MANAGEMENT
Goals of Treatment
Goals in Pain Management

- Involve the patient in the decision-making process
- Agree on realistic treatment goals before starting a treatment plan

Optimized pain relief
- Improved function

Minimized adverse effects
Peri-operative Pain Management Aims to Control Pain and Decrease Likelihood of Developing Chronic Pain

Use of pharmacological agents before, during and after surgery may:

- acute pain
- subsequent development of chronic pain
- morbidity, costs and other consequences of chronic pain

### Importance of Post-operative Pain Management

**Consequences of the failure to adequately relieve pain:**

- Pneumonia
- Delayed readiness for discharge
- Increased patient monitoring/nursing time
- Delayed ambulation

**Proper pain management may lead to:**

- Earlier mobilization
- Decreased hospital stay
- Reduced hospital cost
- Decreased likelihood of developing chronic pain

---

Controlling Post-operative Physiology

Reduced morbidity and accelerated convalescence

Pre-operative information + teaching
Attenuation of intra-operative stress
Pain relief
Exercise
Enteral nutrition
Supportive agents/therapy in high-risk patients

Multimodal Treatment of Pain Based on Biopsychosocial Approach

- Pharmacotherapy
- Stress management
- Intervventional pain management
- Biofeedback
- Education
- Complementary therapies
- Occupational therapy
- Physical therapy
- Sleep hygiene
- Lifestyle management

Non-pharmacological Treatment
Pre-operative Management Issues

Pre-operative preparation may help minimize post-operative pain.

- Comprehensive plan to treat post-operative nausea and vomiting
- Patient and caregiver education
- Assuring the patient that his or her pain level will be monitored
- Familiarizing the patient with the pain scales
- Counseling the patient to overcome fears of addiction

Pre-operative Assessment

- Underlying medical conditions
- Peri-operative pain and/or post-operative nausea and vomiting experience
- Current medications
- Reactions/allergies to analgesics
- Smoking history
- Perceived barriers to pain management
- Pain management preferences
- Previous or ongoing pain
- Ineffective and effective methods of treatment
- Patient attitude to pain medications
- History of substance abuse
- Psychological history
- Patient expectations of pain level
- Patient’s expression of pain

South African Acute Pain Guidelines: Cognitive Behavioral Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Potential utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassurance and provision of information</td>
<td>• Reduces pain and distress after minor procedures</td>
</tr>
<tr>
<td></td>
<td>• May improve pain relief after more major surgery</td>
</tr>
<tr>
<td></td>
<td>• No significant benefit after non-surgical procedures</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>• Not effective in the perioperative setting</td>
</tr>
<tr>
<td>Attentional techniques (e.g., imagery, distraction, music therapy)</td>
<td>• Distraction may reduce analgesic consumption in the perioperative phase</td>
</tr>
<tr>
<td></td>
<td>• Music therapy is ineffective</td>
</tr>
<tr>
<td>Hypnosis</td>
<td>• Evidence that acute procedural pain for minor procedures can effectively be managed by hypnosis</td>
</tr>
</tbody>
</table>
# South African Acute Pain Guidelines: Physical Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Potential utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcutaneous electrical nerve stimulation</td>
<td>• Not thought to be effective in postoperative pain</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>• May reduce analgesic requirements in postoperative pain</td>
</tr>
<tr>
<td>Massage and manual therapy</td>
<td>• No use in postoperative pain</td>
</tr>
<tr>
<td>Heat and cold therapy</td>
<td>• May reduce opioid consumption after orthopaedic trauma</td>
</tr>
<tr>
<td></td>
<td>• No help after other major surgeries</td>
</tr>
</tbody>
</table>

South African Acute Pain Guidelines: Non-pharmacological Management of Sports Injuries

- **Rest**
- **Ice**
- **Compression**
- **Elevation**

Important elements of patient management in the first 48 hours following musculoskeletal injury.

