Care Guide: Cancer Pain

Key Points: Cancer Pain

1. Pain is defined as “an independent and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” Pain occurs in approximately 25% of patients with newly diagnosed malignancies, 33% of patients undergoing treatment, and 75% of patients with advanced cancer. Most importantly, pain is what the patient says it is, and it needs to be addressed adequately in order to improve quality of life.

2. Unrelieved cancer pain denies patients of comfort and greatly affects their activities, motivation, interactions with family and friends, and overall quality of life.

3. Studies have revealed that most physicians underestimate the level of their patient’s pain. It is recommended that all cancer patients should be screened for pain during their initial visit, at regular intervals and whenever new therapy is initiated.

4. Most patients can have their cancer pain successfully controlled with appropriate techniques and safe drugs if the pain management algorithms are applied, monitored, and tailored to the needs of the individual.

5. Pain medications not recommended for use in cancer patients by the NCCN because of inadequate pain control include:
   - Meperidine (Demerol)
   - Placebos
   - Partial agonists (buprenorphine)
   - Mixed agonist-antagonists (albuphine, pentazocine)

Specific Pain Problems

1. For pain associated with inflammation, a trial of NSAIDs or glucocorticoids is indicated.

2. Bone pain without oncologic emergency.
   - Trial of opioids and/or NSAIDs
   - Consider radiation therapy or nerve block for local bone pain
   - For diffuse bone pain: Consider trial of bisphosphonates, hormonal chemotherapy or radioisotopes for responsive tumors
   - Consider physical medicine evaluation
   - For resistant pain, consider anesthetic procedures


4. Neuropathic pain:
   - Trial of tricyclic antidepressants
   - Trial of anticonvulsants-neurontin, tegretol, lyrica
   - Consider topical agents
   - Consider referral to a pain specialist and/or interventional strategies

5. Consider trial of radiation, hormones or chemotherapy for painful lesions
Key Points: Cancer Pain Management

Numerical Patient Rating Scale:

Verbal: What number describes your worst pain in the past 24 hours? __________
      Scale from 0 (no pain) to 10 (worst imaginable pain)

Written: Circle the number that best describes your worst pain in the past 24 hours.
         No pain 0 1 2 3 4 5 6 7 8 9 10 Worst imaginable pain

Categorical: What is the worst pain you have had in the past 24 hours?
            □ None (0) □ Mild (1–3) □ Moderate (4–6) □ Severe (7–10)

COMPREHENSIVE PAIN ASSESSMENT

The self-reporting of pain is the standard. The assessment should consist of an evaluation of the following:

► Pain experience
  • Location, pattern, radiation
  • Intensity (last 24 hours, current, at rest, with movement)
  • Interference with activities (mood, relationships, sleep, appetite)
  • Timing: Onset, duration, course, persistent, or intermittent
  • Description or quality (aching, gnawing, sharp, etc)
  • Aggravating and alleviating factors
  • Other current symptoms
  • Current pain management plan (pharmacologic and non-pharmacologic)
  • Response to current therapy
  • Prior pain therapies
  • Special issues (meaning and consequences of pain, knowledge, beliefs, culture, goals and expectations)

► Medical history
  • Current or prior oncologic treatment, illnesses, conditions
  • Pre-existing chronic pain

► Psychosocial
  • Distress
  • Support
  • Psychiatric history including substance abuse
  • Risk factors for inappropriate use of pain medication
  • Risk for under treatment of pain

► Physical examination
► Laboratory and/or imaging evaluations
► Establish “pain diagnosis” (etiology and pathophysiology) and individualized treatment plan
OPIOID PRESCRIBING: TITRATION AND MAINTENANCE

General Principles

- Morphine is the international “gold standard” for first-line treatment of cancer pain.
- The appropriate dose will relieve the patient’s pain throughout its dosing interval without causing unmanageable side effects.
- Calculate increase based on total opioid dose (around the clock, scheduled or as needed) taken in the previous 24 hours.
- Increase both around the clock and as needed doses. The rapidity of dose escalation should be related to the severity of the symptoms.

