Cancer Pain – Pediatric

Note: This consensus algorithm excludes patients who are in the Pediatric Intensive Care Service (PICS), perioperative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.

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Cancer Pain – Pediatric (Inpatient)

Note: This consensus algorithm excludes patients who are in the Pediatric Intensive Care Service (PICS), perioperative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.

Assess for pain[1] at each visit or interaction using appropriate pain scale[2] to determine baseline pain score

Mild pain and/or PPG met

- Consider consulting Child Life or other complimentary therapies (Appendix A)

For patients not currently taking opioids:

- Consider non-opioids (Appendix E) or if contraindicated, consider weak opioids (Appendix G), as needed for pain

For patients currently taking opioids:

- Continue current analgesic regimen or consider dose changes as clinically indicated
- If patient is currently taking a long-acting opioid, consider adding a short-acting opioid for breakthrough pain. The breakthrough dose is calculated as 10-20% of the total daily dose, given every 1 to 4 hours.
- Manage opioid induced side effects as clinically indicated (Appendix K). For patients on opioids, ensure a scheduled bowel regimen.

→ Reassess pain, PPG, and current score using appropriate pain scale
- If using opioids, reassess opioid side effects every 4 hours or at each interaction and subsequent visit

→ Pain adequately controlled?

Yes →
- Continue current analgesic regimen
- Consider starting/adjusting opioid dose

→ Reassess pain, PPG, and current score using appropriate pain scale
- If using opioids, reassess opioid side effects every 4 hours or at each interaction and subsequent visit

No →

Moderate pain and/or PPG not met

- Consider consulting Child Life or other complimentary therapies (Appendix A)

For patients not currently taking opioids:

- Administer short-acting opioids - choose from weak or strong opioids (Appendix G)

For patients currently taking opioids:

- Consider increasing scheduled opioid dose by 30-50%. If scheduled opioid is increased, recalculate the breakthrough dose as 10-20% of the total daily dose, given every 1 to 4 hours.
- Manage opioid induced side effects as clinically indicated (Appendix K). For patients on opioids, ensure a scheduled bowel regimen.
- Consider specialty consult[3]

→ Reassess pain, PPG, and current score using appropriate pain scale
- Reassess opioid side effects within 1 hour of short-acting opioid administration

→ Pain adequately controlled?

Yes →
- Continue current analgesic regimen
- Consider starting/adjusting opioid dose

No →
- Titrate scheduled and short-acting opioids
- Consult specialty service[3]

→ Reassess pain, PPG, and current score using appropriate pain scale
- Reassess opioid side effects within 1 hour of short-acting opioid administration

Severe pain and Pain crisis, see Page 3

Note: For all patients, consider using appropriate adjuvants (Appendix F) and/or complementary therapies (Appendix A), bowel regimen (Appendix K), patient education (Appendix L), and psychosocial support as appropriate (Appendix M)

PPG = personalized pain goal

[1] See Appendix B for Comprehensive Pain Assessment

[2] See Appendices C and D

[3] Consultation services that specialize in pain management: Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine (Appendix M for description of services)

Department of Clinical Effectiveness V3
Approved by the Executive Committee of the Medical Staff on 03/26/2019

Cancer Pain – Pediatric (Inpatient)

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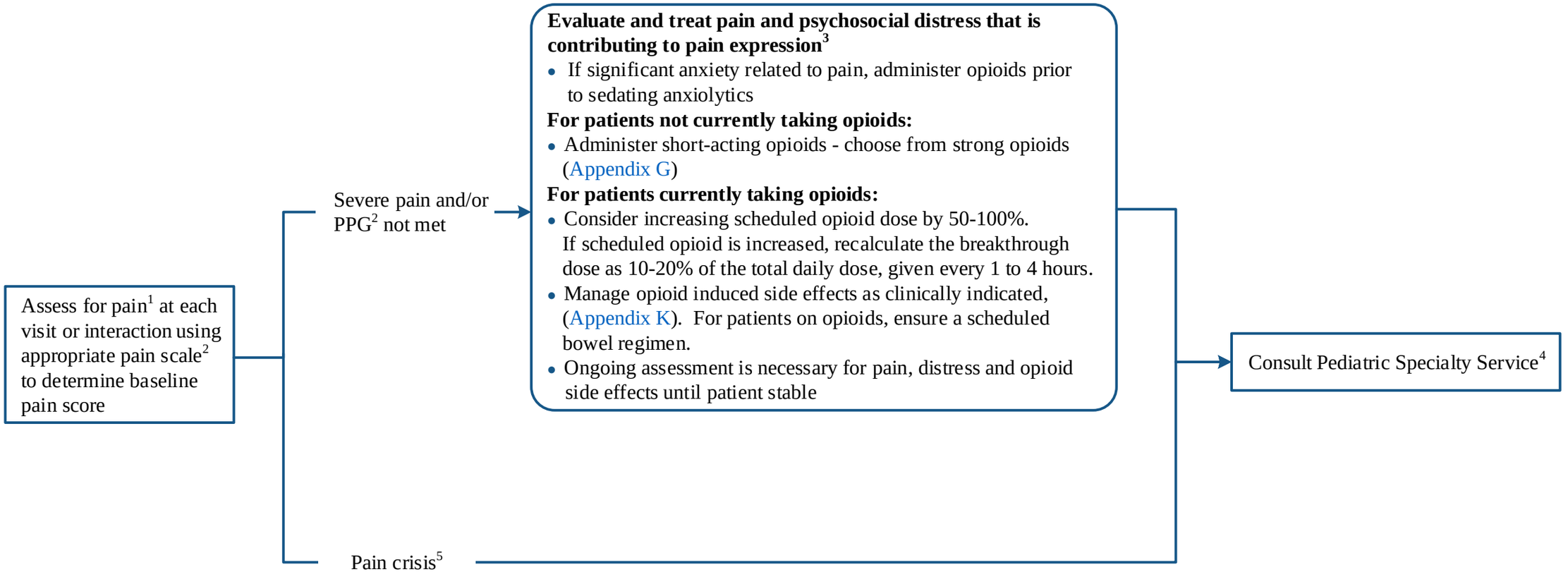


Note: For all patients, consider using appropriate adjuvants (Appendix F) and/or complementary therapies (Appendix A), bowel regimen (Appendix K), patient education (Appendix L), and psychosocial support as appropriate (Appendix M)

