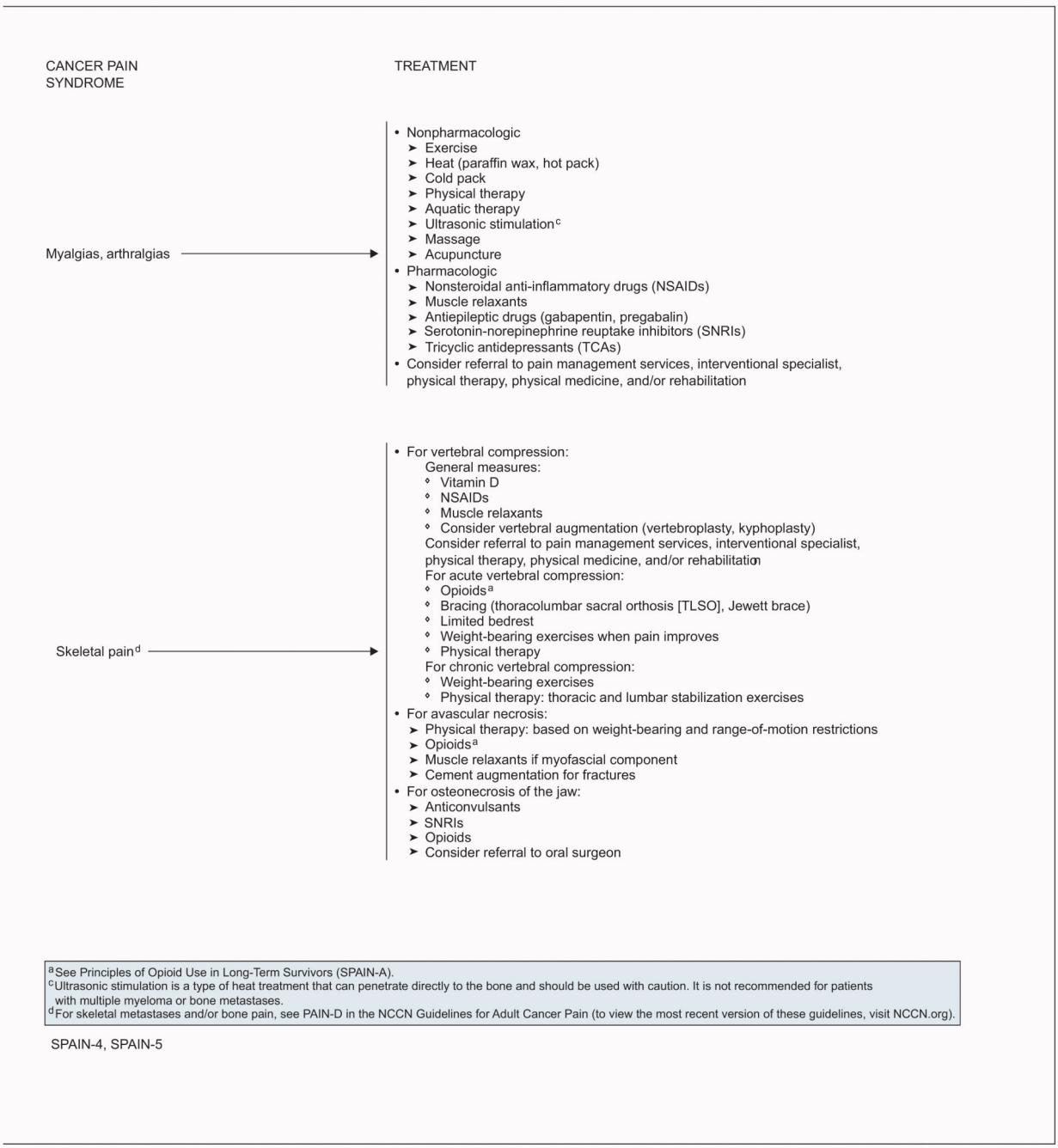

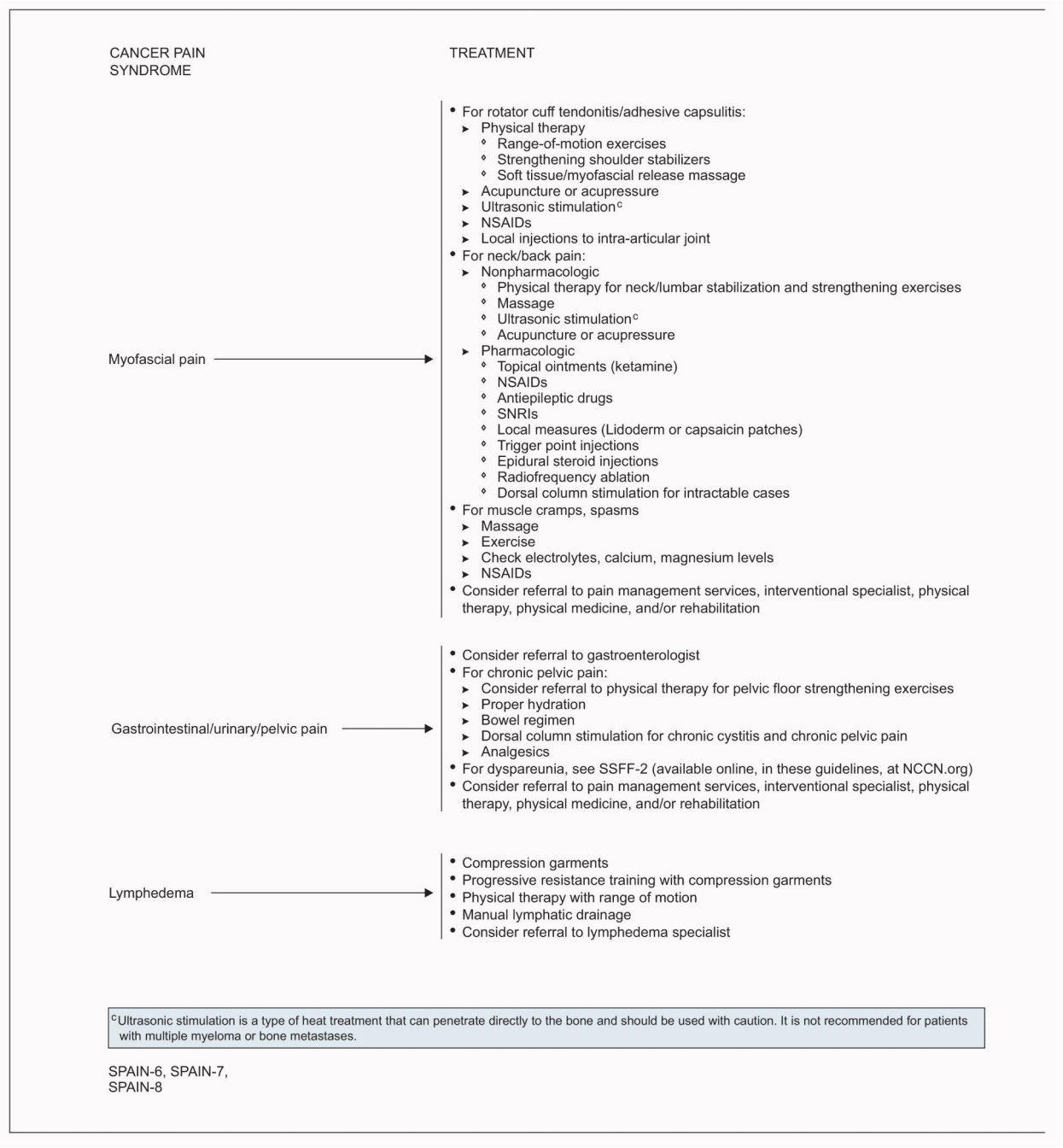

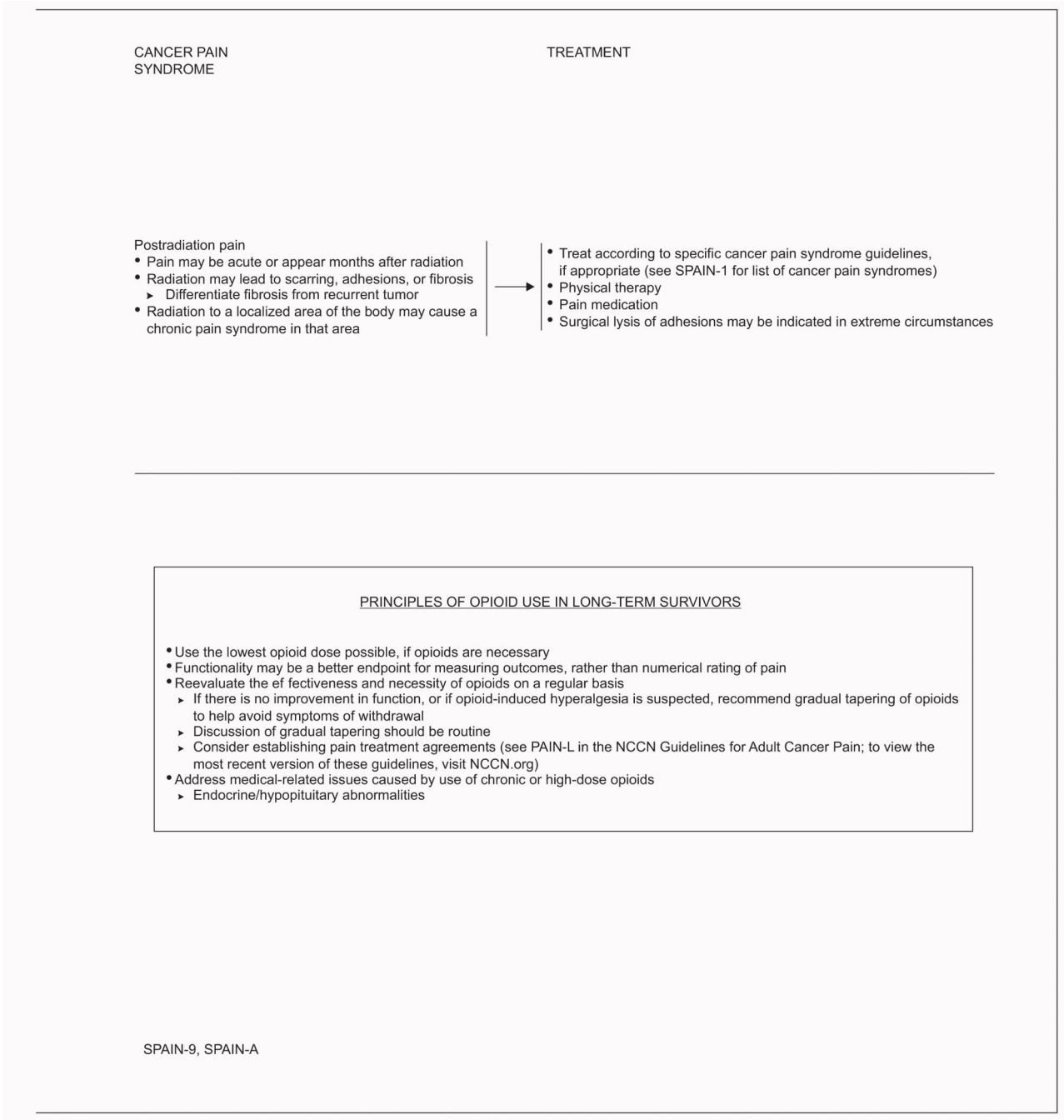

Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated

Individual Disclosures for the NCCN Survivorship Panel

Panel Member	Clinical Research Support/Data Safety Monitoring Board	Advisory Boards, Speakers Bureau, Expert Witness, or Consultant	Patent, Equity, or Royalty	Other	Date Completed
Madhuri Are, MD	None	None	None	None	5/15/13
K. Scott Baker, MD, MS	None	None	None	None	11/22/13
Wendy Demark-Wahnefried, PhD, RD	National Cancer Institute; Harvest for Health Gardening Project for Breast Cancer Survivors; and Nutrigenomic Link between Alpha-Linolenic Acid and Aggressive Prostate Cancer	American Society of Clinical Oncology	None	American Society of Preventive Oncology	11/13/13
Crystal S. Denlinger, MD	Bayer HealthCare; ImClone Systems Incorporated; MedImmune Inc.; OncoMed Pharmaceuticals; Astex Pharmaceuticals; Merrimack Pharmaceuticals; and Pfizer Inc.	Eli Lilly and Company	None	None	1/9/14
