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Practical Approaches to Acute Pain Management

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Practical Approaches to Acute Pain Management

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Owner and Family Nurse Practitioner

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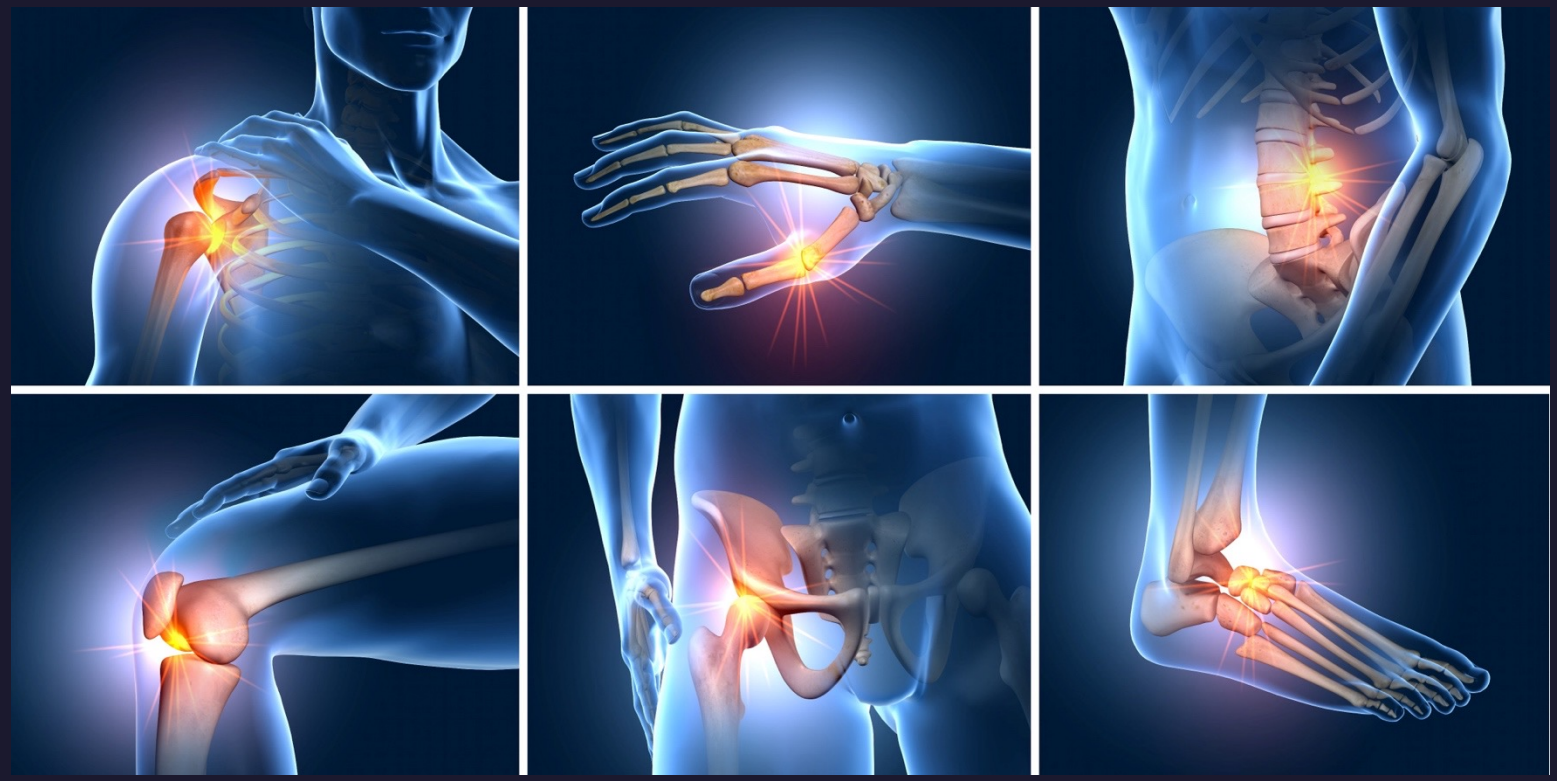

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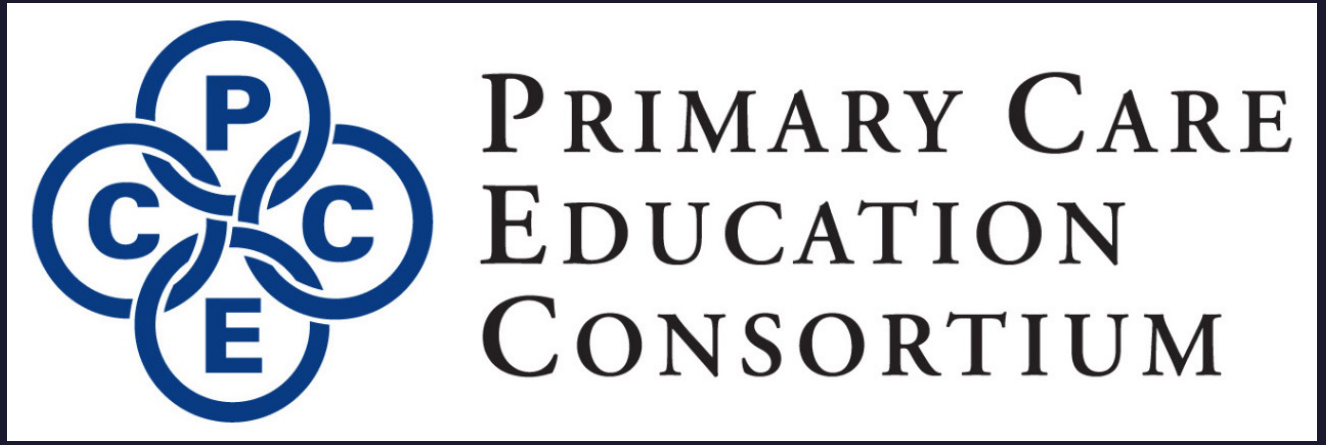


and supported by an educational grant from KOWA PHARMACEUTICALS.

Disclosures

Wendy L. Wright, DNP, discloses that she is on the advisory board and/or speakers bureau for AbbVie, AstraZeneca, Bayer, Biohaven, Exact Sciences, GSK, Indorsia, Moderna, Merck, Pfizer, Sanofi, Seqirus, and Shield Therapeutics.

Robert W. Rhoades, PharmD, medical writer, and **Michael Hanak, MD,** CME Reviewer, have no disclosures to report.

- All relevant financial relationships have been mitigated.

Learning Objectives

Participants in this presentation should be able to…
Recognize and diagnose the etiology of acute pain.
Understand the history and challenges of acute pain management.
Use newer therapies for acute pain management.

Epidemiology and impact of acute pain

What is acute pain?

- Acute pain is often described as being an entirely normal physiologic response to some form of noxious stimulus. It is often even described as being a “healthy” reaction because it allows the organism to know that homeostasis has been disrupted in some form and that a change in behavior is warranted[1]
- Acute pain has been defined as, “the physiologic response to and experience of noxious stimuli that can become pathologic, is normally sudden in onset, time limited, and motivates behaviors to avoid potential or actual tissue injury[2]

1. Meyr AJ, et al. *Clin Podiatr Med Surg*. 2008;25(3):305-v.
2. Dowell D, et al. MMWR Recomm Rep. 2022;71(3):1-95.

The definition of acute pain is quite broad

- Defining acute pain has focused mainly on distinguishing it from chronic pain with a focus on duration:
  - Acute pain is usually sudden in onset and time limited (duration of <1 month) and often is caused by injury, trauma, or medical treatments such as surgery
  - Unresolved acute pain or subacute pain (defined as pain that has been present for 1-3 months) can evolve into chronic pain
  - Chronic pain typically lasts >3 months and can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or unknown cause

Dowell D, et al. *MMWR Recomm Rep*. 2022;71(3):1-95.

Acute pain is an important aspect of patient management in many healthcare settings

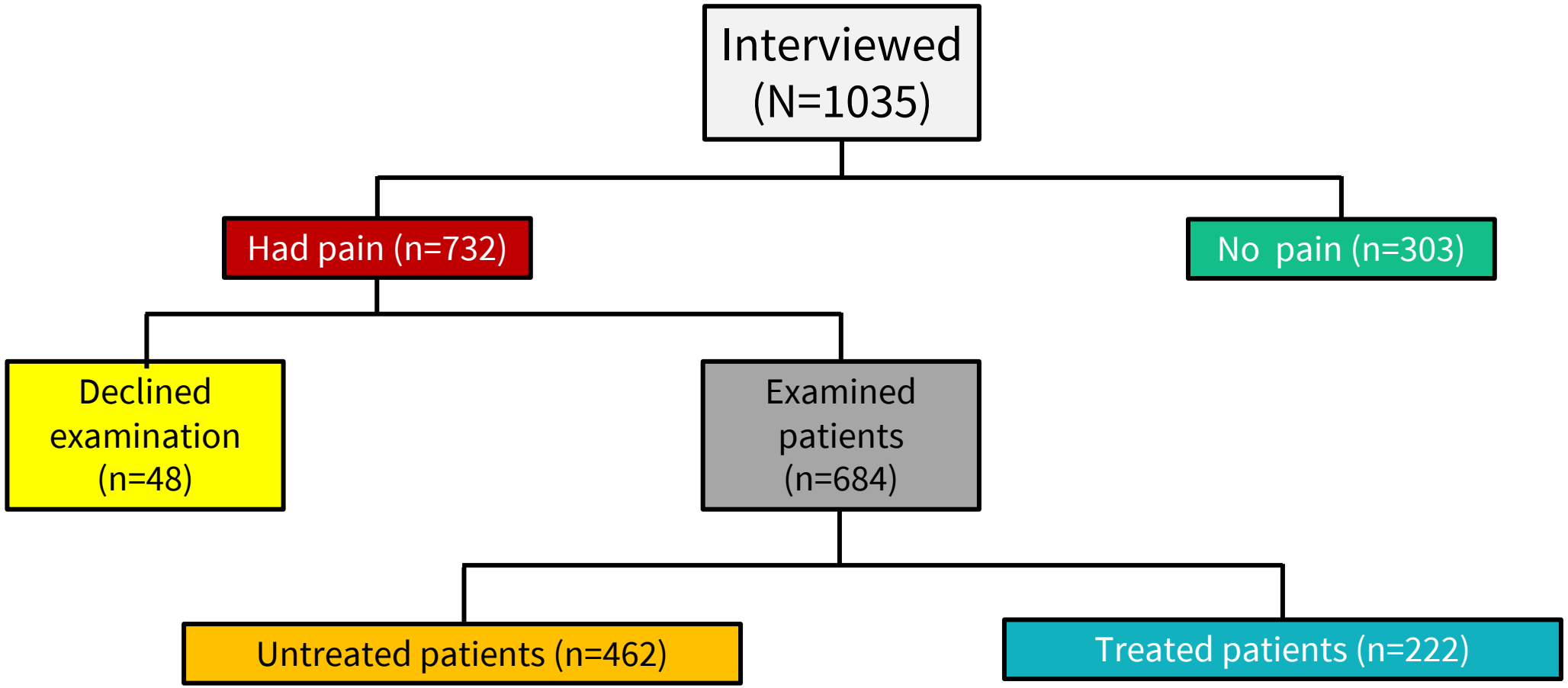
- Primary care[1]
- Orthopaedics[2]
- Emergency department[3]
- Dentistry[4]
- Gynecology[5]
- Surgery[6,7]
- Anesthesiology[6,7]