PPG = personalized pain goal

[1] See Appendix B for Comprehensive Pain Assessment

[2] See Appendices C and D

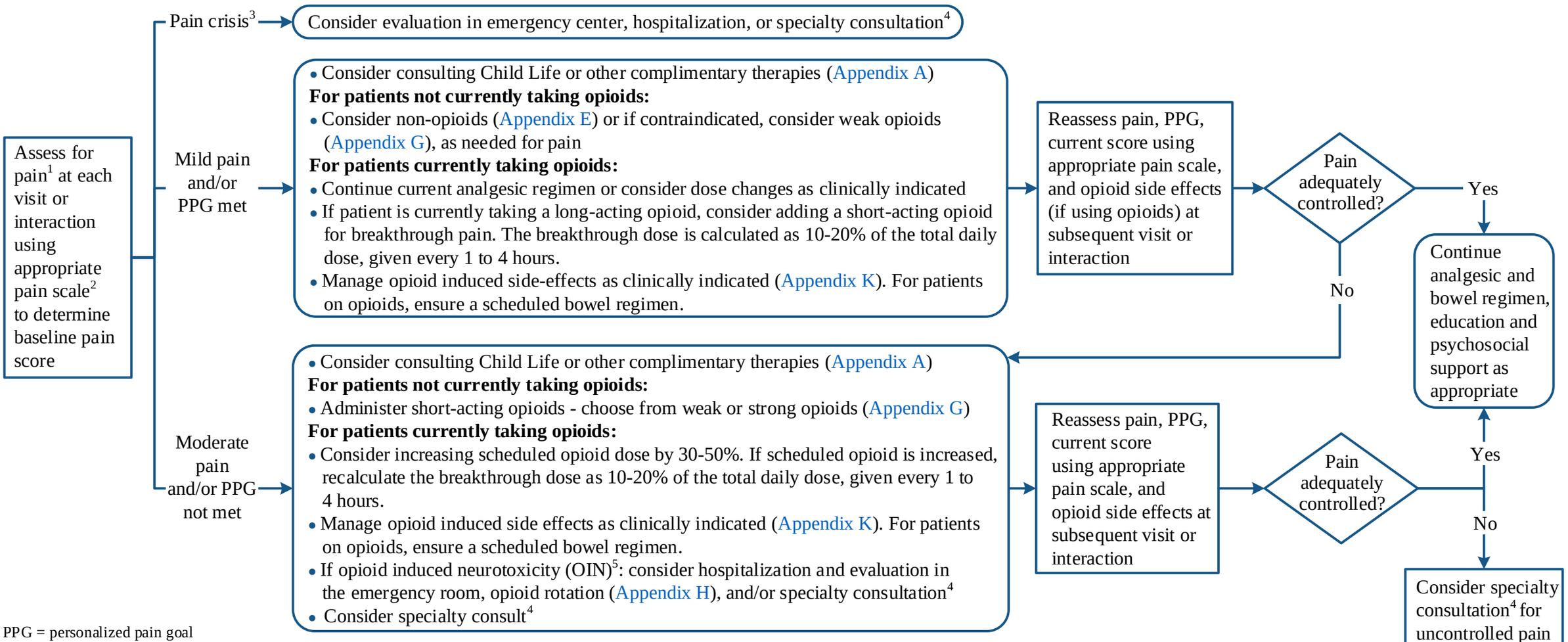
[3] For additional information see the Distress Screening and Psychosocial Management algorithm

[4] Consultation services that specialize in pain management: Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine (Appendix M for description of services)

[5] Pain crisis or emergency is defined as severe pain, new onset, or exacerbation of previously stabilized pain, accompanied by significant distress or if present for more than 24 hours

Cancer Pain – Pediatric (Outpatient)

Note: This consensus algorithm excludes patients who are in the Pediatric Intensive Care Service (PICS), perioperative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.



PPG = personalized pain goal

[1] See Appendix B for Comprehensive Pain Assessment
[2] See Appendices C and D
[3] Pain crisis or emergency is defined as severe pain, new onset, or exacerbation of previously stabilized pain, accompanied by significant distress or if present for more than 24 hours
[4] Consultation services that specialize in pain management: Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine (Appendix M for description of services)
[5] Opioid induced neurotoxicity (OIN) can include drowsiness, cognitive impairment, confusion, hallucinations, and myoclonic jerks (Appendix K)

Note: For all patients, consider using appropriate adjuvants (Appendix F) and/or complementary therapies (Appendix A), bowel regimen (Appendix K), patient education (Appendix L), and psychosocial support as appropriate (Appendix M)

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Note: This consensus algorithm excludes patients who are in the Pediatric Intensive Care Service (PICS), perioperative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.

Quick Pediatric Reference Guide

- Opioid naïve: Includes patients who are not chronically receiving opioid analgesic on a daily basis and therefore have not developed significant tolerance.
- Opioid tolerant: Patients who are chronically receiving opioid analgesics on a daily basis. The FDA identifies this group as "receiving at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer" for adult patients. The pharmaceutical industry's definition of opioid tolerant for pediatric patients is generally a patient receiving the equivalent of 1 mg/kg per day of oral morphine for 1 week or longer.
- Incomplete cross-tolerance: Reduce dose of new opioid by 30 to 50% when switching from one opioid to another to account for tolerance to a currently administered opioid that does not extend completely to other opioids. Consequently, this phenomenon tends to lower the required dose of the new opioid.
- Dose titration: Adjusting the dose of an opioid should be individualized for each patient. Refer to Pages 2 to 4 of this algorithm for titration recommendations.
- Dosing frequency: For long-acting opioids, dosing frequency is typically every 12 hours to 24 hours depending on the agent. Refer to Appendix G for Opioid Dose Considerations.
- Breakthrough pain: Doses of short-acting opioids for breakthrough pain should be 10 to 20% of the total daily dose given every 1 to 4 hours as needed. Breakthrough opioids can be given as frequently as every 1 hour for oral doses or every 15 minutes if IV (assuming normal renal/hepatic function).
- Organ dysfunction: Use additional caution when converting opioids in patients with hepatic, renal, or pulmonary dysfunction. Codeine, morphine, hydromorphone, and oxycodone should be used with caution in patients with decreased renal function.
- Opioids NOT recommended for cancer pain: Meperidine and mixed agonist-antagonists (pentazocine, nalbuphine, butorphanol, dexocine) should be avoided.
- Withdrawal symptoms: Nausea, vomiting, diarrhea, anxiety, and shivering are common symptoms of opioid withdrawal. A gradual taper is recommended when discontinuing opioids.
- Overdose: Symptoms may include respiratory depression, constricted pupils, and decreased responsiveness. Naloxone is used to reverse the effects of an opioid. To administer, dilute 0.4 mg/mL (1 mL) ampule into 9 mL of normal saline for total volume of 10 mL to achieve a 0.04 mg/mL concentration. Give 0.04 mg (1 mL) via slow IV push every 30 to 60 seconds until symptom improvement. DO NOT administer undiluted naloxone due to risk of precipitating rapid withdrawal, which may cause severe pain or seizures.
- Chemotherapy-related, intermittent pain: This type of pain may be managed with weak opioids (*e.g.*, tramadol) or combination opioid preparations (*e.g.*, hydrocodone with acetaminophen, etc.). See Appendix G for Opioid Dose Considerations, or refer to a drug information reference for additional information.
- Constipation is a common side effect with opioid use. Consider starting a bowel regimen in all patients taking opioids. Refer to Appendix K.
- Duration of drug effect: Any residual drug in the patient's system must be accounted for and an assessment of any residual effects from discontinued long-acting opioids must be made before any new opioid is started. For example, fentanyl will continue to be released from the skin 12 to 36 hours after transdermal patch removal.
- The Texas Prescription Monitoring Program is an electronic database that tracks controlled substance prescriptions. It can help identify patients who may be misusing prescription opioids or other prescription medications and who may be at risk for overdose. Clinicians are encouraged to check the Texas PMP prior to initial opioid prescribing and at regular intervals. It can be accessed at https://texas.pmpaware.net/login