Debra L. Friedman, MD, MS	None	None	None	None	5/26/13
Mindy Goldman, MD					Pending
Lee W. Jones, PhD	None	None	None	None	2/2/12
Allison King, MD	None	None	None	None	8/12/13
Grace H. Ku, MD	None	None	None	None	8/13/13
Elizabeth Kvale, MD	None	None	None	None	10/7/13
Terry S. Langbaum, MAS	None	None	None	None	8/13/13
Kristin Leonardi-Warren, RN, ND	None	None	None	None	1/6/14
Jennifer A. Ligibel, MD	None	None	None	None	10/3/13
Mary S. McCabe, RN, BS, MS	None	None	None	None	8/12/13
Michelle Melisko, MD	Celldex Therapeutics; and Galena Biopharma	Agendia BV; Genentech, Inc.; and Novartis Pharmaceuticals Corporation	None	None	10/11/13
Jose G. Montoya, MD	None	None	None	None	12/6/13
Kathi Mooney, RN, PhD	University of Utah	None	None	None	9/30/13
Mary Ann Morgan, PhD, FNP-BC	None	None	None	None	8/19/13
Javid J. Moslehi, MD	None	ARIAD Pharmaceuticals, Inc.; Millennium Pharmaceuticals, Inc.; Novartis Pharmaceuticals Corporation; and Pfizer Inc.	None	None	1/27/14

Panel Member	Clinical Research Support/Data Safety Monitoring Board	Advisory Boards, Speakers Bureau, Expert Witness, or Consultant	Patent, Equity, or Royalty	Other	Date Completed
Tracey O'Connor, MD	None	None	None	None	6/13/13
Linda Overholser, MD, MPH	None	Antigenics Inc.; and Colorado Central Cancer Registry Care Plan Project	None	None	10/10/13
Electra D. Paskett, PhD	Merck & Co., Inc.	None	None	None	6/13/13
Muhammad Raza, MD	None	None	None	None	8/23/12
Karen L. Syrjala, PhD	None	None	None	None	10/3/13
Susan G. Urba, MD	None	Eisai Inc.; and Helsinn Therapeutics (U.S.), Inc.	None	None	10/9/13
Mark T. Wakabayashi, MD, MPH	None	None	None	None	6/19/13
Phyllis Zee, MD	Philips/Respironics	Merck & Co., Inc.; Jazz Pharmaceuticals; Vanda Pharmaceuticals; and Purdue Pharma LP	None	None	3/26/14

The NCCN Guidelines Staff have no conflicts to disclose.