Physiotherapy, including therapeutic ultrasound, followed by rehabilitation form an essential part of treatment from 24 hours after injury.
# Physical Interventions for Acute Pain

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Potential utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcutaneous electrical nerve stimulation</td>
<td>• Certain stimulation patterns effective in some acute pain settings (e.g., post-operative pain)</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>• Reduces post-operative pain as well as opioid-related adverse effects</td>
</tr>
<tr>
<td></td>
<td>• May be effective in some other acute pain settings</td>
</tr>
<tr>
<td>Massage and manual therapy</td>
<td>• Little consistent evidence for use in post-operative pain</td>
</tr>
<tr>
<td>Heat and cold therapy</td>
<td>• Evidence for benefits from post-operative local cooling is mixed</td>
</tr>
</tbody>
</table>

## Cognitive Behavioral Interventions for Acute Pain

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Potential utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassurance and provision of information</td>
<td>• Evidence that information is effective in reducing procedure-related pain is tentatively supportive and not sufficient to make recommendations</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>• Evidence is weak and inconsistent</td>
</tr>
</tbody>
</table>
| Attentional techniques (e.g., imagery, distraction, music therapy) | • Listening to music produces a small reduction in post-operative pain and opioid requirement  
  • Immersive virtual reality distraction is effective in reducing pain in some clinical situations |
| Hypnosis                                    | • Evidence of benefit is inconsistent                                               |
| Coping methods/behavioral instruction       | • Training prior to surgery reduces pain, negative affect and analgesic use         |
**Australian Guidelines: Non-pharmacological Treatment of Acute Neck Pain**

**Recommended**
- Exercise/advice to stay active
- Multimodal therapy
- Pulsed electromagnetic therapy

**Not recommended**
- Collars

**Insufficient evidence**
- Acupuncture
- Cervical manipulation
- Cervical passive mobilisation
- Electrotherapy
- Gymnastics
- Biopsychosocial rehabilitation
- Neck school
- Patient education
- Traction
- TENS

*TENS = transcutaneous electrical nerve stimulation*

Australian Guidelines: Non-pharmacological Treatment of Acute Shoulder Pain

Recommended
- Exercise
- Therapeutic ultrasound

Conflicting/insufficient evidence
- Acupuncture
- Extracorporeal shock wave treatment
- Manual therapy
- Surgery
- Transcutaneous electrical nerve stimulation

Australian Guidelines: Non-pharmacological Treatment of Acute Knee Pain

**Recommended**
- Exercise/advice to stay active
- Foot orthoses
- Injection therapy

**Not recommended**
- Laser therapy

**Insufficient evidence**
- Patellofemoral orthoses
- Acupuncture
- Electrical stimulation

Non-pharmacological Treatment of Acute Pain: Summary of Guideline Recommendations

• No real consensus regarding non-pharmacological treatment modalities
• Pre-operative patient education may help management of post-operative pain

Pharmacological Treatment
Ideal Characteristics for Acute Analgesic Therapy

- Ideal drug characteristics for acute pain therapy:
  - Rapid onset
  - Long duration
  - Effective analgesia
  - Limited adverse effects
Patients Prefer Avoiding Side Effects to Complete Pain Control

Relative Importance Placed by Patients on Different Attributes of Acute Pain Therapy

- Pain control: 41%
- Setting and route of administration: 12%
- Side effect type: 28%
- Side effect severity: 19%

## Proportion of Patients Experiencing Adverse Events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>25 (50%)</td>
</tr>
<tr>
<td>Mental cloudiness/dizziness</td>
<td>41 (82%)</td>
</tr>
<tr>
<td>Itching</td>
<td>27 (54%)</td>
</tr>
<tr>
<td>Nightmares/hallucinations</td>
<td>16 (32%)</td>
</tr>
<tr>
<td>Mood changes/alterations</td>
<td>17 (34%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>35 (70%)</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>24 (48%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>16 (32%)</td>
</tr>
</tbody>
</table>

So how do we treat acute pain?

Treat according to pain mechanisms involved

Multimodal analgesia
Multimodal or Balanced Analgesia

- Improved analgesia
- ↓ doses of each analgesic
- ↓ severity of side effects of each drug

Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug


Potentiation

Opioid

Acetaminophen
nsNSAIDs/coxibs
α2δ ligands
Ketamine
Clonidine
Nerve blocks

Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Synergistic or Additive Effects of Analgesics Used Together

- Agents with different mechanisms of action can potentially have additive or synergistic effects:
  - Acetaminophen/NSAIDS + opioids
  - Opioids + local anesthetics
  - Centrally acting agents + NSAIDS
  - Opioids + $\alpha_2\delta$ ligands (e.g., dexamethasmatomidine)

***NSAID = non-steroidal anti-inflammatory drug***

American Society of Anesthesiologists Task Force on Acute Pain Management Recommendations