APPENDIX A: Complementary and Integrative Therapy

Integrative Medicine refers to an evidence-informed approach to bringing these complementary approaches into conventional medical care. Complementary approaches may be provided safely by individuals with proper training. Such approaches can provide support to patients and their caregivers. Benefits can include helping to provide relief for symptoms such as: pain, nausea, and anxiety. Complementary approaches may offer also opportunities for increased socialization, motivation, and improving coping skills. Services provided include the risks and benefits of using herbs and supplements, acupuncture, oncology massage, meditation, music therapy, nutrition, exercise, and health psychology. Integrative Medicine consultation services are available in the outpatient and inpatient setting. Inside Integrative Medicine is a monthly newsletter with the latest news on complementary therapies, research and a monthly activities/group class calendar for the Integrative Medicine Center; group classes are available at no cost to patients and caregivers.

Arts in Medicine Program

Zachary E. Gresham, MA – Program Manager
(713) 792-5192 office
Email: zegresham@mdanderson.org
The Arts in Medicine program connects pediatric patients and their families to visual arts, music, theater, and dance through community collaborations, large-scale projects, and one-on-one experiences. Services are rendered via an informal referral process for patients and families.

Pediatric School

Daniel Smith, M.Ed., Manager
(713) 792-7681 office
Email: dlsmith4@mdanderson.org
Education program offers art class daily, one day utilizing a pottery wheel, Google expeditions, cooking classes, and writers in the schools. Kids' yoga class is provided by Child Life.

Pediatric Clinical Psychology Services

Pediatric clinical psychology services are initiated by consultation. The Pediatric On-Call Schedule denotes provider and contact information.
Psychological interventions can be provided to patients who are struggling through acute or chronic pain.

APPENDIX B: Comprehensive Pediatric Pain Assessment

The comprehensive pain assessment should include the following:

1. **Pain**:
   a. For each site of pain, determine intensity level using the appropriate pain scales based on age and developmental level (Appendix C FLACC Behavioral Pain Assessment Categories and Appendix D Wong-Baker FACES Pain Rating Scale).
   b. Evaluation of medical history includes: oncologic or other significant medical illnesses, medication history, relevant imaging and laboratory studies.
   c. Physical examination.
   d. Assess for presence of sedation and common opioid side effects (Appendix K).
2. **Function**:
   a. Evaluate patient's ability to ambulate, perform activities of daily living (ADL), range of motion (ROM), deep breathing, and coughing.
   b. Assess restrictions related to pain.
   c. Report patient's evaluation of functional ability.
3. **Psychosocial issues**:
   a. Evaluate patient distress, family support, psychiatric history, patient/family knowledge and beliefs surrounding pain and its management, and risk factors for under treatment of pain (underreporting, prior treatment of pain and response to other pain medications, concerns about addiction to pain medications or side effects, extremes of age, gender, cultural barriers, communication barriers, and prior history of drug abuse).
   b. Report patient's assessment of psychological distress.
4. **Personalized Pain Goal (PPG):**
   a. Determine the verbal or written goal stated by the patient describing the desired level/intensity of pain that will allow the patient to achieve comfort in physical, functional, and psychosocial domains.

In addition to Comprehensive Pain Assessment, rule out or treat pain related to oncologic emergencies[1].

[1] Pain related to an oncologic emergency requires assessment and treatment (*e.g.*, surgery, corticosteroids, radiation therapy, antibiotics) along with an emergent consultation.
Oncologic emergencies include:

- Bowel obstruction/perforation
- Brain metastasis
- Leptomeningeal metastasis
- Fracture or impending fracture of weight-bearing bone
- Epidural metastasis/spinal cord compression
- Pain related to infection

APPENDIX C: FLACC Behavioral Pain Assessment
(For patients less than 3 years of age or non-verbal or as clinically appropriate)

FLACC Behavioral Pain Assessment

Categories	Scoring		
	0	**1**	**2**
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry, (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching hugging or being talked to, distractible	Difficulty to console or comfort

Each of the five categories is scored from 0-2, resulting in a total score between 0 and 10.

The FLACC scale was developed by Sandra Merkel, MS, RN, Terri Voepel-Lewis, MS, RN and Shobha Malviya, MD at C. S. Mott Children's Hospital, University of Michigan Health System, Ann Arbor, MI.

APPENDIX D: Wong-Baker FACES® Pain Rating Scale
(For patients 3 to 18 years old or as clinically appropriate)

Instructions for Usage

Explain to the person that each face represents a person who has no pain (hurt), or some, or a lot of pain.

Face 0 doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little bit more. Face 6 hurts even more. Face 8 hurt a whole lot. Face 10 hurts as much as you can imagine, although you don't have to be crying to have this worst pain.

Ask the person to choose the face that best depicts the pain they are experiencing.

APPENDIX E: Non-opioids for Pediatric Pain Management[1]

CAUTION: All of these agents are antipyretic and may mask fever; use caution in patients receiving myelosuppressive chemotherapy. Non-steroidal anit-inflammatory drugs (NSAIDs) may have antiplatelet effects that can increase the risk of bleeding in patients who are thrombocytopenic or receiving myelosuppressive chemotherapy and likely to become thrombocytopenic. Non-acetylated salicylates (*e.g.*, salsalate, choline magnesium salicylate) and the COX-2 selected NSAID (celecoxib) may have less effects on platelets, but should still be used with caution in a patient receiving myelosuppressive chemotherapy.

Non-opioids include: acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs); they may be used alone or in combination with opioids for pain management. NSAIDs are useful adjuvant analgesics for bone pain.

Recommended Starting Doses: The choice of non-opioid must depend on the individual risk/benefit balance for each patient. The mechanism of action and side effect profile of each option is different.