10 most common reasons for primary care visits in developed countries[1]

1. Hypertension
2. Upper respiratory tract infections
3. Depression or anxiety
4. **Back pain**
5. Routine health maintenance
6. Arthritis (excluding back)
7. Dermatitis
8. Acute otitis media
9. Diabetes
10. Cough

1. Bartol TG. *Medscape*. 2019. https://www.medscape.com/viewarticle/908364.
2. Delaney LD, et al. J Bone Joint Surg Am. 2020;102 Suppl 1(Suppl 1):3-9.
3. Mura P, et al. *J Pain Res*. 2017;10:2781-2788.
4. Kim SJ, Seo JT. *J Periodontal Implant Sci*. 2020;50(2):68-73.
5. Overcarsh P, et al. *Clin Obstet Gynecol*. 2019;62(1):59-66.
6. Garcia-Ramirez PE, et al. *Rev Colomb Anestesiol*. 2018;46(2):93-97
7. van Boekel RLM, et al. *Sci Rep*. 2021;11(1):16459.

Many patients with acute pain do not receive any treatment



63% of patients who presented with pain were not treated

Mura P, et al. *J Pain Res*. 2017;10:2781-2788.

Ineffectively treated acute pain adversely affects multiple organ systems

System	Effects
Cardiovascular	• Tachycardia, systemic hypertension, increased systemic vascular resistance, increased myocardial work, increased oxygen consumption
Pulmonary	• Hypoxia, hypercapnia, atelectasis, decrease in cough, flow volume, and ventilation/perfusion ratio
Gastrointestinal	• Nausea, vomiting, ileus, fasting
Renal	• Oliguria, urinary retention
Endocrine	• Increased adrenergic activity and increased metabolism
Central nervous system	• Anxiety, fear, sedation, fatigue, vagal inhibition
Extremities	• Skeletal muscle spasm, limited mobility
Immune	• Lowered immune response

Carrillo-Torres O, et al. *Revista Medica del Hospital General de Mexico*. 2018;81(4):276-281.

Acute pain reduces quality of life

- Higher post-surgical pain severity is associated with greater reductions in quality of life
  - 166 patients undergoing general or orthopedic surgery were assessed 7 days post surgery
  - Pain assessment tools used:
    - Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R)
    - 12-item Short-Form health survey (SF-12)
    - EuroQoL (EQ-5D)
  - At 7 days post surgery, 27 (16%) patients experienced pain for more than half of the day ($P = .02$)
    - Severity of pain on the APS-POQ-R was highly correlated with a decrease in HRQoL measured by the PCS and MCS on the SF-12 and by the EQ-5D, even after adjusting for confounders (age, gender, pre-operative HRQoL)

HRQoL is strongly associated with pain severity

Taylor RS, et al. *Pain Pract*. 2013;13(7):515-523.

HRQoL, health-related quality of life; MCS, Mental Component Score of SF-12; PCS, Physical Component Score of SF-12.

Acute pain assessment

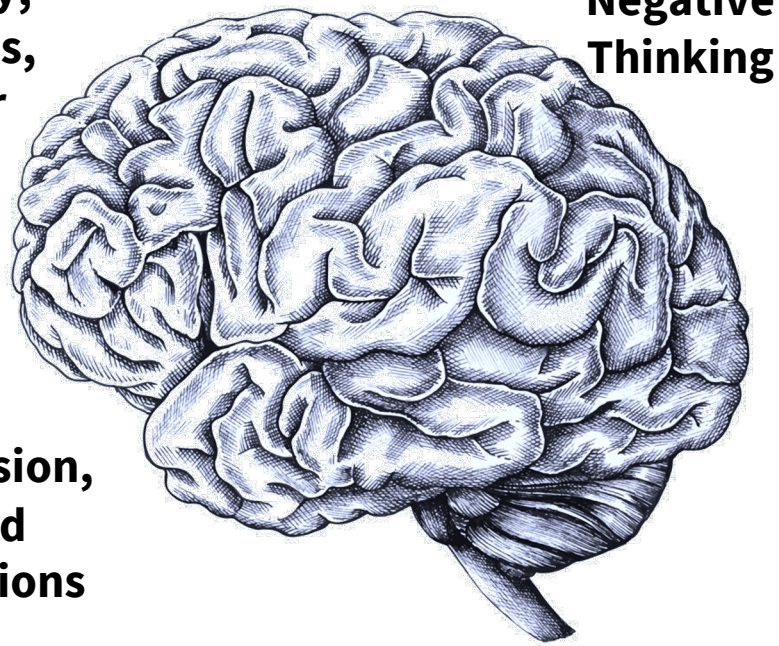
Pain is a complex experience

Inflammation

Poor Coping

Anxiety, Distress, Anger

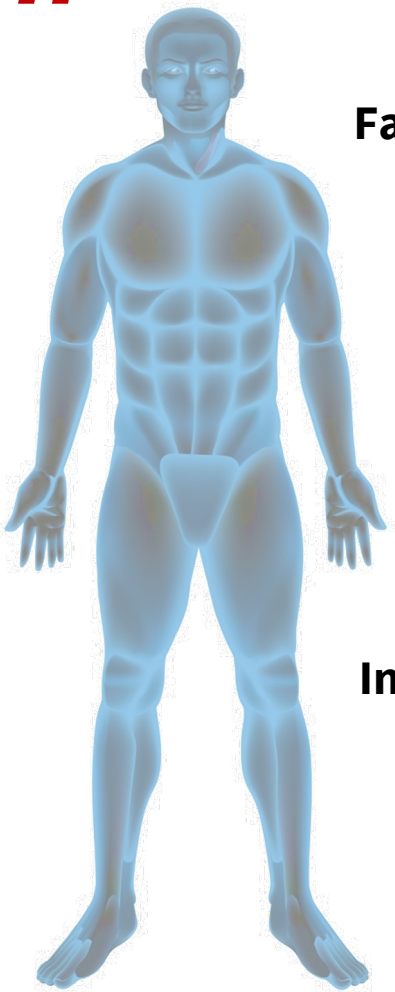
Negative Thinking



Depression, Mood Alterations

Pain

Fatigue



Reduced Activity, Avoidance Withdrawal

Delayed Healing

Inflammation, Muscle Weakness

Graphics from brgfx/Freepik. Art compilation courtesy of Robert W. Rhoades.

Pain assessment should be multidimensional

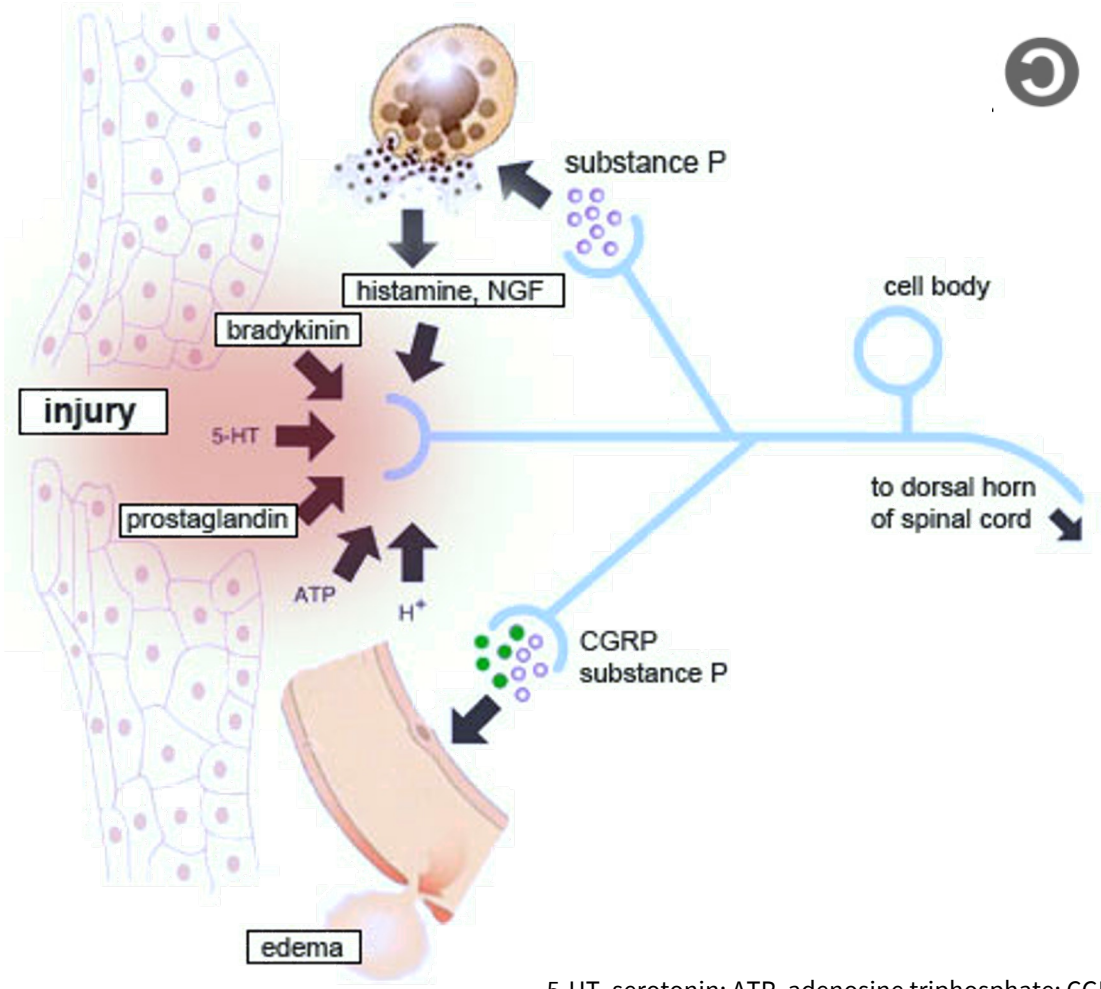
Scales for pain assessment

Pain Scale	Description	Intended population
Visual Analog Scale	Numerical rating scale (1-10)	Adults who are able to self-report pain
Wong-Baker Faces	Scale utilizing facial expressions linked to pain severity	Patients 3 years of age and above
Pain Assessment in Advanced Dementia (PAINAD)	Utilizes non-verbal cues to assess pain	Patients with dementia, unable to self-report
Behavioral Pain Scale	Observational assessment	Critically ill, sedated patients
Defense and Veterans Pain Rating Scale (DVPRS)	Combination graphic and numerical tool	Adults who are able to self-report pain

Pain pathways

Acute pain: what happens in the site of damage?