• Advocate the use of multimodal analgesia

• “Unless contraindicated, all patients should receive around-the-clock regimen of NSAIDs, COX-2 inhibitors, or acetaminophen”

NSAID = non-steroidal anti-inflammatory drug

Improved Outcomes with Adapted Post-operative Pain Management

• Incidence of pulmonary complications:
  – Surgery lower limbs: 12% vs. 28%
  – Abdominal and vascular: 10% vs. 17%
  – Thoracic surgery: 15% vs. 31%

• Incidence of cardiac complications:
  – Abdominal surgery: 15% vs. 24%

• Better gastrointestinal function
  • Duration of paralytic ileus: 56 h vs. 103 h
    (8 randomized controlled trials)

• Fewer thromboembolic complications
  – DVT incidence: 29% vs. 62%
  – 4 randomized controlled trials: hip, knee, prostatectomy, peripheral vascular surgery
Analgesics Should Be Given at Regular Intervals During Acute Pain Episodes

![Graph showing mean pain intensity scores for around-the-clock dosing and PRN dosing after surgery.](graph)

Mechanism-Based Pharmacological Treatment of Nociceptive/Inflammatory Pain

Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug


Noxious stimuli

nsNSAIDs/coxibs, opioids

Peripheral sensitization

Inflammation

nsNSAIDs/coxibs, opioids

α2δ ligands

Acetaminophen

Antidepressants

nsNSAIDs/coxibs, opioids

Opioids

Descending modulation

Ascending input

Spinal cord

Brain

Perception

Opioids

Transduction

Transmission

Nociceptive afferent fiber

Descending modulation

Central sensitization
Acetaminophen

• Action at molecular level is unclear
• Potential mechanisms include:
  – Inhibition of COX enzymes (COX-2 and/or COX-3)
  – Interaction with opioid pathway
  – Activation of serotoninergic bulbospinal pathway
  – Involvement of nitric oxide pathway
  – Increase in cannabinoid-vanilloid tone

What are NSAIDs (nsNSAIDs/coxibs)?

**NSAID =** Non-Steroidal Anti-Inflammatory Drug

- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

<table>
<thead>
<tr>
<th>Examples of nsNSAIDs:</th>
<th>Examples of Coxibs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Diclofenac</td>
<td>– Celecoxib</td>
</tr>
<tr>
<td>– Ibuprofen</td>
<td>– Etoricoxib</td>
</tr>
<tr>
<td>– Naproxen</td>
<td>– Parecoxib</td>
</tr>
</tbody>
</table>

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

How do nsNSAIDs/coxibs work?

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Gastrointestinal cytoprotection, platelet activity

Inflammation, pain, fever

Pain relief

Arachidonic acid

COX-1 (constitutive)

COX-2 (induced by inflammatory stimuli)

Coxibs

nsNSAIDs

COX-2 Is Expressed in the CNS

- Prostaglandins in the CNS are important in central sensitization and hyperalgesia\(^1\)
- Peripheral inflammation leads to central induction of COX-22
  - Occurs even with complete sensory nerve block\(^3\)
  - Humoral signal (IL-6?) may play a role in signal transduction across blood-brain barrier\(^3\)
  - IL-1beta plays an important role centrally\(^3\)
  - Elevation of prostaglandins in CSF lead to hyperalgesia\(^3\)
  - Inhibition of IL-1beta synthesis or receptors reduce CSF levels of COX-2, prostaglandin and hyperalgesia\(^3\)
  - Inhibition of COX-2 centrally has similar effects\(^3,4\)

CNS = central nervous system; CSF = cerebrospinal fluid; IL = interleukin
1. Taiwo YO, Levine JD. Brain Res 1986; 373(1-2):81-4;
COX-2 Results in Sensitization to Pain

- **Peripheral Sensitization**
  - COX-2 is expressed following tissue injury
  - Prostaglandins produced increase nociceptor sensitivity to pain

- **Central Sensitization**
  - Peripheral inflammation leads to induction of COX-2 in CNS
  - Occurs even with complete sensory nerve block, possibly due to a humoral signal
  - Prostaglandins produced by COX-2 in CNS cause further sensitization to pain

- **Result:** hyperalgesia and allodynia

*CNS = central nervous system*

COX-2 Is Involved in Central Sensitization

• Central induction of COX-2 result in increased prostaglandin production

• PGE2 stimulation of EP receptors in the dorsal horn will:
  – Activate PKC, phosphorylating and further enhancing NMDA channel opening
  – Directly activate certain dorsal horn neurons by opening EP2 receptor linked ion channels
  – Reduced inhibitory transmission of glycinergic inter-neurons
  – Increased depolarization and excitability of dorsal horn neurons