Drug	Recommended Starting Dose	Maximum Daily Dose	Comments
Acetaminophen	10 – 15 mg/kg (max 1,000 mg) PO every 4-6 hours	Less than 12 years old: 5 doses (75 mg/kg) per day Greater than or equal to 12 years: 4,000 mg[2]	Available PO, IV or per rectum[3]. At higher doses, can cause fatal hepatotoxicity and renal damage. Avoid use in hepatic dysfunction. Does not have anti-inflammatory effect.
	12.5 mg/kg (max 650 mg) IV every 4 hours **or** 15 mg/kg (max 1,000 mg) IV every 6 hours	4,000 mg[2]	IV acetaminophen is formulary restricted
Ibuprofen	4 – 10 mg/kg (max 800 mg) PO every 6-8 hours	Less than 12 years old: 40 mg/kg Greater than or equal to 12 years: 3,200 mg	Inhibits platelet aggregation and can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk[4].
Celecoxib	10 to 25 kg: 50 mg twice daily Greater than 25 kg: 100 mg twice daily	400 mg	May not affect platelet aggregation. Can cause renal insufficiency.
Ketorolac	Single-dose treatment: 0.5 mg/kg (max 15 mg) IV once Multiple-dose treatment: 0.5 mg/kg (max 30 mg) IV every 6 hours	120 mg Max 5 days	Limit treatment to 5 days. Use is contraindicated in patients with advanced renal impairment or patients at risk for renal failure due to volume depletion. Inhibits platelet aggregation; can cause gastrointestinal side effects.

[1] The following medications are not approved in children: aspirin and naproxen
[2] Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily
[3] Rectal route is contraindicated in neutropenic patients
[4] Patients at high risk of serious gastrointestinal side effects or renal damage from NSAIDs include: smokers, previous history of peptic ulcer, currently receiving corticosteroids, anticoagulants, or presence of existing renal disease, cardiac or liver impairment

APPENDIX F: Adjuvant "Co-analgesics" for Pediatric Neuropathic Pain Syndromes and Chronic Pain[1]

Drug Class and Uses	Medication	Recommended Starting Dose	Maximum Daily Dose	Comments
Anticonvulsants (various NP types)	Gabapentin	**Day 1:** 5 mg/kg (max 300 mg) PO at bedtime **Day 2:** 5 mg/kg (max 300 mg) PO twice a day **Day 3:** 5 mg/kg (max 300 mg) PO three times a day	Dose may be further titrated to a maximum of 3,600 mg/day	Used in PHN and NP. May cause drowsiness, dizziness, and peripheral edema. Dose adjust for renal impairment.
	Topiramate	6-12 years (weight greater than or equal to 20 kg): 15 mg PO daily for 7 days, then 15 mg PO twice a day. Greater than or equal to 12 years: 25 mg PO at bedtime for 7 days, then 25 mg PO twice a day and titrate up to 50 mg PO twice a day	200 mg	Used in NP. May cause acidosis, drowsiness, dizziness, and nausea. Dose adjust for renal and/or hepatic impairment.
Tricyclic Antidepressants (TCA) (various NP types)	Amitriptyline	0.1 mg/kg PO at bedtime; titrate as tolerated over 3 weeks to 0.5 – 2 mg/kg at bedtime	25 mg	Consider for continuous and shooting neuropathic pain. Caution use in frail patients, those with glaucoma or arrhythmias. May cause sedation, arrhythmias, dry mouth, orthostasis, and urinary retention. Consider duloxetine for NP or DN. Caution use in patients with seizures; avoid MAOIs, other SSRIs or SNRIs due to potential for serotonin syndrome. Duloxetine may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to this risk. Taper slowly.

DN = diabetic neuropathy
FM = fibromyalgia
MAOI = monoamine oxidase inhibitors
NP = neuropathic pain
PHN = post herpetic neuralgia
SNRIs = serotonin-norepinephrine reuptake inhibitors
SSRIs = selective serotonin reuptake inhibitors
TCAs = tricyclic antidepressants
TGN = trigeminal neuralgia

[1] The following medications are not approved in children: pregabalin, carbamazepine, oxcarbazepine, tiagabine, nortriptyline, desipramine, duloxetine, venlafaxine and tizanidine

Continued on Next Page

APPENDIX F: Adjuvant "Co-analgesics" commonly used for Pediatric Neuropathic Pain Syndromes and Chronic Pain[1]- continued

Drug Class and Uses	Medication	Recommended Starting Dose	Maximum Daily Dose	Comments
Muscle Relaxants (muscle pain, spasm)	Baclofen[2]	**Less than 2 years old:** 2.5 – 5 mg PO every 8 hours; titrate dose every 3 days to max daily dose **2–7 years old:** 7.5 – 10 mg PO every 8 hours; titrate dose every 3 days in increments of 5 – 15 mg/day to max daily dose **Greater than or equal to 8 years old:** 10 – 15 mg PO every 8 hours; titrate dose every 3 days in increments of 5 – 15 mg/day to max daily dose	**Less than 2 years old:** 40 mg **2–7 years old:** 60 mg **Greater than or equal to 8 years old:** 80 mg	Caution use in patients with seizures, cardiovascular disease, glaucoma, myasthenia gravis, renal or hepatic impairment, patients on TCAs or MAOIs. May cause anticholinergic effects and significant drowsiness. Methocarbamol: may repeat course after drug free interval of 48 hours.
	Cyclobenzaprine	**Greater than or equal to 15 years old:** 5 mg PO three times daily	30 mg	
	Metaxalone	**Greater than 12 years old:** 400 mg PO three times daily	3,200 mg	
	Methocarbamol	**Greater than or equal to 16 years old:** 500 mg PO four times daily 1,000 mg IV every 8 hours	4,000 mg IV for 3 days maximum if PO not possible	
Corticosteroids (inflammation, nerve compression)	Dexamethasone	0.25 mg/kg IV or PO every 6 hours Standard dose 4 – 16 mg/day	16 mg	May cause impaired healing, infection, thrush, hyperglycemia, weight gain, myopathy, stomach upset, psychosis, emotional instability.