- Pain occurs when intense stimuli activate high-threshold nerve fibers called nociceptors that relay the pain signals via multiple ascending pathways to the brain
- When tissue is injured, multiple substances (e.g., bradykinin, histamine, prostaglandins, and others) are released and bind to receptors of primary afferents that signal pain
- Pain fibers, themselves may release substances (substance P, CGRP) that promote inflammation and increase pain



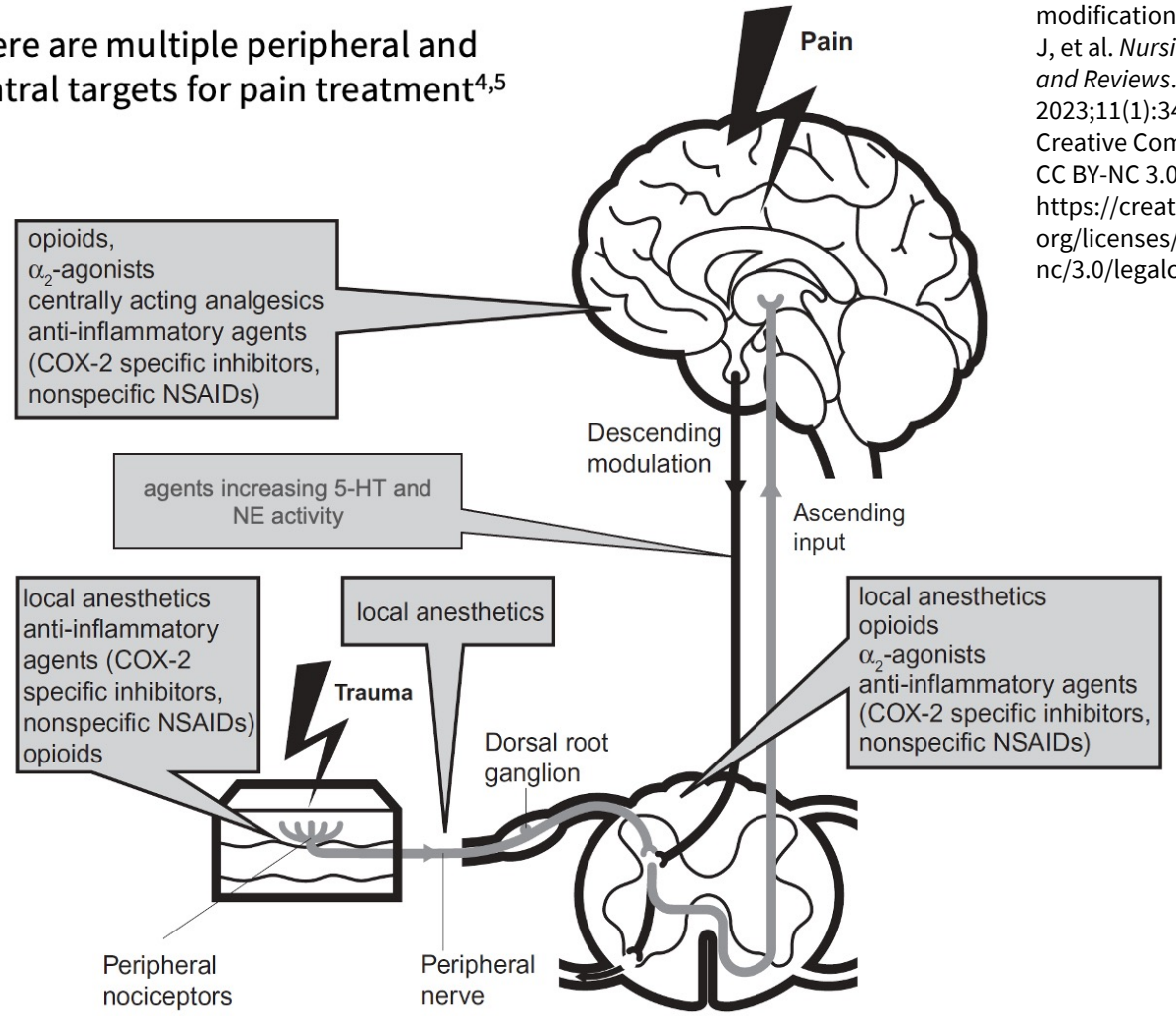
5-HT, serotonin; ATP, adenosine triphosphate; CGRP, calcitonin gene-related peptide; NGF, nerve growth factor.

Canadian Institutes of Health. The Brain From Top to Bottom. 2023. https://thebrain.mcgill.ca/flash/a/a_03/a_03_m/a_03_m_dou/a_03_m_dou.html

Ascending and descending pain pathways

- The serotonergic (5-HT) system plays a critical role in the modulation of nociception mainly through descending pain circuits[1]
- Descending noradrenergic projections inhibit nociceptive transmission in the spinal cord via activation of specific receptors on peripheral nociceptors and spinal neurons[2]
- The response to peripheral nociceptive stimuli can be modified in the spinal cord by the release of local endogenous modulators such as endogenous opioids[3]

There are multiple peripheral and central targets for pain treatment[4,5]



5-HT, serotonin; COX, cyclo-oxygenase; NE, norepinephrine; NSAID, nonsteroidal anti-inflammatory drug.

1. Tao ZY, et al. *Neural Plast*. 2019;2019:1389296.
2. Tavares I, et al. *Front Pain Res* (Lausanne). 2021;2:696515.
3. Kaczmarski P, et al. *Int J Mol Sci*. 2022;23(16):9080.
4. O'Brien J, et al. *Nursing: Research and Reviews.* 2013;3:9-22.
5. Kwon M, et al. *Pain Pract*. 2014;14(7):656-667.

Treating acute pain

Acute pain treatment goals

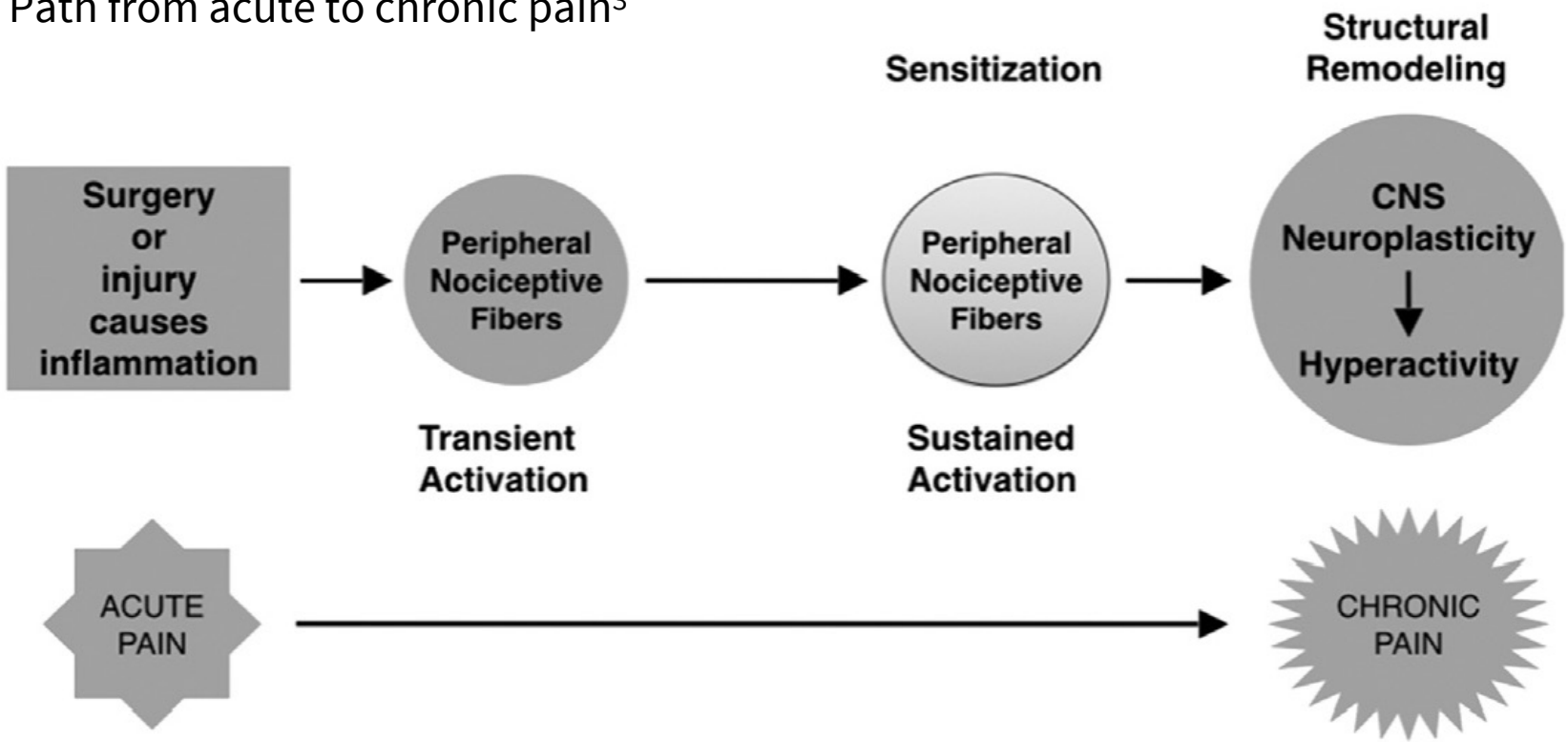
- The primary aim of acute pain management is to provide treatment that reduces the patient's pain, with minimal adverse effects, while allowing them to maintain function[1-3]
- A secondary aim is to prevent acute pain from progressing to chronic pain by interrupting the pain cycle[4,5]

1. Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.
2. Inter-Agency Task Force. 2019. Available at: https://www.hhs.gov/sites/default/files/pain-mgmt-best-practices-draft-final-report-05062019.pdf.
3. Dowell D, et al. MMWR Recomm Rep. 2022;71(3):1-95.
4. Feizerfan A, Sheh G. *Continuing Education in Anaesthesia, Critical Care & Pain*. 2015;15(2): 98-102.
5. Sinatra R. Pain Med. 2010;11(12):1859-1871.