NMDA = N-methyl-D-aspartate; PGE2 = prostaglandin E2; PKC = protein kinase C
COX-2 Inhibition Minimizes Sensitization

• Signal for COX-2 induction likely to persist with peripheral inflammation
• To minimize sensitization, COX-2 should be inhibited centrally and in the periphery
  – As early as possible
  – Continued until peripheral inflammation resolved
• Ideal COX-2 inhibitor should be able to act in periphery as well as centrally
  – Should readily cross blood-brain barrier

Adverse Effects of nsNSAIDs/Coxibs

All NSAIDs:
- Gastroenteropathy
  - Gastritis, bleeding, ulceration, perforation
- Cardiovascular thrombotic events
- Renovascular effects
  - Decreased renal blood flow
  - Fluid retention/edema
  - Hypertension
- Hypersensitivity

Cox-1-mediated NSAIDs (nsNSAIDs):
- Decreased platelet aggregation

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

What is the cardiovascular risk associated with the use of nsNSAIDs/coxibs in acute pain (i.e., for 7–10 days)?

Risk of Death/Myocardial Infarction within First 7 Days of nsNSAID/Coxib Treatment in Patients with Previous Death/Myocardial Infarction

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug
Gastrointestinal Risk with nsNSAIDs/Coxibs

Pooled Relative Risks and 95% CIs of Upper Gastrointestinal Complications

CI = confidence interval; coxib = COX-2 inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Risk Factors for Gastrointestinal Complications Associated with nsNSAIDs/Coxibs

- History of GI bleeding/perforation: 13.5
- Concomitant use of anticoagulants: 6.4
- History of peptic ulcer: 6.1
- Age ≥60 years: 5.5
- Single or multiple use of NSAID: 4.7
- Helicobacter pylori infection: 4.3
- Use of low-dose ASA within 30 days: 4.1
- Alcohol abuse: 2.4
- Concomitant use of glucocorticoids: 2.2
- Smoking: 2.0

Odds ratio/relative risk for ulcer complications

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; GI = gastrointestinal; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; SSRI = selective serotonin reuptake inhibitor
What is the gastrointestinal risk associated with the use of nsNSAIDs/coxibs in acute pain (i.e., for 7–10 days)?

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>During week 1 (53 cases, 22 controls)</td>
<td>11.7</td>
<td>6.5–21.0</td>
</tr>
<tr>
<td>After week 1 until discontinuation</td>
<td>5.6</td>
<td>4.6–7.0</td>
</tr>
<tr>
<td>First week after discontinuation</td>
<td>3.2</td>
<td>2.1–5.1</td>
</tr>
</tbody>
</table>

CI = confidence interval; coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Effects of nsNSAIDs/Coxibs + ASA on Platelet Function

- Baseline
- 12 hours after NSAID
- 24 hours after last NSAID, 22 hours after ASA 300 mg

n = 24 healthy subjects
ASA = acetyl salicylic acid; coxib = COX-2-inhibitor;
NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Guidelines Regarding ASA + NSAID Use

• Individuals taking low-dose ASA (75–162 mg/day) for vascular protection should avoid the concomitant use of nsNSAIDs
• If a patient taking low-dose ASA for vascular protection requires an anti-inflammatory drug, coxibs should be chosen over nsNSAIDs
• Both coxibs and nsNSAIDs increase cardiovascular risk and, if possible, should be avoided in patients at risk of ischemic vascular events

ASA = acetyl salicylic acid; coxib = COX-2-inhibitor;
NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug
**Canadian Consensus on Prescribing NSAIDs**

*In high-risk patients, a coxib and an nsNSAID + PPI show similar reductions of rebleeding rates, but these reductions may be incomplete.*

†Most patients on ASA + naproxen would need an added PPI, but naproxen alone may be appropriate for some patients at very low gastrointestinal risk.

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID; PPI = proton pump inhibitor.