MAOI = monoamine oxidase inhibitors
TCAs = tricyclic antidepressants
[1] The following medications are not approved in children: pregabalin, carbamazepine, oxcarbazepine, tiagabine, nortriptyline, desipramine, duloxetine, venlafaxine and tizanidine
[2] Intrathecal formulation not on MD Anderson formulary

APPENDIX G: Pediatric Opioid Dose Considerations[1] (Weaker medications are listed at the beginning of Appendix G)

Opioid	Initial Short-Acting Dose in an Opioid Naïve Patient		Onset (minutes)	Peak Effect (hours)	Duration (hours)	Initial Scheduled Dosing in Opioid Naïve Patient	Available Oral Dose Formulations	Comments
	Route	Dose						
Tramadol	PO	1 – 2 mg/kg (max 25-50 mg)	30 – 60	1.5	3 – 7	Short-acting: every 4-6 hours	Short-acting: 50 mg tablets Long-acting: 100, 200, 300 mg tablets	Not be used in children less than 12 years of age. Increased risk of serotonin syndrome.[2] May lower seizure threshold. Maximum daily dose 400 mg; consider lower doses if history or increased risk of seizures.. Use with caution in renal dysfunction.[3]
Hydrocodone	PO	0.1 – 0.2 mg/kg (max 5-10 mg)	10 – 20	1 – 3	4 – 8	Short-acting: every 6 hours	Short-acting in combination with acetaminophen: 5, 7.5, 10 mg tablets; 2.5 mg/5 mL liquid	Hydrocodone used for pain is only available in combination with acetaminophen or ibuprofen.[4] Use with caution in renal dysfunction.

[1] The following medications are not approved in children: tapentadol and oxymorphone
[2] When used with TCAs, MAOIs, SSRIs, SNRIs, or 2D6 or 3A4 inhibitors
[3] Avoid use of tramadol ER when creatinine clearance is less than 30 mL/minute
[4] Note: Must consider all forms of acetaminophen or ibuprofen medications (combination and individual) when determining total daily dosing. Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily.

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APPENDIX G: Pediatric Opioid Dose Considerations[1] – continued (Weaker medications are listed at the beginning of Appendix G)

Opioid	Initial Short-Acting Dose in an Opioid Naïve Patient		Onset (minutes)	Peak Effect (hours)	Duration (hours)	Initial Scheduled Dosing in Opioid Naïve Patients	Available Oral Dose Formulations	Comments
	Route	Dose						
Morphine	PO	0.2 – 0.5 mg/kg (max 5-15 mg)	30	0.5 – 1	3 – 6	Short-acting: PO: every 4 hours IV: every 4 hours Long-acting: varies by product	Short-acting: 15, 30 mg tablets; 10 mg/5 mL, 20 mg/5 mL, 20 mg/mL liquid Long-acting: 15, 30, 60, 100 mg tablets	Available as tablet or liquid preparation. Short-acting preparations can be given via PEG tube. Avoid use in renal dysfunction.
	IV/SC	0.05 – 1 mg/kg (max 2-3 mg)	5-10	N/A	N/A			
Oxycodone	PO	0.1 – 0.2 mg/kg (max 5-10 mg)	10 – 15	0.5 – 1	3 – 6	Short-acting: every 4 hours Long-acting: every 12 hours	Short-acting: 5, 15, 30 mg tablets; 5 mg/5 mL and 20 mg/mL liquid Long-acting: 10, 15, 20, 30, 40, 60, 80 mg tablets	Available alone or in combination with acetaminophen[2] (*e.g.*, oxycodone 5 mg with acetaminophen 325 mg in Percocet®). Use with caution in renal dysfunction.
Hydromorphone	PO	0.03 – 0.06 mg/kg (max 1-3 mg)	15 – 30	0.5 – 1	3 – 5	Short-acting: every 4 hours IV/SC: every 4 hours	Short-acting: 2, 4, 8 mg tablets; 1 mg/mL liquid Long-acting: 8, 12, 16, 32 mg tablets	Use with caution in renal dysfunction.
	IV/SC	0.01 – 0.015 mg/kg (max 0.5-1.5 mg)	15 – 30	N/A	4 – 5			

[1] The following drugs are not approved in children: tapentadol and oxymorphone

[2] Must consider all forms of acetaminophen (combination and individual) when determining total daily dosing. Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily dosing.

APPENDIX H: Equianalgesic Opioid Dose Conversion[1]

Note: The equianalgesic doses (oral and parenteral) can be affected by interpatient variability, type of pain (for example, acute versus chronic), chronic administration, and tolerance. The following table should serve as a guide when switching from one opioid to another. It is recommended to reduce the dose of the new opioid by 30 to 50% to account for incomplete cross tolerance, and to periodically monitor for efficacy and adverse reactions and the dose adjusted accordingly.

Opioid	Oral Dose (PO)	Parenteral Dose (IV/SC)	Conversion Factor: Parenteral to Oral Opioid	Conversion Factor: Oral Opioid to Oral Morphine
Morphine	30 mg	12 mg	2.5	1
Oxycodone	20 mg	N/A	N/A	1.5
Hydrocodone	30 mg	N/A	N/A	1
Oxymorphone	10 mg	1 mg	10	3
Hydromorphone	7.5 mg	3 mg	2.5	4
Fentanyl[2]	N/A	120 mcg	N/A	Should be managed by clinicians experienced in pain management
Methadone and buprenorphine should only be initiated and managed by clinicians experienced in pain management. Consider consult to pain specialists if needed.				

[1] This Equianalgesic Opioid Dose Conversion chart is based on the Centers for Disease Control and Prevention (CDC) recommendations (https://www.cdc.gov/drugoverdose/resources/data.html)

[2] See Appendix I for transdermal fentanyl conversion

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APPENDIX H: Equianalgesic Opioid Dose Conversion - continued

Steps for Opioid Rotation:

1. Stop current opioid regimen.
2. Calculate total dose of current opioid (scheduled and breakthrough doses) used in the previous 24 hour period.
3. Calculate the dose of the new opioid using the equianalagesic dose conversion table (from previous page) and conversion equation (below).

$$\frac{\text{Equianalgesic dose per route of CURRENT opioid}}{\text{24 hour dose per route of CURRENT opioid}} = \frac{\text{Equianalgesic dose per route of NEW opioid}}{\text{24 hour dose per route of NEW opioid}}$$

4. Calculate for incomplete cross-tolerance between opioids. Decrease the target dose from step 3 by 30-50% to obtain the new opioid dose.
5. Calculate scheduled pain dose. Divide the new opioid dose (from step 4) by number of doses to be given over 24 hours and administer as scheduled doses.
6. Calculate breakthrough pain dose as 10-20% of calculated new opioid dose to administer as needed every 1 hour.
7. Titrate new opioid regimen until adequate analgesia is achieved.

Opioid Rotation Example: Rotation from morphine PCA (total daily dose of 120 mg IV) to oral oxycodone.