For example:

- Pain 7-10 Consider increasing dose by 50-100%
- Pain 4-6  Consider increasing dose by 25-50%
- Pain 1-3  Consider increasing dose by 25%

- Switch from fixed-combination opioids to single-entity opioids when acetaminophen dose > 4 g/d.
- If patient is experiencing unmanageable side effects and pain is < 4, consider downward dose titration by approximately 25% and re-evaluate.
- Equilibrium achieved in about 5 half-lives.

Principles of Maintenance Opioid Therapy

Consider converting from short-acting to sustained release opioids for control of chronic persistent pain when 24 h opioid requirement is stable. Examples include:

- Extended-release morphine sulfate tablets q 8-24 h depending on brand. Capsules q 8-24 h.
- Extended-release oxycodone hydrochloride tablets q8-12 h.
- Transdermal fentanyl delivery system q 48-72 h.

Provide rescue doses of short-acting opioids for pain not relieved by sustained release opioids including acute exacerbations of pain, activity, or position-related pain or pain at the end of dosing interval:

- Use short-acting form of sustained release opioid whenever possible.
- Allow immediate-release rescue doses of 10-20% of 24 h oral dose (mg) every 1 h prn.
- The 24 h adult oral morphine dose equivalent of transdermal fentanyl is 2 x mcg/h dose.
- Consider oral transmucosal fentanyl citrate for brief episodes of acute exacerbation of pain not attributed to inadequate dosing of around the clock opioid. Data does not support a specific transmucosal fentanyl dose. Initiate with a 200 mcg unit.

Increase dose of sustained-release opioid if, (a) patient persistently needs doses of as needed opioids, or (b) dose of around the clock opioid fails to relieve pain at peak effect or at end of dose.
Approximate Oral and Parenteral Dose Equivalents of Opioids Based on Single Dose Data

<table>
<thead>
<tr>
<th>Opioid Analgesic</th>
<th>Oral Dose</th>
<th>Parenteral Dose</th>
<th>Typical Dose Frequency</th>
<th>Transdermal Dose</th>
<th>Half Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>100 mg</td>
<td>50 mg</td>
<td>q 3 – 4 h</td>
<td></td>
<td>2.9 h</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>15 mg</td>
<td>N/A</td>
<td>q 3 – 4 h</td>
<td></td>
<td>3.8 ± .3 h</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>7.5 – 10 mg</td>
<td>N/A</td>
<td>q 3 – 4 h</td>
<td></td>
<td>3.2 h</td>
</tr>
<tr>
<td>Morphine</td>
<td>15 mg</td>
<td>5 mg</td>
<td>q 3 – 4 h</td>
<td></td>
<td>1.5 – 2 h</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4 mg</td>
<td>0.75 – 1.5 mg</td>
<td>q 3 – 4 h</td>
<td></td>
<td>2.5 h</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>2 mg</td>
<td>1 mg</td>
<td>q 6 – 8 h</td>
<td></td>
<td>11 – 30 h</td>
</tr>
<tr>
<td>Methadone</td>
<td>10 mg</td>
<td>5 mg</td>
<td>q 6 – 8 h</td>
<td></td>
<td>15 – 30 h</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>N/A</td>
<td>50 mcg</td>
<td>q 2 – 3 h</td>
<td>q 48 – 72 h</td>
<td>1 – 3 h</td>
</tr>
</tbody>
</table>

World Health Organization (WHO) 3-Step Pain Ladder *

**STEP 1 Medications** *(similar to Visual pain scale 1-3)*
(Note: Potential adverse effects should be noted, particularly the renal and gastrointestinal adverse effects of the NSAIDs)
- ASA (Aspirin)
- Acetaminophen (Tylenol)
- NSAIDs (nonsteroidal anti-inflammatory drugs)
  - Ibuprofen (Advil, Motrin)
  - Naproxen (Alleve, Naprosyn)
  - Celecoxib (Celebrex)
  - Ketorolac (Toradol)
- Tramadol (Ultram)