Failure to effectively manage acute pain can lead to chronic pain

- Persistent nociceptive stimulation may cause various changes in pain physiology leading to pain sensitization[1-3]
- Cellular changes in the periphery and central nervous system result in peripheral and central sensitization[1-3]
- Cerebral reorganization and pathophysiological changes in neurons are associated with a hyper-excitable state[1-3]

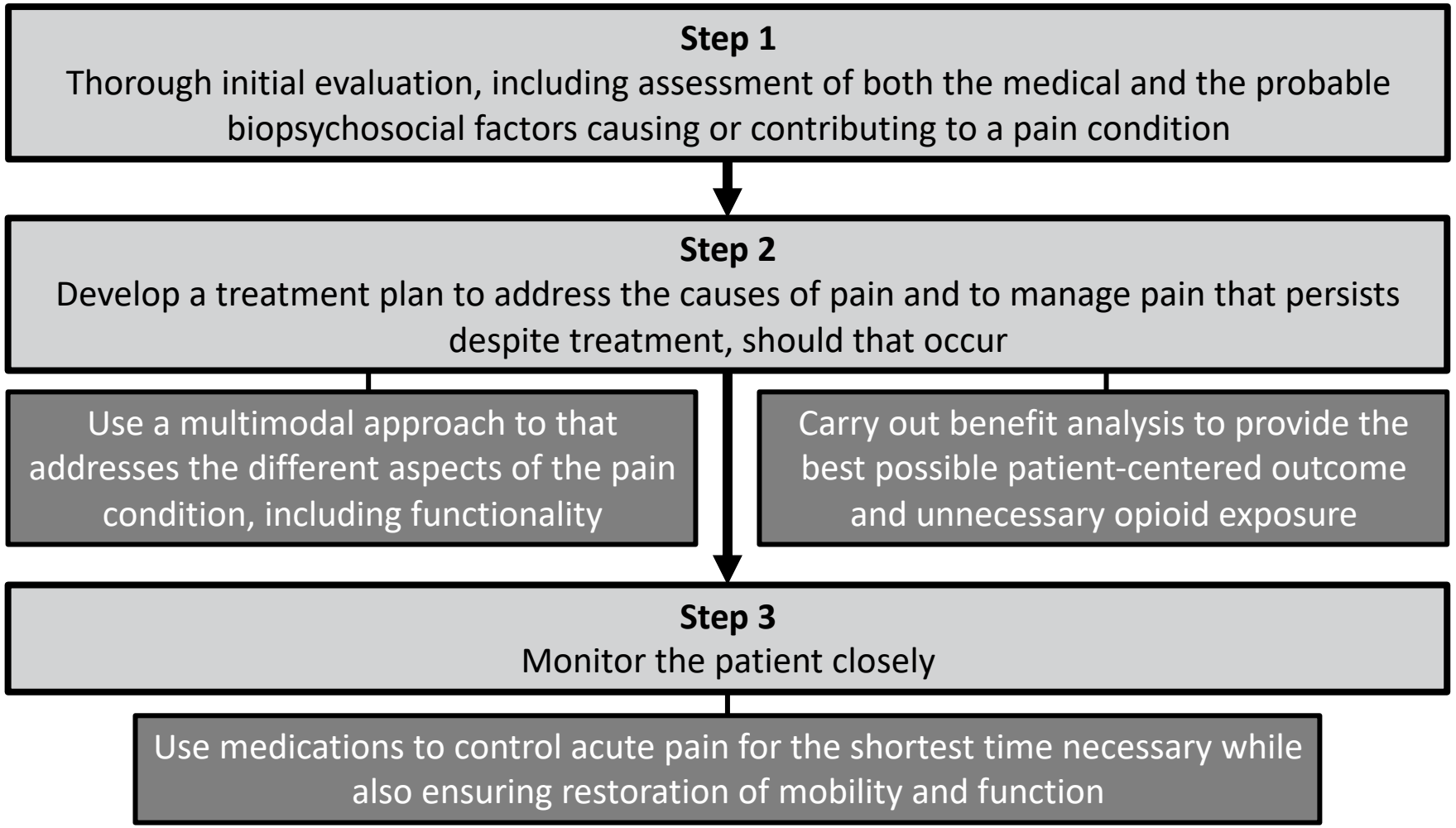
Path from acute to chronic pain[3]



1. Feizerfan A, Sheh G. *Continuing Education in Anaesthesia, Critical Care & Pain*. 2015;15(2): 98-102.
2. Sinatra R. *Pain Med*. 2010;11(12):1859-1871.
3. Pozek JP, et al. *Med Clin North Am*. 2016;100(1):17-30.

CNS, central nervous system.

Developing a strategy to meet acute pain treatment goals[1,2]



1. Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.
2. Inter-Agency Task Force. 2019. Available at: https://www.hhs.gov/sites/default/files/pain-mgmt-best-practices-draft-final-report-05062019.pdf.

Key points of agreement across treatment guidelines for acute pain[1-3]

- A multimodal and multidisciplinary approach to pain management attending to the physical health, behavioral health, long-term services and supports, and expected health outcomes and well-being of each person is critical
- NSAIDs, acetaminophen, or a combination is an effective initial treatment approach for acute pain syndromes
- Opioids should be used only for severe or refractory acute pain:
  - They should in combination with other medications (e.g., medications that work on opioid and monoamine receptors or with the use of acetaminophen/opioid or NSAID/opioid combinations)

1. Dowell D, et al. *MMWR Recomm Rep*. 2022;71(3):1-95.
2. Qaseem A, et al. *Ann Intern Med*. 2020;173(9):739-748.
3. Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.

Centers for Disease Control Guidance for the treatment of acute pain – focus on opioids

1	• Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risks to the patient.
2	• Nonopioid therapies are preferred for subacute and chronic pain.
3	• When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release and long-acting (ER/LA) opioids.
4	• When opioids are initiated for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage.

Dowell D, et al. *MMWR Recomm Rep*. 2022;71(RR-3):1-95.

Centers for Disease Control Guidance for the treatment of acute pain – focus on opioids

5	• For patients already receiving opioid therapy, clinicians should carefully weigh benefits and risks and exercise care when changing opioid dosage.
6	• When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.
7	• Clinicians should evaluate benefits and risks with patients within 1–4 weeks of starting opioid therapy for subacute or chronic pain or of dosage escalation.
8	• Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss risk with patients.

Dowell D, et al. *MMWR Recomm Rep*. 2022;71(RR-3):1-95.

Centers for Disease Control Guidance for the treatment of acute pain – focus on opioids

9	• When prescribing initial opioid therapy for acute, subacute, or chronic pain, and periodically during opioid therapy for chronic pain, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose.
10	• When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances.
11	• Clinicians should use particular caution when prescribing opioid pain medication and benzodiazepines concurrently.
12	• Clinicians should offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder.

Dowell D, et al. *MMWR Recomm Rep*. 2022;71(RR-3):1-95.

Medications used for the treatment of acute pain

Acetaminophen

Medication/dosing	Pain level/ Best use	Risk	Comments
Orally or rectally: 325 to 1,000 mg every 4-6 hrs IV: ≥50 kg, 650 mg every 4 hrs or 1,000 mg every 6 hrs; <50 kg, 12.5 mg per kg every 4 hrs or 15 mg per kg every 6 hrs Maximum: 75 mg per kg per day, not to exceed 4,000 mg per day	• Mild to moderate • Mild osteoarthritis, generalized headache, ankle sprain	• Liver toxicity	• Well tolerated First-line in patients with renal and hepatic impairment and CVD • ≤2,000 mg per day in patients with advanced hepatic disease and severe alcohol use disorder • May be combined with NSAIDs for postoperative pain

Amaechi O, et al. *Am Fam Physician*. 2021;104(1):63-72.

COX, cyclo-oxygenase; CVD, cardiovascular disease; IM, intramuscular; IV, intravenous; NSAID. nonsteroidal anti-inflammatory drug.

Medications used for the treatment of acute pain

Nonselective NSAIDs

Medication/dosing	Pain level/ Best use	Risk	Comments
Ibuprofen: 200-400 mg every 6-8 hrs Maximum: 1,200 mg per day	• Mild to moderate • Migraine, low back pain, dysmenorrhea, renal colic, postoperative pain	• Cardiovascular, gastrointestinal, renovascular events, bronchospasm (aspirin)	• Anti-inflammatory effects • Consider adding proton pump inhibitor or switching to a selective COX-2 NSAID to decrease gastrointestinal risk • May have a ceiling analgesic effect
Naproxen: 250 mg every 6-8 hrs or 500 mg every 12 hrs Maximum: 1,000 mg per day			
Diclofenac: 50 mg every 8 hrs Maximum: 150 mg per day			
Ketorolac Orally: 10 mg every 4-6 hrs IM: 30-60 mg as a single dose or 15-30 mg every 6 hrs IV: 10-15 mg every 6 hrs Maximum: oral 40 mg per day; IM/IV 120 mg per day			
Meloxicam: 7.5-15 mg per day Maximum: 15 mg per day			

Amaechi O, et al. *Am Fam Physician*. 2021;104(1):63-72.

COX, cyclo-oxygenase; CVD, cardiovascular disease; IM, intramuscular; IV, intravenous; NSAID. nonsteroidal anti-inflammatory drug.

Medications used for the treatment of acute pain

	Medication/dosing	Pain level/ Best use	Risk	Comments
Selective COX-2 NSAIDs	Meloxicam: 7.5 mg per day Celecoxib (Celebrex): 100-200 mg per day	• Mild to moderate • Migraine, low back pain, dysmenorrhea, renal colic, postoperative pain	• Cardiovascular, renovascular events	• More expensive than nonselective NSAIDs Celecoxib has a U.S. Food and Drug Administration boxed warning for increased risk of cardiovascular disease
Acetaminophen + NSAID	See individual medications	• Mild to moderate May continue use for severe pain • Pain refractory to either agent alone, postoperative pain	• See individual medications	• Combinations have superior effectiveness vs. single agents Effective for postoperative pain Combining medications has lower risk of adverse effects than high doses of single agents

Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.