1. Stop current opioid regimen.
2. Calculate dose of current opioid (scheduled and breakthrough doses) used in the previous 24 hours which equals 120 mg IV morphine.
3. Calculate the dose of the new opioid using the equianalagesic dose conversion table and conversion equation (below).

a. Calculate IV morphine to PO morphine based on conversion table and conversion equation :

$$\frac{\text{10 mg IV morphine}}{\text{120 mg IV morphine over 24 hours}} = \frac{\text{30 mg PO morphine}}{\text{X mg PO morphine over 24 hours}} \quad X = 360 \text{ mg PO morphine}$$

b. Calculate PO morphine to PO oxycodone based on conversion table:

$$\frac{\text{30 mg PO morphine}}{\text{360 mg PO morphine}} = \frac{\text{20 mg PO oxycodone}}{\text{X mg PO oxycodone}} \quad X = 240 \text{ mg PO oxycodone}$$

4. Calculate for incomplete cross-tolerance. After a 30-50% dose reduction, the oxycodone dose calculated above should be between 120 and 168 mg per day.
5. Calculate scheduled pain dose. Extended release (ER) oxycodone is dosed every 12 hours; recommend ER oxycodone 60 mg every 12 hours (based on tablet availability).
6. Calculate breakthrough pain dose as 10-20% of 120 mg oxycodone dose and administer as needed every 1 hour.
   Immediate release (IR) oxycodone is between 12 and 24 mg per dose and may be administered every 1 to 4 hours.
   Based on tablet availability recommend IR oxycodone 10 to 20 mg every 1 to 4 hours as needed for breakthrough pain.
7. Titrate new opioid regimen until adequate analgesia is achieved.

APPENDIX I: Fentanyl

Dosage Forms	Onset	Peak	Duration	Doses Available per Formulary	Comments
Parenteral (IV/Subcutaneous)	Almost immediate	Several minutes	0.5-1 hour	50 mcg/mL (5 mL vial for injection) PCA syringe supplied as 2,750 mcg/55 mL	
Transdermal patch[1]	12-24 hours	24-72 hours	48-72 hours	12 (delivers 12.5), 25, 50, 75, 100 mcg/hour	Bioavailability 90%; Do *not* cut patch, apply heat, or use in patients who develop fever – results in faster onset, shorter duration, and possible overdose.
Transmucosal lozenge (Actiq®)	5-15 minutes	20-40 minutes	Related to blood level	200, 400, 600 mcg	Bioavailability: 50%
Sublingual tablet (Abstral®)	5-15 minutes	30-60 minutes	2 hours	100, 200, 300, 400, 600, 800 mcg	Bioavailability: 54%

Drug specific characteristics:

- Fentanyl is 80 to 100 times more potent than morphine. Fentanyl is not recommended for initial use in opioid naïve patients since its use may lead to fatal respiratory depression.
- Transdermal fentanyl should only be used in patients with stable opioid requirements. Due to the long systemic half-life of 17 hours, the dose may be difficult to titrate if pain is not well-controlled.
- When initiating transdermal fentanyl, patients should use short-acting opioids as needed until efficacy is obtained (peak effect 24-72 hours).
- Titrate patients on transdermal fentanyl no more frequently than every 3 days after initial dose, and then every 6 days thereafter. Initial evaluation of maximum analgesic effect should not be made before 24 hours.
- Caution use with CYP450 3A4 inhibitors, which can increase fentanyl plasma concentrations.
- May be used in patients with renal dysfunction.
- Prior to processing initial prescriptions for **rapid onset fentanyl**, the prescriber must register with the TIRF REMS Access Program and complete a Prescriber and Patient agreement.

[1]After transdermal patch removal, continued absorption of fentanyl occurs from the skin. Delayed administration of another long-acting opioid should be considered due to persistent serum levels of fentanyl. Due to differences in bioavailability, fentanyl products are not interchangeable on a mcg to mcg basis.

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APPENDIX I: Fentanyl - continued

IV Fentanyl Dosing:

Morphine to IV fentanyl conversion: 1 mg of IV morphine or 2.5 mg of oral morphine = 10 micrograms of IV fentanyl

Example: Conversion from oral morphine ER 90 mg every 12 hours to IV fentanyl

1. 24 hour morphine dose is 90 + 90 = 180 mg
2. Decrease 180 mg by 30 % for incomplete tolerance = 126 mg
3. 1 mg IV morphine = 2.5 mg oral morphine = 10 micrograms IV fentanyl, then new 24 hour morphine dose of 126 mg = 24 hour IV fentanyl dose of 504 micrograms
4. Divide 24 hour fentanyl dose calculated by 24 hours = 21 micrograms/hour

Thus an appropriate starting dose for IV fentanyl/hour (as basal rate in PCA) is 20 micrograms/hour.

Transdermal Fentanyl (TDF) Dosing:

Option 1: 2 mg oral morphine is approximately 1 mcg ***per hour*** transdermal fentanyl
Example: Total daily dose of morphine 100 mg translates to approximately 50 mcg transdermal patch, to be applied every 72 hours

Option 2: calculate the total daily dose of morphine and then use the following table to select the appropriate patch strength

Oral Morphine (mg/day)	Transdermal Fentanyl (mcg/hour)
25	12
50	25
75	37
100	50
125	62
Each additional 25 mg/day	An additional 12 mcg/hour

- **Note**: This table should **NOT** be used to convert from TDF to other therapies because this conversion to **TDF** is conservative. Use of this table for conversion to other analgesic therapies can overestimate the dose of the new agent.
- To convert patients to another opioid, remove the transdermal fentanyl patch and titrate the dose of the new analgesic based upon the patient's report of pain until adequate analgesia has been attained. Upon system removal, 17 hours or more are required for a 50% decrease in serum fentanyl concentrations.
- Must prescribe short-acting opioid for breakthrough pain

APPENDIX J: Pediatric Patient Controlled Analgesia (PCA)

Suggested initial PCA settings: All opioid doses must be individualized

1. Opioid naïve patients

Opioid	Demand (PCA) Dose (Dose Range)	Lock-out Interval (Minutes)	1-hour Dose Limit (Optional)	Continuous Dose (Basal)
Morphine (milligrams)	0.01 – 0.03 mg/kg	6-8 minutes	5 doses per hour	0 – 0.03 mg/kg/hour
Hydromorphone (milligrams)	0.003 – 0.004 mg/kg	6-8 minutes	5 doses per hour	0 – 0.004 mg/kg/hour
Fentanyl (micrograms)	0.5 – 1 mcg/kg	6-8 minutes	5 doses per hour	0 – 0.5 mcg/kg/hour

a. Patient should be alert and demonstrate ability to administer demand dose for pain. If concerns about cognitive failure or significant anxiety, consider Specialty Consultation: Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine (Appendix M for description of services).

b. Carefully consider adding continuous (basal) dose after 12-24 hours if using frequent demand doses or if pain not controlled. Suggested basal dose is 30-50% of average hourly dose.
Example: The 12 hour total morphine demand dose is 20 mg, calculate continuous dose as
20/12 = 1.7 mg/hour then 1.7 X 0.3 (30%) = 0.5 mg/hour basal rate.

c. Nurse bolus as needed for pain; nurse bolus interval (hours) per physician discretion