**STEP 2 Medications** *(similar to Visual pain scale 4-6)*
- Codeine preparations with/without Tylenol
- Acetaminophen + Hydrocodone (Vicodin)
- Aspirin + Oxycodone (Percodan)
- Acetaminophen + Oxycodone (Percocet)

**STEP 3 Medications** *(similar to Visual pain scale 7-10)*
- Morphine preparations
- Fentanyl (Duragesic)
- Hydromorphone (Dilaudid)
- Methadone (Dolophine)
- Levorphanol (Levo-Dromoran)

* American College of Physicians Guidelines on Cancer Pain
MANAGEMENT OF OPIOID SIDE EFFECTS

Side effects usually improve over time with the exception of constipation. A multi-system assessment is necessary. Pain is rarely treated in isolation in patients with cancer and side effects may be from other treatments or cancer itself

**Constipation**

*Preventive measures:*
- Prophylactic medications
  - Stimulate laxative + stool softener (senna + docusate, 2 tablets q am)
  - Increase dose of laxative when increasing dose of opioids
- Maintain fluids
- Maintain dietary fiber (psyllium compounds are unlikely to control opioid induced constipation and are not recommended)
- Exercise, if appropriate

*If constipation develops:*
- Assess for cause and severity of constipation
- Rule out obstruction
- Treat other causes
- Titrate as needed to maximal dose of laxative (senna + docusate, 4 tablets bid) with goal of one non-forced bowel movement q 1-2 days
- Consider co-analgesic to allow reduction of the opioid dose

*If constipation persists:*
- Reassess for cause and severity of constipation
- Check for impaction
- Consider adding another agent such as magnesium hydroxide, 30-60 mL qd; bisacodyl, 2-3 tablets PO qd, or 1 rectal suppository qd; lactulose, 30-60 mL qd; sorbitol, 30 mL q2 h x 3, then prn, or magnesium citrate, 8 oz PO qd, polyethelene glycol (1 capful/8 oz water PO bid)
- Fleet, saline or tap water enema
- Consider use of a prokinetic agent (e.g., metoclopramide, 10-20 mg PO qid)
- When response to laxative therapy has not been sufficient for opioid-induced constipation in patients with advanced illness, consider Methylnaltrexone, 0.15 mg/kg sq, maximum one dose per day
- Consider neuraxial analgesics or neuroablative techniques to potentially reduce opiate dose

**Nausea (Refer to Antiemesis Care Guide)**
**Sedation**

*If sedation develops and persists for more than 1 week after initiating opioids:*
- Assess for other causes of sedation (e.g., CNS pathology, other sedating medications, hypercalcemia, dehydration, sepsis, hypoxia)
- Decrease the dose of opioid if pain control can be maintained at a lower dose
- Consider changing the opioid
- Consider co-analgesic to allow reduction of the opioid dose
- Consider a lower dose of opioid given more frequently to decrease peak concentrations
- Consider the addition of caffeine, 100-200 mg PO q6; methylphenidate, 5-10 mg 1 – 3 /day; or dextroamphetamine, 5-10 mg PO 1 – 3 /day; or modafinil, 100 – 200 mg PO qd. (Limit dosing to morning and early afternoon to avoid insomnia)

*If sedation persists despite several changes of opioids and the above measures:*
- Reassess cause and severity of sedation
- Consider neuraxial analgesics or neuroablative techniques to potentially reduce opiate dose

**Delirium**
- Assess for other causes of delirium including hypercalcemia, CNS, metastases, other psychoactive medications, etc.
- Consider changing the opioid
- Consider co-analgesic to allow reduction of the opioid dose
- Consider haloperidol, 0.5-2 mg PO q4-6 h or alternative neuroleptic agents

**Motor and Cognitive Impairment**
- Studies have shown that stable doses (>2 wk) are not likely to interfere with psychomotor and cognitive function but should be monitored

**Respiratory Depression**
- Use reversing agents cautiously.
- If respiratory problems or acute changes in mental status occur, consider naloxone administration. Consider another reason for neurological status changes if unresponsive to naloxone.