Medications used for the treatment of acute pain

Opioid + Acetaminophen or NSAID*

Medication/dosing	Pain level/ Best use	Risk	Comments
Hydrocodone/acetaminophen: 2.5 mg/325 mg-10 mg/325 mg every 4-6 hrs Maximum: 4,000 mg per day of acetaminophen	• Persistent moderate to severe pain • Pain refractory to other agents, postoperative pain, fracture pain	• See individual medications	• Superior effectiveness compared with single agent Opioid sparing effect with decreased risk of adverse events
Hydrocodone/ibuprofen: 2.5 mg/200 mg-10 mg/ 200 mg every 6-8 hrs Maximum: 1,200 mg per day of ibuprofen			
Oxycodone/acetaminophen 2.5 mg/325 mg-10 mg/ 325 mg every 4-6 hrs Maximum: 4,000 mg per day of acetaminophen			

Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.

Medications used for the treatment of acute pain

Dual-action opioid medications

Medication/dosing	Pain level/ Best use	Risk	Comments
Tramadol: 25 mg every 4-6 hrs, titrated to 50 to 100 mg as needed Maximum: 400 mg per day	• Persistent moderate to severe pain • Pain refractory to other agents, with goal of limiting more potent opioids	• Dizziness, sedation, constipation, opioid use disorder, serotonin syndrome, tramadol decreases the seizure threshold	• Adverse effects comparable to full agonists with less pain relief
Tapentadol : 50 to 100 mg every 4-6 hrs Maximum: 600 mg per day			

Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.

IV, intravenous.

Medications used for the treatment of acute pain

Full agonist opioids

Medication/dosing	Pain level/ Best use	Risk	Comments
Oxycodone: 5 mg orally every 4-6 hrs as needed	• Persistent severe pain • Short course for severe acute pain, pain refractory to other medications	• Nausea, emesis, constipation, sedation, respiratory depression, opioid use disorder	• Limit prescription to 3-day course • Continue other medication classes as tolerated • Higher doses may be required for patients taking chronic opioid therapy or naltrexone
Morphine: 1-4 mg IV every 4 hrs titrated up as needed; 10-15 mg IV every 4-6 hours for severe pain Maximum: limited by opioid-related adverse effects			
Hydromorphone Orally: 2-4 mg every 4-6 hrs IV: 0.2-1 mg every 2-3 hours Maximum: reserve for severe pain; use caution with dosing to prevent oversedation			

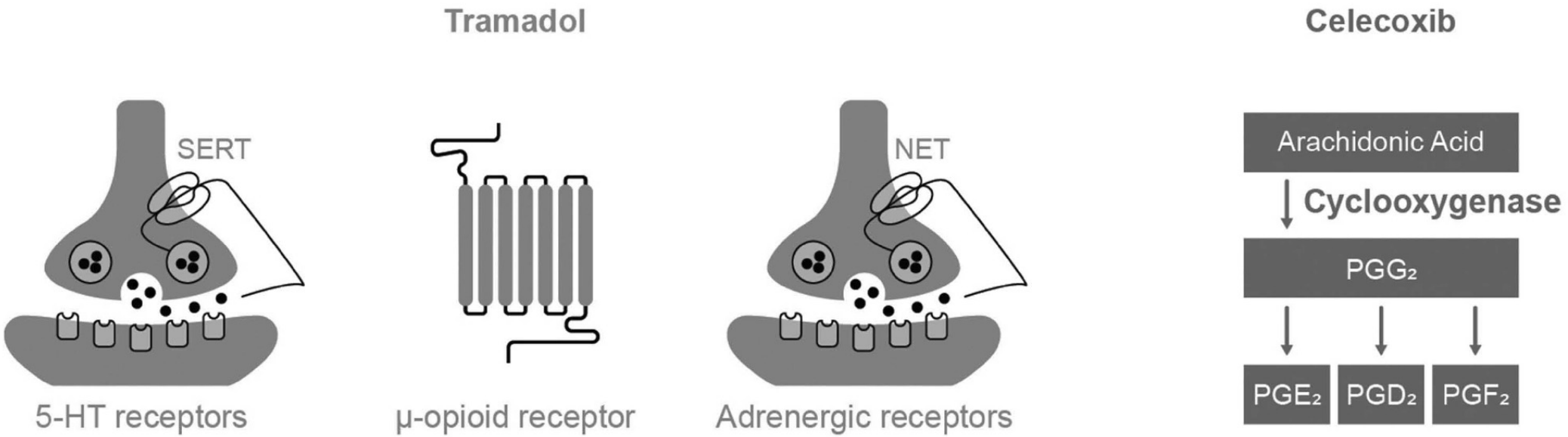
Amaechi O, et al. Am Fam Physician. 2021;104(1):63-72.

IV, intravenous.

Newer approaches to acute pain treatment

Attacking multiple targets with an optimized celecoxib-tramadol combination

Cellular actions of tramadol and celecoxib



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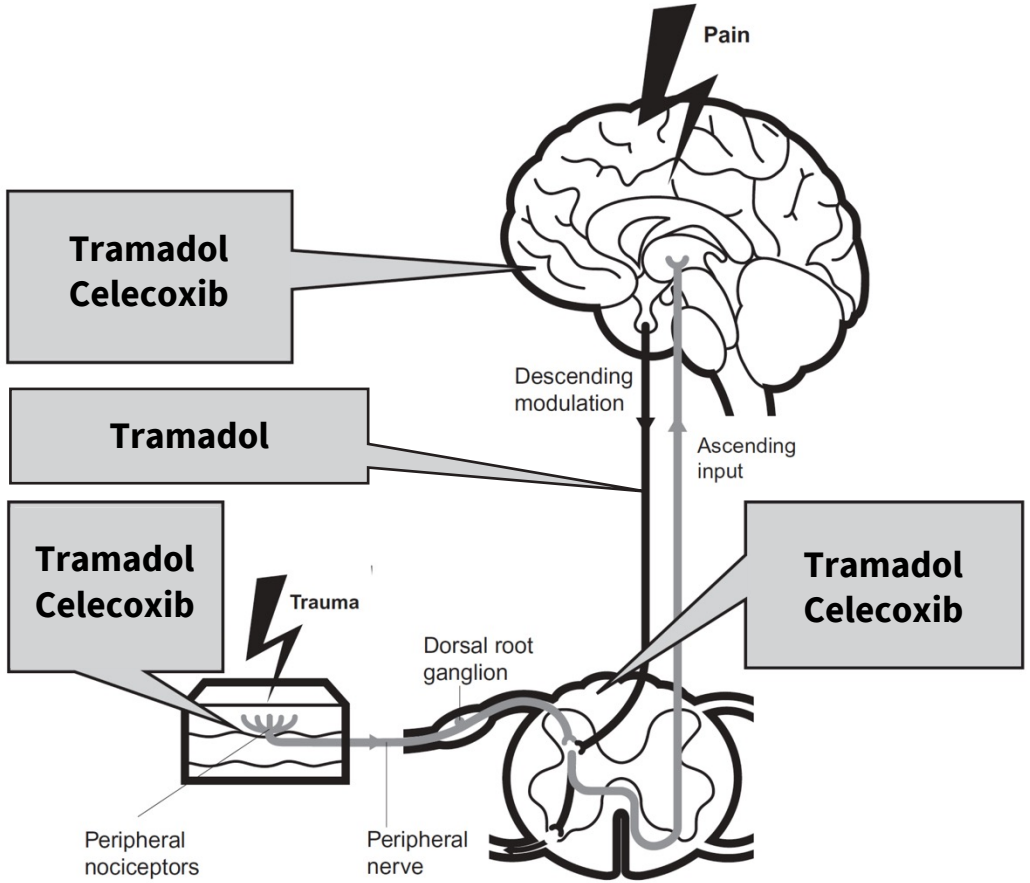
5-HT, 5-hydroxytryptamine; NET, norepinephrine transporter; PG, prostaglandin; SERT, serotonin transporter.

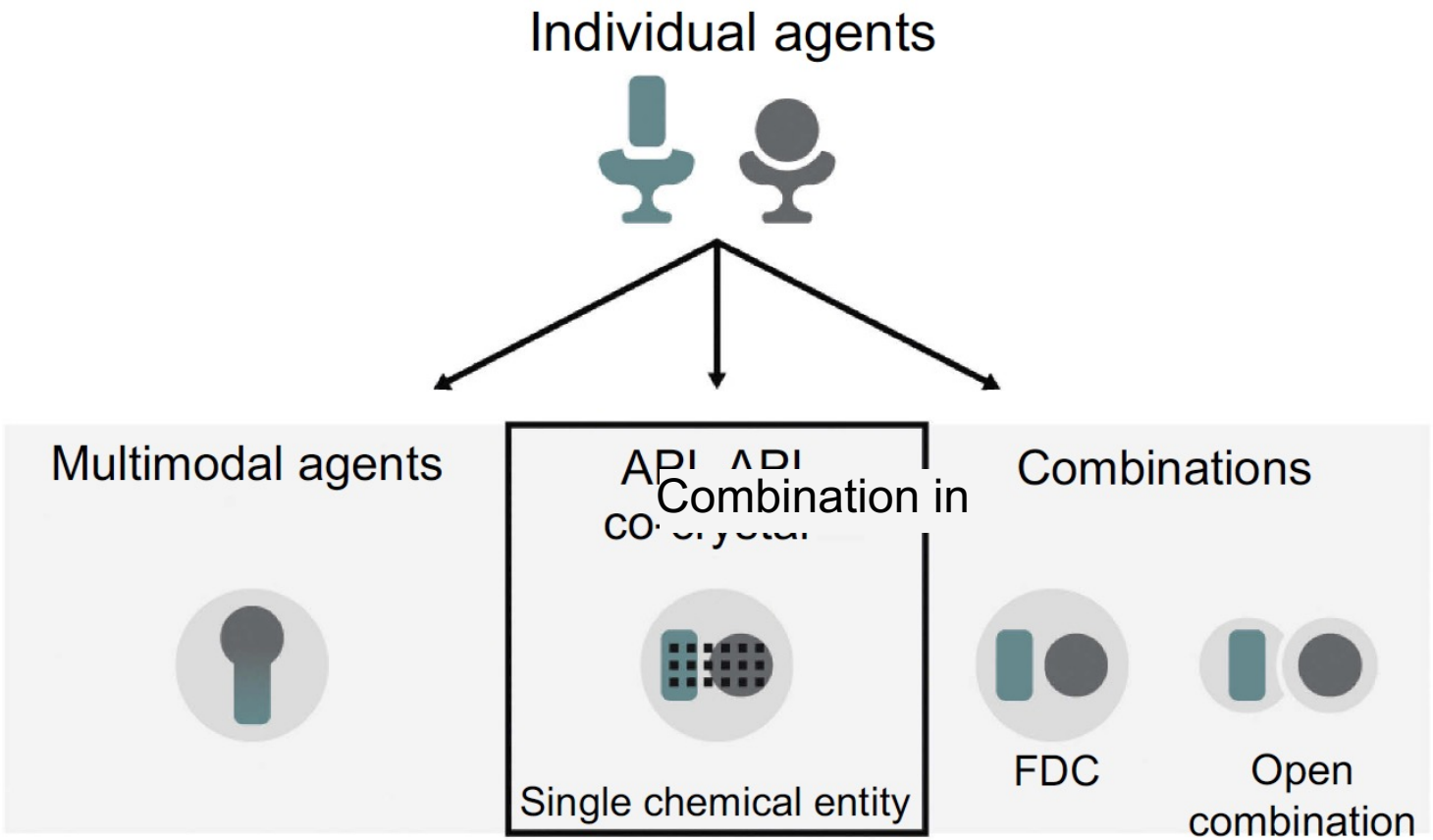
Attacking multiple targets with an optimized celecoxib-tramadol combination

The combination of tramadol modulates pain signalling at multiple levels[1-3]



1. O'Brien J, et al. *Nursing: Research and Reviews.* 2013;3:9-22.
2. Kwon M, et al. *Pain Pract*. 2014;14(7):656-667.
3. Almansa C, et al. *J Pain Res*. 2019;12:2679-2689.