2. Opioid tolerant patients (currently receiving opioid therapy)

PCA orders should take into account the patient's current opioid regimen, clinical situation (severity and etiology of the pain, side effects from opioids, baseline drowsiness, need for opioid rotation). If there are significant side effects, drowsiness, confusion, respiratory or central nervous system concerns, it is recommended to call for Specialty Consultation: Acute Pain, Cancer Pain, Palliative/Supportive Care (see Appendix M for description of services) for PCA ordering.

a. Calculate total dose of opioid (scheduled and breakthrough doses) used in the previous 24 hour period.

b. Use equianalgesic opioid dose conversion table (Appendix H) to calculate dose of IV opioid being considered for PCA. Decrease dose by 30-50% to adjust for lack of complete cross tolerance to obtain new IV dose.

c. Divide new IV dose (from above step) by 24 hours, to obtain hourly (basal) dose.

d. Calculate demand (PCA) dose as 10-20% of new IV opioid dose to use as needed every hour for breakthrough pain.

APPENDIX K: Pediatric Opioid Side Effects – Prevention and Management

Side Effect	Prevention	Management
Sedation	• Discontinue other sedating medications if appropriate • Educate all patients receiving opioids that drowsiness may occur for a few days following initiation or increase in opioid regimen	• Consider rotation or dose reduction of opioid if sedation persists • Consider psychostimulant: 1. Methylphenidate 2.5 – 5 mg PO once or twice daily (last dose no later than 4 pm to avoid insomnia). Suggested time 8 am and 12 noon daily **or** 2. Modafinil 100 mg once or twice daily
Opioid Induced Neurotoxicity Risk factors: • High opioid dose • Dehydration • Renal failure • Preexisting borderline cognition and/or delirium • Use of other psychoactive drugs	Eliminate nonessential CNS activating or depressing drugs (*e.g.*, benzodiazepines)	• Consider reversible causes such as metabolic disorders, liver or renal dysfunction, dehydration, hypercalcemia, organic brain disease; treat as appropriate. • Consider one or more of the following: 1. Opioid rotation (see Appendix G) 2. Opioid dose reduction or discontinuation 3. Discontinue other offending drugs (benzodiazepines) 4. Hydration 5. Symptomatic treatment with haloperidol 1 – 5 mg PO, IV, or SC every 4 hours as needed • Avoid using naloxone even if delirium is thought to be due to opioid use
Respiratory depression	• Monitor sedation and respiratory status (respiratory rate and oxygen saturation) during the first 24 hours in opioid naïve patients • Titrate opioids cautiously • Consider dose reduction or opioid rotation if patient has excessive sedation	• Call primary team, HOLD opioids, and provide supplemental oxygen • If patient minimally responsive or unresponsive and respiratory rate less than or equal to 6 bpm, administer naloxone. Recommended dose: Naloxone 0.4 mg diluted in 9 mL saline, 1 mL IV push, repeat 1-2 minutes until patient more awake and respiratory status improves. *(Half life of naloxone is short and patient may need naloxone infusion for long acting opioids. If no change with naloxone, rule out other causes for the respiratory depression.)* • If patient is actively dying, DNR (do not resuscitate) and receiving comfort care, naloxone administration may not be appropriate

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APPENDIX K: Pediatric Opioid Side Effects – Prevention and Management - continued

Side Effect	Prevention	Management
Nausea, Vomiting	• Titrate opioid dose slowly and steadily • Provide antiemetics available with opioid prescription • Metoclopramide 0.1 – 0.2 mg/kg (maximum 10 mg) PO every 6 hours • Patients at high risk of nausea-consider scheduled antiemetics for 5 days and then change to as needed	1. Investigate for other causes of nausea (*e.g.*, constipation, bowel obstruction, chemotherapy or other medications) and treat per guidelines. Initiate scheduled antiemetics. Example: Metoclopramide 0.1 – 0.2 mg/kg (maximum 10 mg) PO, IV, or SC every 6 hours 2. Add or increase non-opioid or adjuvant medications for additional pain relief so opioid dose can be reduced 3. If analgesia is satisfactory, reduce opioid dose by 25% 4. Consider opioid rotation if nausea remains refractory
Constipation	Unless alterations in bowel patterns such as bowel obstruction or diarrhea exist, all patients receiving opioids should be started on laxative bowel regimen and receive education for bowel management 1. Stimulant laxative plus stool softener: For example: Senokot-S (senna 8.6 mg plus docusate 50 mg), - 2 to 6 years: ½ tablet once daily (maximum 1 tablet twice daily) - 6 to 12 years: 1 tablet once daily (maximum 2 tablets twice daily) - Greater than 12 years: 2 tablets twice daily and titrate to a maximum of 9 tablets/day 2. Ensure adequate fluids, dietary fiber and exercise if feasible 3. Prune juice followed by warm beverage may be considered	1. Assess potential causes of constipation (such as recent opioid dose increase, use of other constipating medications, new bowel obstruction) 2. Increase Senokot-S (or senna and docusate tablets if using separate) and add 1 or both of the following: a. Milk of Magnesia oral concentrate (1,200 mg/5 mL) 15 – 30 mL PO once or twice daily b. Polyethylene glycol (Miralax®) 0.7 – 1.5 g/kg (maximum 17 g/dose) in 4-8 ounce beverage daily 3. If no response to above, perform digital rectal exam (DRE) to rule out low impaction (do not perform if neutropenic, thrombocytopenic, or post-operative bowel surgery) Continue above steps **and** • If impacted: Disimpact manually if stool is soft. If not, soften with mineral oil fleet enema before disimpaction. Follow up with milk of molasses enemas until clear with no formed stools. • Consider use of short-acting analgesics before disimpaction. • If not impacted on rectal examination, patient may still have higher level impaction. Consider abdominal imaging and/or administer milk of molasses enema along with magnesium citrate - 2 to 6 years: 60 – 90 mL once or in divided doses - 6 to 12 years: 90 – 210 mL once or in divided doses - Greater than 12 years: 240 mL once 4. Methylnaltrexone may be given to patients who meet the following criteria: • Patient experiencing opioid-induced constipation • Patient has not demonstrated an adequate response to other laxative therapy • Patient does not have a known or suspected mechanical gastrointestinal obstruction

APPENDIX L: Pain Management Education for Pediatric Patients and Family Prior to Discharge

Management of cancer pain is an integral component of cancer care. Patient education in the following areas should be provided to patients.