**Pruritus**

*If pruritus develops*
- Assess for other causes (other medications, etc)
- Consider antihistamine administration

*If pruritus persists*
- Consider changing to another opioid if other management has failed
- Consider adding to analgesic regimen: nalbuphine, 0.5 – 1 mg IV every 6 hours as needed

*Consider continuous infusion of naloxone for the relief of pruritus without decreasing analgesic effect*
UNIVERSAL SCREENING

If pain present
- Screen for pain
- If no pain
  - Re-screen at each Subsequent visit

If pain present
- Quantify pain intensity and characterize quality
  - See pain rating Scale
- Ask patient to describe characteristics of pain (i.e., burning, aching, etc)
- Severe uncontrolled pain is a medical emergency and should be addressed promptly

Assess for pain
- Comprehensives pain assessment in order to identify pain
  - Etiology
  - Pathophysiology
  - Specific cancer pain syndrome
  - Determine patient goals for comfort, function

MANAGEMENT OF PAIN

Pain not related to an oncologic emergency
- Opioid naïve patients **

Pain related to an oncologic emergency:
- Opioid tolerant patients ***
  - Analgesics as specified above plus specific treatment for oncologic emergency (e.g., surgery, steroids, RT, antibiotics)

Anticipated painful events and procedures

- Bone fracture or impending fracture of weight bearing bone
- Brain metastasis
- Epidural metastasis
- Leptomeningeal metastasis
- Pain related to infection
- Obstructive or perforated viscus (acute abdomen)

Provide consistent adequate analgesia for all pain related events, procedures and anxiety

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Healthways, Inc., Science and Medical Integrity, SD/AP
** Opioid-Naïve Patients**

<table>
<thead>
<tr>
<th>PAIN INTENSITY</th>
<th>MANAGEMENT OF PAIN IN OPIOID-NAÏVE PATIENTS*</th>
</tr>
</thead>
</table>
| For *ALL* levels of pain | • Recognize and treat analgesic side effects  
|                        | • Consider adding co-analgesics for specific pain syndrome  
|                        | • Provide psychosocial support  
|                        | • Provide patient and family education  
|                        | • Optimize non-pharmacologic interventions  
| Severe Pain 7 – 10 | • Manage for all levels of pain as above  
|                    | **AND**  
|                    | • Rapidly titrate short-acting opioid  
|                    | ► Oral peak effect in 60 minutes  
|                    | ► 5 – 15 mg short-acting morphine sulfate  
|                    | ► Increase or decrease dose based on pain score  
|                    | ♦ Begin bowel regimen  
| Moderate Pain 4-6 | • Manage for all levels of pain as above  
|                    | **AND**  
|                    | • Titrate short-acting opioid  
|                    | ♦ Begin bowel regimen  
| Mild Pain 1 -3 | • Manage for all levels of pain as above  
|                    | **AND**  
|                    | • Consider non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen without opioid if patient is not on analgesics  
|                    | or  
|                    | • Consider titrating short-acting opioid  
|                    | ♦ Begin bowel regimen  

Re-evaluate pain at each contact and as needed to meet patient goals for comfort and function.

* Opioid naïve patients are those who do not meet the criteria for opioid tolerant patients described by the U.S. FDA.