Co-crystallization results in a single chemical entity



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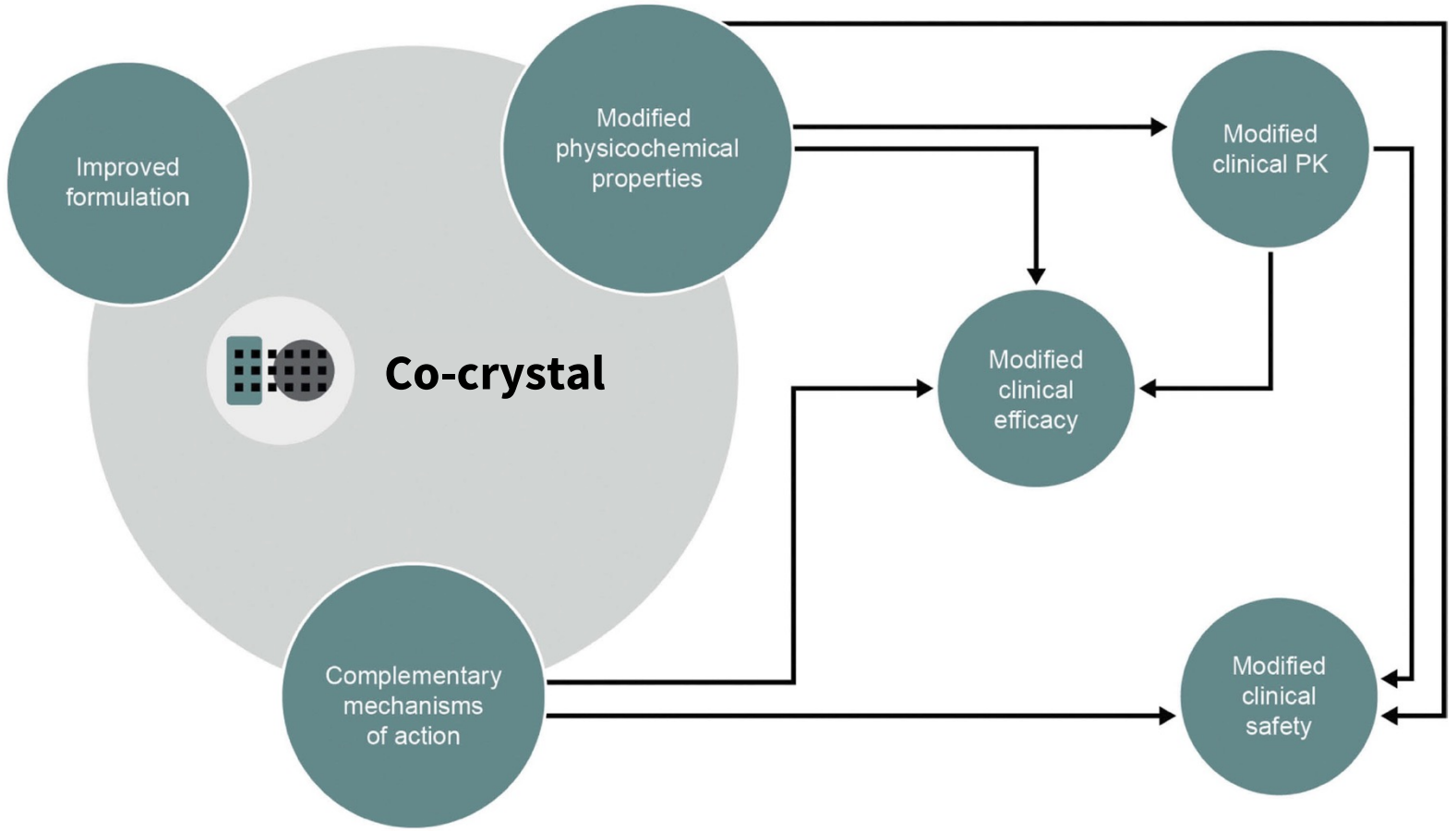
FDC, fixed dose combination.

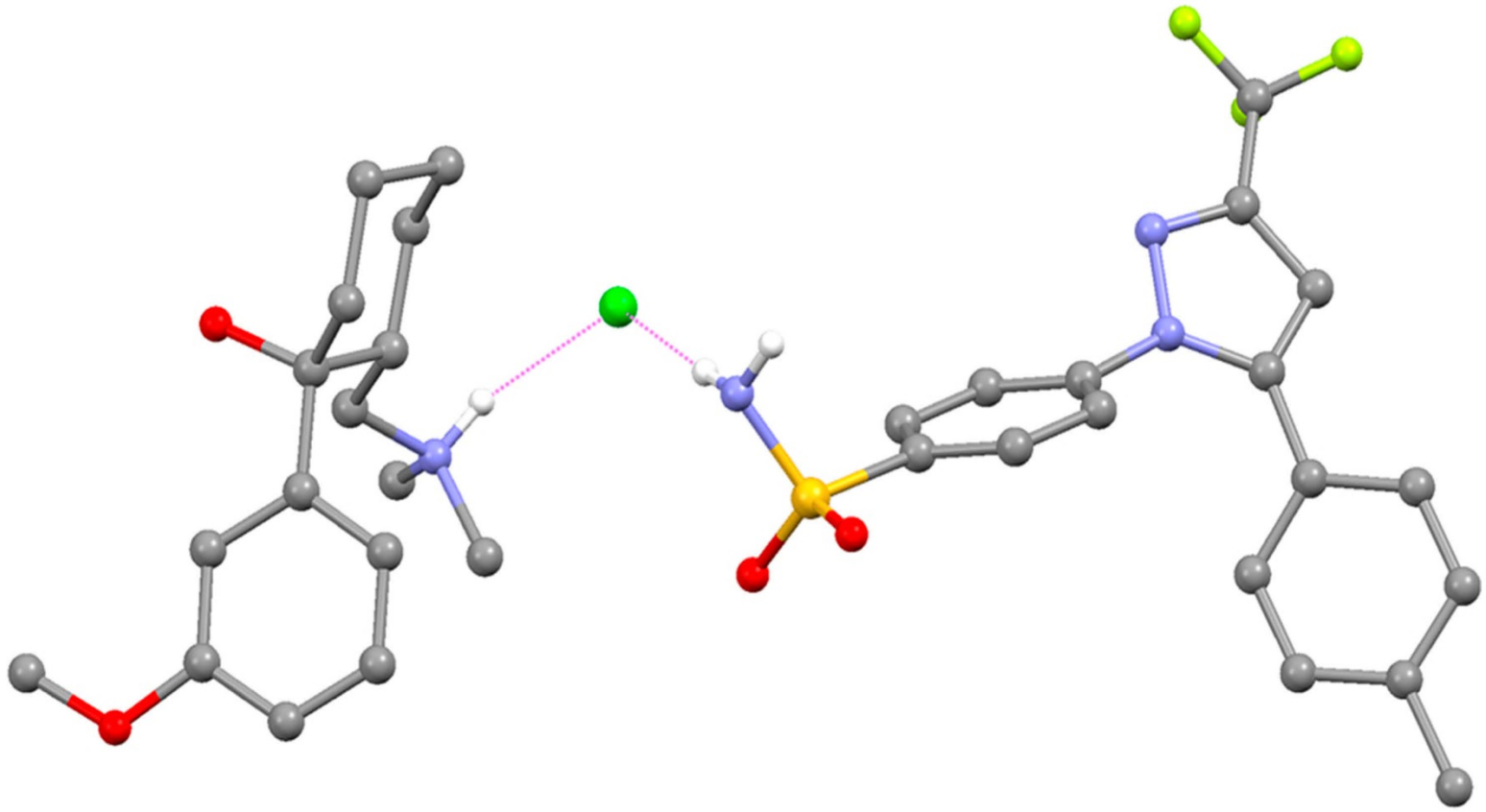
Advantages of co-crystallization for delivery of combination therapy



FDC, fixed dose combination; PK, pharmacokinetic.