Guidelines for nsNSAIDs/Coxibs Use Based on Gastrointestinal Risk and ASA Use

<table>
<thead>
<tr>
<th>Gastrointestinal risk</th>
<th>Not elevated</th>
<th>Elevated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not on ASA</td>
<td>nsNSAID alone</td>
<td>Coxib</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nsNSAID + PPI</td>
</tr>
<tr>
<td>On ASA</td>
<td>Coxib + PPI</td>
<td>Coxib + PPI</td>
</tr>
<tr>
<td></td>
<td>nsNSAID + PPI</td>
<td>nsNSAID + PPI</td>
</tr>
</tbody>
</table>

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor
Drug-Drug Interactions with nsNSAIDs/Coxibs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycoside antibiotics</td>
<td>Renal clearance inhibited</td>
<td>Monitor antibiotic concentration and adjust dose as necessary</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>Increased risk of bleeding</td>
<td>Monitor prothrombin time Avoid ASA use</td>
</tr>
<tr>
<td>Antihypertensive agents (with some NSAI Ds)</td>
<td>Reduced antihypertensive effect Potential hyperkalemia with diuretics and ACE-Is</td>
<td>Monitor blood pressure, cardiac function and potassium concentration</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Renal clearance inhibited</td>
<td>Monitor digoxin concentration and adjust dose as necessary</td>
</tr>
</tbody>
</table>

ACE-I = angiotensin-converting enzyme inhibitor; ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID

### Drug-Drug Interactions with nsNSAIDs/Coxibs (cont’d)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Increased lithium concentration</td>
<td>Monitor lithium concentrations</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Increased methotrexate concentration</td>
<td>Monitor methotrexate concentration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Avoid NSAIDs with high-dose methotrexate</td>
</tr>
<tr>
<td>Phenytoin (with ibuprofen)</td>
<td>Increased phenytoin levels</td>
<td>Monitor phenytoin concentration and adjust dose as necessary</td>
</tr>
<tr>
<td>Probenecid (with naproxen)</td>
<td>Reduced clearance of naproxen</td>
<td>Monitor for adverse effects</td>
</tr>
</tbody>
</table>

*Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID*

How Opioids Affect Pain

Modify perception, modulate transmission and affect transduction by:

- Altering limbic system activity; modify sensory and affective pain aspects
- Activating descending pathways that modulate transmission in spinal cord
- Affecting transduction of pain stimuli to nerve impulses

Rationale for Peri-operative Opioid Use

• Used for over 2000 years, and continue to be the gold standard for moderate-to-severe pain
• Opioids bind with receptors located on cells throughout the peripheral and central pain pathways
• Very potent central and peripheral analgesia
• In addition to producing analgesia, opioids alter the emotional component of the painful experience
• Offer convenient administration – oral, sublingual, intramuscular, intravenous, epidural and intrathecal

# Opioids and Pain Management

<table>
<thead>
<tr>
<th>Opioid Receptor</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mu</strong></td>
<td>Supraspinal analgesia, respiratory depression, sedation, miosis, euphoria, cardiovascular effects, pruritis, nausea/vomiting, decreased gastrointestinal motility, dependence, tolerance</td>
</tr>
<tr>
<td><strong>Delta</strong></td>
<td>Analgesia, euphoria, dysphoria, psychotomimetic effects</td>
</tr>
<tr>
<td><strong>Kappa</strong></td>
<td>Spinal analgesia, dysphoria, psychotomimetic effects, miosis, respiratory depression, sedation</td>
</tr>
</tbody>
</table>

Opioids Modulate Control of “ON” and “OFF” Cells

- Opioid stimulation of mu-receptors on “ON” cells
  - Reduced “ON” cell activity
  - Reduced facilitation of pain transmission at dorsal horn
  - Less pain

- Opioid stimulation of mu-receptors on GABA-ergic interneurons innervating “OFF” cells
  - Reduced GABA-ergic interneuron activity
  - Reduced inhibition of “OFF” cells
  - Increased “OFF” cell inhibition of pain transmission at dorsal horn
  - Less pain

GABA = γ-aminobutyric acid
Segmental Opioid Spinal Control

Endogenous opioid peptides:
- 3 classes: mu, delta and kappa
- Laminae I and II
- Principle mechanism: presynaptic inhibition (>70% mu receptor sites located on primary afferent terminals) → ↓ cAMP → ↓ neurotransmitter release
- Postsynaptic: decrease evoked activity of neurotransmitters and projection neurons (inward potassium channels) → ↓ hyperexcitability

Aδ fiber

C fiber

Nociceptive-specific projection neuron

5-HT = serotonin; cAMP = cyclic adenosine 3',5'-monophosphate; CCK = cholecystokinin; GABA = y-aminobutyric acid

Supraspinal Effect of Opioids

Enhance activity of descending inhibitory neurons → serotonin, norepinephrine at spinal level

Opioid R

Glutamate

Substance P

Calcium
Voltage-dependent calcium channels

Dorsal horn

PAG, RVM, etc.