1. **General Pain Education:** Specific teaching information is available in Patient Education-On Line (Patient Packet 1). Education should include the following:
   A. Relief of pain is important and there is no benefit to suffering with pain
   B. Expect optimal treatment for pain and side effects
   C. Pain can usually be well controlled with oral medications. There are many options available to control pain.
   D. Communication with healthcare team is critical to pain management and avoiding serious side effects. Communication should include:
      - Patient understanding about how to rate their pain type, severity/intensity, and personalized pain goals (PPG). A numeric pain scale should be provided with explanation.
      - Potential problems or side effects of pain medications
      - Concerns about difficulty in obtaining medications (such as cost or inadequate quantity of tablets)
2. **Specific information related to Opioid Use** (such as morphine and related medications). Specific teaching information is available in Patient Education-On Line (Patient Packet 2).
   A. Morphine and morphine-like medications are often used to relieve pain
   B. When opioids are used to treat cancer pain, addiction is rarely a problem
   C. Taking opioids now will not alter later effectiveness
   D. Discuss potential side effects of opioids, and their prevention and management
   E. Prevention of constipation will be needed by most patients
   F. Opioids are controlled substances that need to be properly safeguarded in the home
   G. Opioids must be used with caution, and should not be mixed with alcohol or illicit substances

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APPENDIX L: Pain Management Education for Pediatric Patients and Family Prior to Discharge - continued

3. Pain Education Discharge/Resource Checklist:

A. A written plan for pain medications, listing all medications to be used with dosage and frequency. Provide patient with print out of updated medication reconciliation.

B. Written information on who to call (provider, service, phone number) for pain issues and plan for follow up care. Instruct patient/caregiver to call if:

- Problems in obtaining prescriptions or taking the medication
- New pain, change in pain, or pain not relieved with medication
- Nausea and vomiting that prevents eating for 1 day
- No bowel movements for 3 days
- Difficulty arousing the patient from sleep easily during daytime
- Confusion

C. MD Anderson has multiple resources for pain management

- Online resources – http://www.mdanderson.org/departments/patedu/ or via https://my.mdanderson.org. Please ask for a guide to the website.
- Specialty services for pain management at MD Anderson include: Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine (Appendix M for description of services). Referral from primary service is required.
  Pain Management, Supportive Care, and Integrative Medicine have clinics 5 days a week. Integrative Medicine services such as acupuncture, massage, and mind-body therapies are available through Online Consults or by calling 713-794-4700. Website: http://www.mdanderson.org/departments/integrative-medicine-program. Located in the Main Building, Floor 1, outside and east of Clark Clinic main entrance - Main, free-standing building located outside and east of the Clark Clinic main entrance, near the Aquarium (R1.2000); Mays Clinic, Floor 2, near The Tree Sculpture
- The Learning Center(s) provide the latest information about health, cancer, and cancer prevention. Available resources include:
  - Journals, consumer health magazines and newsletters
  - Online journals, electronic books and databases
  - Free booklets
  - Topic-specific binders
  - Books, audios and videos
  - DVDs and videotapes

Law Learning Center, Main Building, Floor 4, Elevator A R4.1100 713-745-8063
Levit Learning Center, Mays Clinic, Floor 2, Near Tree Sculpture ACB2.1120 (Mon-Fri 9-4 pm 713-563-8010).

APPENDIX M: Pediatric Specialty Services Consultation Guidelines

MD Anderson offers several coordinated pain specialty core services, consisting of Acute Pain, Pain Medicine, Palliative/Supportive Care, Pediatric ICU and Integrative Medicine. Guidelines for consultation to these services include the following:

A. For a patient whose pain remains uncontrolled for more than 24 hours, consider a consult to one of the specialty core services.

Included in this group are:

- Substance use disorders - except tobacco (current or past history)
- Emotional, behavioral, and mental disorders
- Cognitive disorders
- Communicative disorders
- Developmental disabilities
- Vision and hearing impairments and disabilities
- Refractory symptoms and dying patient

B. For postoperative and perioperative pain: Acute Pain Medicine and Integrative Medicine

C. For acute pain in inpatients: Pain Medicine in cases of pre-existing chronic pain

D. For patients with chronic pain and no evidence of active cancer: Pain Medicine (Chronic Pain) and Integrative Medicine

E. For patients with evidence of active cancer with pain as the sole or predominant symptom: Pain Medicine or Palliative/Supportive Care Service; consider Integrative Medicine

F. For patients with evidence of active cancer and pain accompanied by multiple symptoms: Palliative/Supportive Care; consider Integrative Medicine

G. For patients with pain in the context of cancer in the palliative stage or end of life: Palliative/Supportive Care; consider Integrative Medicine

H. For patients who need continuous infusions of medications when other measures previously listed have failed and pain is therefore intractable: Pediatric ICU

I. For patients with suspected opioid addiction, request a consult to one of the specialty core services for a referral to a treatment program. See Appendix N for Treatment Services.

APPENDIX N: Treatment Services

Note: Most treatment facilities require insurance coverage or sufficient money to cover treatment. If patient has insurance, call the customer service number to find a facility in-network to avoid a large out-of-pocket debt.

- Treatment Facilities for Alcohol and Drug Abuse
  Houston, Texas
  (1-800-304-2219)
- Bay Area Recovery Center
  1807 FM 517
  East Dickinson, Texas 77539
  (713) 705-3457
- The Council on Alcohol and Drugs
  Houston, Texas
  www.councilonrecovery.org
- Clearinghouse for treatment, education, and recovery groups, *etc.*
  303 Jackson Hill St.
  Houston, Texas 77007
  (713) 914-0556, (281) 866-7557
- UT Health Houston Behavioral and Biomedical Science Building
  941 East Rd. First floor
  Houston, Texas 77054
  (713) 500-3784
- Hazelden Betty Ford
  Multiple locations around the country
  1-866-831-5700
- The Treehouse
  Scurry, Texas (South of Dallas)
  (888) 683-1406
- St. Joseph Hospital
  1401 St. Joseph Parkway
  Houston, Texas 77002
  (713) 575-1000 (800) 466-0792
- West Oaks Hospital (Dr. George Santos)
  www.westoaks.org
  6500 Hornwood
  Houston, Texas 77074
- UT Health Harris County Psychiatric Center (HCPC)
  2800 South MacGregor Way
  Houston, TX 77021
  713-741-5000
- SAMHSA, Substance Abuse and Mental Health Services Administration
  Behavioral Health Treatment Services Locator: www.findtreatment.samhsa.gov
  Enter patient's address and zip code on website
  (800) 622 4357
- The Menninger Clinic
  12301 S. Main St.
  Houston, Texas 77035-6207
  (713) 275-5000
- Narcotics Anonymous
  www.na.org
  Houston area Narcotics Anonymous
  www.hascona.org
  (713) 661-4200

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Evidence regarding specific clinical outcomes associated with the use of this or similar pain algorithms applied in comprehensive cancer centers is sparse. Other algorithms or approaches may produce similar or better outcomes.

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