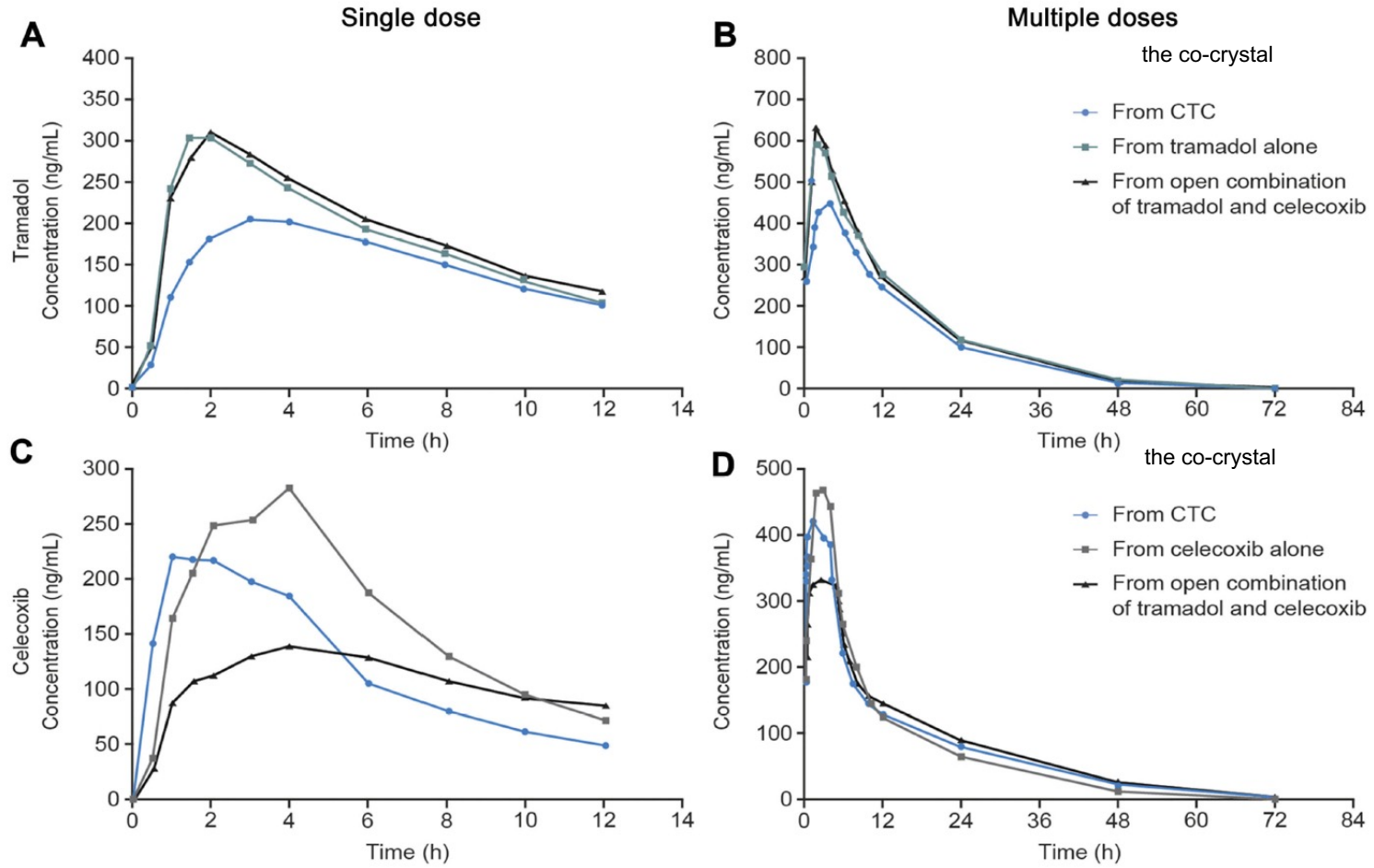
Celecoxib-tramadol co-crystal

- Evolution of crystal engineering
- Crystal engineering is the application of chemistry of bringing 2 molecules together
- Leveraging the concept of “self-assembly” by forces of attraction into a unique single, crystalline solid
- Rationally designed to problem solve and enhance properties of pharmaceutical substances



The pharmacokinetic advantage of the co-crystal

- Tramadol from the co-crystal has a lower maximum plasma concentration vs tramadol taken alone or concomitantly with celecoxib and a delayed or longer time to maximum plasma concentration vs monotherapy or an open combination. This minimizes the overall daily opioid exposure in patients and is aligned with the CDC recommendations[1,2]
- Celecoxib absorption is accelerated with the co-crystal vs celecoxib alone, and tramadol-mediated interference of celecoxib absorption is minimized with the co-crystal vs concomitant administration of celecoxib and tramadol.
- The celecoxib portion of the co-crystal has a higher maximum concentration vs the open combination with tramadol and the time to maximum concentration is shorter/earlier than noted with open combination[1]

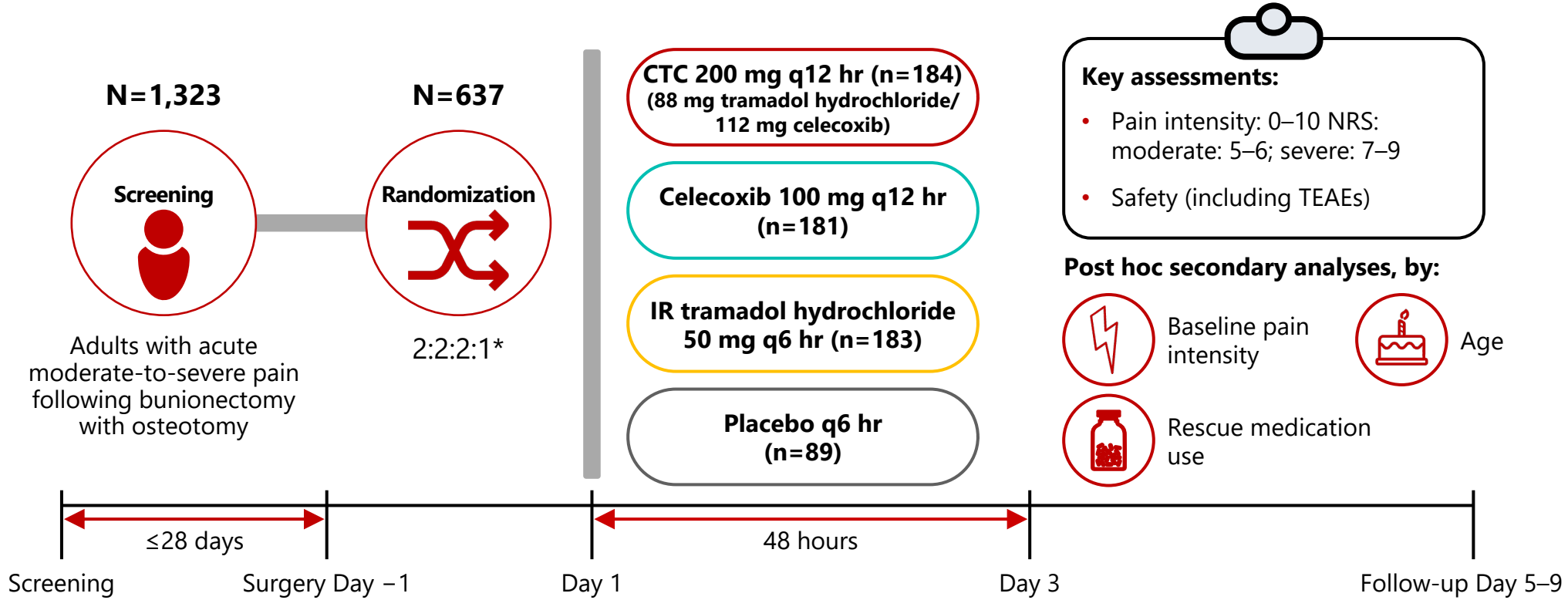


The pharmacokinetic profiles of tramadol (A) and (B) and celecoxib (C) and (D) were modified after administration of the co-crystal compared with administration of the commercially available, single-entity reference products alone or in open combination[3]

1. Viscusi ER, et al. *Pain Pract*. 2023;23(1):8-22.
2. Dowell D, et al. *MMWR Recomm Rep*. 2022;71(3):1-95.
3. Almansa C, et al. *J Pain Res*. 2019;12:2679-2689.

Evaluation of the first co-crystal for acute pain – study design

Phase 3, randomized, double-blind, factorial, active- and placebo-controlled trial (NCT03108482) at 6 clinical research centers in the USA

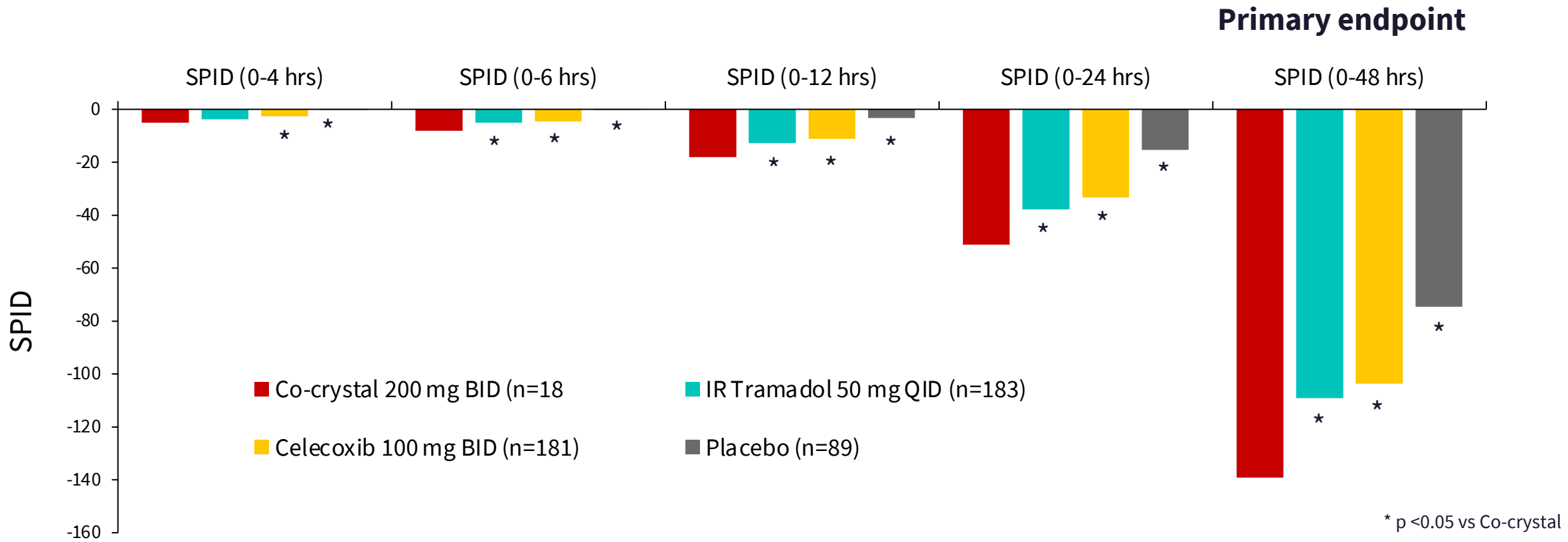


*Randomization was stratified by study center and baseline pain intensity (moderate vs severe).

Primary endpoint: Sum of pain intensity differences (SPID) over 0–48 hours

BID, twice daily; CTC, celecoxib-tramadol co-crystal; NRS, numeric rating scale; QID, four times per day; SPID, sum of pain intensity difference; TEAE, treatment-emergent adverse event.