Enhance inhibitory descending pathways

Brain

Lamina V

Lamina I

C fiber

PAG = periaqueductal gray; RVM = rostral ventromedial medulla; SG = substantia gelatinosa
**Activity of Tramadol, Enantiomers and M1 Metabolite**

<table>
<thead>
<tr>
<th></th>
<th>Uptake Inhibition</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mu-opioid</td>
<td>5HT</td>
</tr>
<tr>
<td>Tramadol*</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>(+) enantiomer</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>(-) enantiomer</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>M1 metabolite#</td>
<td>++++</td>
<td>+/-</td>
</tr>
</tbody>
</table>

*Distribution to brain; #Distribution to spinal cord

**5HT = serotonin; NA = noradrenaline**

Opioids Can Induce Hyperalgesia

- **Primary hyperalgesia**
  - Sensitization of primary neurons $\rightarrow$ decrease threshold to noxious stimuli within site of injury
  - May include response to innocuous stimuli
  - Increase pain from suprathreshold stimuli
  - Spontaneous pain

- **Secondary hyperalgesia**
  - Sensitization of primary neurons in surrounding uninjured areas
  - May involve peripheral and central sensitization

Opioids Can Induce Allodynia

- Pain evoked by innocuous stimuli
- Central sensitization →
  pain produced by Aβ fibers
- Possibly mediated by spinal NMDA receptors

NMDA = N-methyl-D-aspartate
# Adverse Effects of Opioids

<table>
<thead>
<tr>
<th>System</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting, constipation</td>
</tr>
<tr>
<td>CNS</td>
<td>Cognitive impairment, sedation, lightheadedness, dizziness</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Orthostatic hypotension, fainting</td>
</tr>
<tr>
<td>Other</td>
<td>Urticaria, miosis, sweating, urinary retention</td>
</tr>
</tbody>
</table>

*CNS = central nervous system*

Most Hospital Adverse Events Involve an Opioid

• In a 10-year hospital review study of adverse events with over 60,000 patients:
  – 59% of the 4452 adverse events reported involved an opioid
  – Adverse event rate of 2.7% resulted in an average half-day (0.53) increase in length of stay
  – Increased length of stay of 0.53 days would increase the average hospital cost by $840 per patient*

*Applied to the median-cost patient in the non-adverse event group
Additional Opioid Use Concerns

- Abuse and addictive potential
- Tolerance and physical dependence
- Administrative burden in distribution and monitoring due to scheduled status

# Drug-Drug Interactions with Opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Opioid(s)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Fentanyl</td>
<td>Reduced fentanyl clearance, respiratory depression</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Methadone</td>
<td>Increased opioid metabolism (may induce withdrawal)</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Morphine</td>
<td>Reduced analgesic effect, increase dose if needed</td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ketoconazole,</td>
<td>Fentanyl</td>
<td>Reduced fentanyl clearance and respiratory depression</td>
</tr>
<tr>
<td>itroconazole)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines</td>
<td>All</td>
<td>Increased sedation</td>
</tr>
<tr>
<td>Antiretrovirals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopinavir</td>
<td>Methadone</td>
<td>Increased opioid metabolism (may induce withdrawal)</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Fentanyl</td>
<td>Reduced fentanyl clearance, respiratory depression</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Fentanyl</td>
<td>Reduced fentanyl clearance, respiratory depression</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Methadone</td>
<td>Zidovudine metabolism inhibited</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(metoprolol,</td>
<td>Propoxyphene</td>
<td>Increased plasma levels of beta-blockers</td>
</tr>
<tr>
<td>propanolol)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Drug-Drug Interactions with Opioids (cont’d)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Opioid(s)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyrophenones</td>
<td>All</td>
<td>Increased sedation</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Methadone, Propoxyphene</td>
<td>Increased opioid metabolism (may induce withdrawal)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased carbamazepine levels, potential toxicity</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Meperidine, morphine</td>
<td>Increased opioid effects</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Methadone, morphine</td>
<td>Possible toxicity due to inhibition of desipramine metabolism</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Propoxyphene</td>
<td>Possible toxicity due to increased doxepin levels</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Methadone</td>
<td>Increased opioid metabolism (may induce withdrawal)</td>
</tr>
<tr>
<td>MAOIs</td>
<td>Meperidine</td>
<td>Excitatory response (includes seizures, arrhythmia, hyperpyrexia)</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Methadone</td>
<td>Increased opioid metabolism (may induce withdrawal)</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Codeine</td>
<td>Decreased analgesia</td>
</tr>
<tr>
<td>TCAs</td>
<td>All</td>
<td>Increased sedation</td>
</tr>
</tbody>
</table>