*Opioid naïve patients are those who do not meet the criteria for opioid tolerant patients described by the U.S. FDA.*
*** MANAGEMENT OF PAIN IN OPIOID-TOLERANT PATIENTS

Monitor for acute and chronic adverse effects

<table>
<thead>
<tr>
<th>OPIOID-TOLERANT PATIENTS*</th>
<th>INITIAL DOSE</th>
<th>SUBSEQUENT DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain ≥ 4 or As indicated for uncontrolled pain (patient goals not met)</td>
<td>Calculate previous 24 h total oral requirement and administer 10 – 20% (peak effect for oral medicine is 60 minutes)</td>
<td>Reassess efficacy and side-effects at 60 minutes</td>
</tr>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

Pain score increased           Consider IV titration and/or subsequent management and treatment
≥ 4                           
Calculate previous 24 h total oral requirement and administer 10 – 20% (peak effect for oral medicine is 60 minutes) Reassess efficacy and side-effects at 60 minutes Pain score unchanged or increased Increase dose by 50 – 100%

Pain score decreased to 4 – 6 Repeat same dose

Pain score decreased to 0 – 3 Continue at current effective dose as needed over initial 24 h Subsequent management and treatment

* U.S. FDA: “patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for one week or longer.”
## SUBSEQUENT PAIN MANAGEMENT AND TREATMENT IN OPIOID-TOLERANT PATIENTS*

<table>
<thead>
<tr>
<th>Pain Level</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For ALL pain</strong></td>
<td>• Provide psychosocial support&lt;br&gt;• Provide patient and family education</td>
</tr>
<tr>
<td><strong>Severe Pain</strong></td>
<td>• See management for <em>all</em> levels of pain above&lt;br&gt;• Re-evaluate opioid titration&lt;br&gt;• Re-evaluate working diagnosis with a comprehensive pain assessment&lt;br&gt;• Consider specific pain syndrome problems&lt;br&gt;• Consider pain specialist consultation&lt;br&gt;• Re-evaluate co-analgesics, as indicated</td>
</tr>
<tr>
<td>7 – 10</td>
<td>Achieved → See <strong>Ongoing Care</strong></td>
</tr>
<tr>
<td><strong>Moderate Pain</strong></td>
<td>• See management for <em>all</em> levels of pain above&lt;br&gt;• Continue opioid titration&lt;br&gt;• Consider specific pain syndrome problems&lt;br&gt;• Consider pain specialist consultation&lt;br&gt;• Continue co-analgesic titration</td>
</tr>
<tr>
<td>4 – 6</td>
<td>Re-evaluate patient’s goals of comfort and function at each contact</td>
</tr>
<tr>
<td><strong>Mild Pain</strong></td>
<td>• See management for <em>all</em> levels of pain above&lt;br&gt;• Re-assess and modify regimen to minimize side-effects&lt;br&gt;• Co-analgesics as needed</td>
</tr>
<tr>
<td>0 – 3</td>
<td>Re-screen and re-assess&lt;br&gt;Not achieved → Consider interventional strategies</td>
</tr>
</tbody>
</table>

* Opioid tolerant includes patients who are chronically receiving opioid analgesic on a daily basis
ONGOING CARE

Clinician responsibilities

• Convert to oral medications (if feasible) including extended-release agent with rescue doses
• Routine follow-up
  ► Assess pain during each outpatient contact or at least each day for inpatients or more frequently based on:
    △ Patient’s condition
    △ Institutional standards
    △ Regulatory requirements
• Provide written follow-up plan, including prescribed medications
• Ensure adequate access to prescribed medications, especially during transition between sites of care
• Instruct the patient on the importance of the following:
  ► Follow documented pain plan
  ► Maintain clinic appointments
  ► Contact clinician if pain worsens or side effects inadequately controlled
• Process realistic goals, revise, and review
• Address system barriers
  ► Obtain assistance from social workers
• Maintain communication and coordinate care with pain specialist and relevant providers
• On-call/as needed availability

GOALS OF TREATMENT

Achieved → Continue routine follow-up

Not achieved →

• Re-screen and re-assess
• Consider interventional pain specialist referral
References:

1. NCCN: Practice Guidelines in Oncology Adult Cancer Pain - v. 1. 2010