Efficacy of celecoxib-tramadol co-crystal for acute pain treatment – efficacy



- The co-crystal provided greater efficacy than tramadol or celecoxib, with lower rescue medication use (including significantly less use of rescue opioid)

BID, twice daily; IR, immediate release; NRS, numeric rating scale; QID, four times per day; SPID, sum of pain intensity difference. TEAE, treatment-emergent adverse event.

Safety of the Co-crystal for acute pain treatment

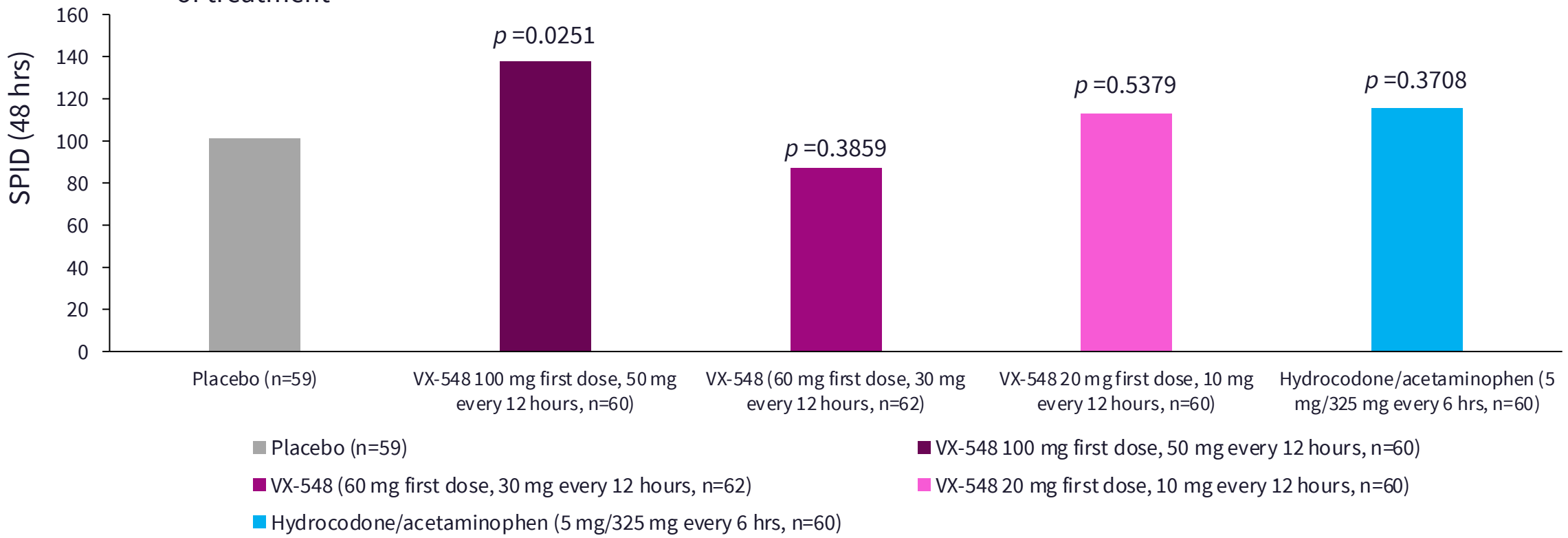
	Co-crystal (n=163)	Tramadol (n=183)	Celecoxib (n=182)	Placebo (n=89)
Patients with ≥1 TEAE	116 (63.4)	116 (63.4)	95 (52.2)	51 (57.3)
Patients with drug-related TEAE	69 (37.7)	89 (48.6)	40 (22.0)	22 (24.7)
Patients with TEAE by severity				
Mild	73 (39.9)	64 (35.0)	70 (38.5)	34 (38.2)
Moderate	41 (22.4)	48 (26.2)	23 (12.6)	15 (16.9)
Severe	2 (1.1)	4 (2.2)	2 (1.1)	2 (2.2)
Patients with serious TEAE	0	0	0	0
Patients with TEAE leading to discontinuation	3 (1.6)	3 (1.6)	0	0
Most common TEAE occurring in ≥5% of patients in any group				
Nausea	55 (30.1)	69 (37.7)	30 (16.5)	17 (19.1)
Dizziness	31 (16.9)	34 (18.6)	9 (4.9)	13 (14.6)
Vomiting	29 (15.8)	30 (16.4)	4 (2.2)	2 (2.2)
Headache	21 (11.5)	33 (18.0)	20 (11.0)	6 (6.7)
Somnolence	15 (8.2)	10 (5.5)	4 (2.2)	3 (3.4)
Decreased appetite	6 (3.3)	11 (6.0)	1 (0.5)	0
Constipation	4 (2.2)	13 (7.1)	9 (4.9)	3 (3.4)

Viscusi ER, et al. *Pain Pract*. 2023;23(1):8-22.

TEAE, treatment-emergent adverse event.

Phase 2 results for the NaV1.8 antagonist VTX-548 in acute pain

- Randomized, double-blind, placebo-controlled, dose-ranging trial that evaluated three different doses of VX-548 administered orally over 36 hours in 274 patients with acute pain following bunionectomy surgery
- The primary endpoint was the time-weighted Sum of the Pain Intensity Difference (SPID) over the first 48 hours of treatment

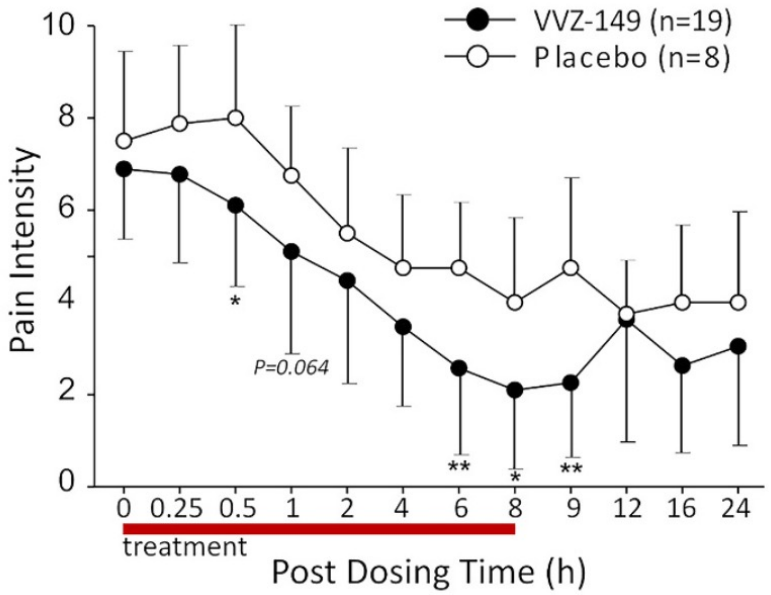


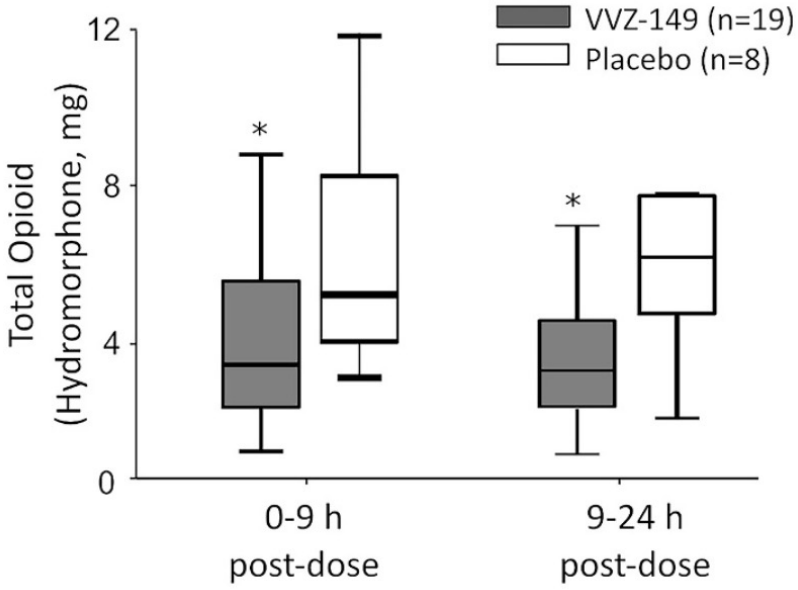
p-values are vs placebo

Vertex. 2022. https://investors.vrtx.com/node/29386/pdf.

Opiranserin (VVZ-149)

- VVZ-149 is a small molecule that inhibits the glycine transporter type 2 and the serotonin receptor 5-hydroxytryptamine 2A.
- It has been evaluated in a randomized, parallel group, double-blind phase 2 clinical that included 60 patients undergoing laparoscopic colorectal surgery.
- VVZ-149 significantly decreased pain intensity and opioid use in patients among patients who required rescue opioids.





* p <0.05, ** p <0.01 for the difference between treatments

Brand Names of Drugs for Reference

Drug	Brand Name
Acetaminophen	Tylenol
Acetaminophen + hydrocodone	Vicodin HP
Acetaminophen + ibuprofen	Advil Dual Action
Acetaminophen + oxycodone	Percocet
Celecoxib	Celebrex
Celecoxib-tramadol co-crystal	Seglentis
Diclofenac	Voltaren
Hydromorphone	Dilaudid

Drug	Brand Name
Ibuprofen	Advil
Ibuprofen + hydrocodone	Ibudone
Ketorolac	Toradol
Meloxicam	Mobic
Morphine	Avinza
Naproxin	Aleve
Oxycodone	Oxycontin
Pregabalin	Lyrica
Tapentadol	Nucynta
Tramadol	Ultram

Summary

- Acute pain is very common and effective management is essential to preserve/restore function and quality of life and to prevent acute pain from progressing to chronic pain
- All current guidelines support a multimodal approach to pain management and reserving limited use of opioids to patients with severe pain that cannot be managed with other agents
- There are a number of new agents/formulations recently approved or in development for the treatment of acute pain
  - The recently approved co-crystal formulation of celecoxib and tramadol provides a single-medication multimodal approach with demonstrated efficacy and safety in multiple types of acute pain
  - Blockade of sodium channels also appears to hold promise for the treatment of acute pain

Special Resource Toolkit

Visit the website via the QR code to the right or the URL below for more information on this topic and to review the presentation.

Practical Approaches to Acute Pain Management

URL: https://pceconsortium.org/toolkit/pain

Post-presentation Survey:

Please complete the survey by using the QR code to the right or the URL below.

Practical Approaches to Acute Pain Management

https://www.pcmg-us.org/survey/post/pain6