MAOI = monoamine oxidase inhibitor; TCA = tricyclic antidepressant

## Coagulation and Post-operative Pain Management

### Bleeding

- Some patients may have increased risk for bleeding due to:
  - Inherited disorder (e.g., von Willibrand disease)
  - Acquired disorder (e.g., vitamin K deficiency)
  - Medication use (e.g., antiplatelet)
- Risk should be assessed and managed pre-, peri- and post-operatively

### Clotting

- Elevated risk of postoperative DVT in patients undergoing some forms of surgery
- Prophylaxis with anticoagulant therapy should be considered in these patients
- NSAIDs may enhance anticoagulant effects
  - Close monitoring is warranted

---

DVT = deep vein thrombosis; NSAID = non-steroidal anti-inflammatory drug
Special Considerations for Post-operative Management in the Elderly

• Wide variation in drug metabolism among older patients
• Increased risk of complications due to NSAIDs
• Frequently on numerous other medications (increased risk of drug-drug interactions)
• Mindset may reflect historical perspectives
• May under-report pain due to stoicism or reluctance to ask for analgesia
• Frequent pre-existing pain (e.g., osteoarthritis)
• Potential cognitive impairment

NSAID = non-steroidal anti-inflammatory drug
Analgesia for Post-operative Pain Based on Type of Surgery

**Surgical procedures**

**Minor surgery**
- Acetaminophen
- nsNSAIDs/coxibs*
- Wound infiltration
- Regional block analgesia
- Weak opioid or rescue analgesic, if necessary

**Moderate surgery**
- Acetaminophen
- nsNSAIDs/coxibs*
- Wound infiltration
- Peripheral nerve block or IV opioid

**Major surgery**
- Acetaminophen
- nsNSAIDs/coxibs*
- Wound infiltration
- Epidural or major peripheral nerve or plexus block or IV opioid

*Unless contraindicated
Coxib = COX-2-specific inhibitor; IV = intravenous; nsNSAID = non-selective non-steroidal anti-inflammatory drug

**PROSPECT: Management of Post-operative Pain***

High-intensity pain (VAS ≥50)
- nsNSAID/coxib + acetaminophen ± strong opioid

Moderate-intensity pain (VAS 30–50)
- nsNSAID/coxib + acetaminophen ± weak opioid

Low-intensity pain (VAS ≤30)
- nsNSAID/coxib + acetaminophen ± weak opioid

*Note: specific recommendations vary depending on type of surgery
Coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale

PROSPECT: Management of Abdominal Hysterectomy Postoperative Pain

Expected high-intensity pain (VAS ≥50)
- Low risk: strong opioid (IV PCA) + coxib/NSAID
- High risk: strong opioid + epidural LA

Expected moderate-intensity pain (VAS 30-50)
- Low risk: coxib/nsNSAID + acetaminophen ± weak opioid
- High risk: consider step-down to coxib/nsNSAID + acetaminophen ± weak opioid

Expected low-intensity pain (VAS ≤30)
- All: coxib/nsNSAID + acetaminophen ± weak opioid

Coxib = COX-2-specific inhibitor; IV = intravenous; LA = local anesthetic; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale.

**PROSPECT: Management of Colonic Resection Post-operative Pain**

### Patients undergoing open surgery

<table>
<thead>
<tr>
<th>Multimodal rehabilitation protocols + thoracic epidural analgesia (if not contraindicated)</th>
</tr>
</thead>
</table>

### All patients

<table>
<thead>
<tr>
<th>Expected high-intensity pain (VAS $\geq 50$): strong opioid (IV PCA) + coxib/nsNSAID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected moderate-intensity pain (VAS 30-50): consider step-down to coxib/nsNSAID + acetaminophen ± weak opioid</td>
</tr>
<tr>
<td>Expected low-intensity pain (VAS $\leq 30$)</td>
</tr>
</tbody>
</table>

**Coxib = COX-2-specific inhibitor; IV = intravenous; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale**

PROSPECT: Management of Hemorrhoid Surgery Post-operative Pain

Coxibs/nsNSAIDs + acetaminophen

Moderate- to high-intensity pain

Low- to moderate-intensity pain

Oral strong opioids

Oral weak opioids

Laxatives
Oral metronidazole

Coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug;

PROSPECT = Procedure Specific Postoperative Pain Management

PROSPECT: Management of Herniorrhaphy Post-operative Pain

**Coxibs/nsNSAIDs**

+ acetaminophen

**High-intensity pain (VAS ≥50)**

- Add strong opioid

**Moderate-intensity pain (VAS 30-50)**

- Add weak opioids

*Use weak opioids when nsNSAIDs/coxibs are contraindicated*  
Coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale

PROSPECT: Management of Laparoscopic Cholecystectomy Post-operative Pain

High-risk pulmonary patients:
- Epidural analgesia + strong opioids (in early postoperative period)

Routine surgery:
- Coxib/nsNSAID + acetaminophen; opioid for rescue analgesia
- Early discharge (<24 hours)

Coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug;
PROSPECT = Procedure Specific Postoperative Pain Management
**PROSPECT: Management of Non-cosmetic Breast Surgery Post-operative Pain**

- **High-intensity pain** (VAS ≥50):
  - Coxib/nsNSAID + acetaminophen + strong opioids (titrated to effect)

- **Moderate or low-intensity pain** (VAS <50):
  - Coxib/nsNSAID + acetaminophen + weak opioids

For major breast surgery, consider continuing paravertebral block from intra-operative period.

---

**Coxib** = COX-2-specific inhibitor; **nsNSAID** = non-selective non-steroidal anti-inflammatory drug; **PROSPECT** = Procedure Specific Postoperative Pain Management; **VAS** = visual analog scale

Note: the above recommendations are based on evidence from unimodal interventions. The optimal combinations of these interventions remain unknown at present time.
Coxib = COX-2-specific inhibitor; IV = intravenous; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale
**PROSPECT: Management of Total Hip Arthroplasty Post-operative Pain**

*By catheter techniques, using patient-controlled regional analgesia; **Establish epidural infusion as the nerve block regresses using patient-controlled epidural analgesia

**Coxib = COX-2-specific inhibitor; IV = intravenous; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale

PROSPECT: Management of Total Knee Arthroplasty Post-operative Pain

**High-intensity pain (VAS ≥50)**
- Coxib/nsNSAID + acetaminophen + IV PCA strong opioids (titrated to effect)

**Moderate- or low-intensity pain (VAS <50)**
- Coxib/nsNSAID + acetaminophen ± weak opioids (titrated to effect)

*For all: cooling and compression techniques*

Coxib = COX-2-specific inhibitor; IV = intravenous; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale

South African Acute Pain Guidelines: 
Pain Measuring and Monitoring Protocol

Chose appropriate unidimensional scale

Monitor pain every 15 minutes and adjust analgesic treatment accordingly, until patient is pain free

Monitor pain hour for 6 hours

Continue with 4-hourly assessment

If pain intensity increases to >5/10:
1. Contact relevant physician
2. Adjust pain treatment
3. Go back to 15-minute and then hourly monitoring schedule

In the meantime:
1. Look for complication that might cause pain
2. Monitor medication’s side effects

South African Acute Pain Guidelines: Acute Pain Treatment Ladder

**Mild Pain (VAS 1–5)**
- Acetaminophen 1 g q6h
- NSAID (if not contraindicated)
- Codeine 30–60 mg q6h or
- Tramadol 50–100 mg q6h

**Moderate Pain (VAS 6–7)**
- Acetaminophen 1 g q6h and
- NSAIDs (regular) (if not contraindicated) and
- Codeine (regular) and/or
- Tramadol 50–100 mg q6h and/or
- Morphine 0.1–0.2 mg/kg q4h and/or
- PCA/nerve block/ neuroaxial blockade

**Severe Pain (VAS 8–10)**
- Morphine (regular or continuous) and
- Acetaminophen 1 g q6h and
- NSAIDs (if not contraindicated) and/or
- PCA/nerve block/ neuroaxial blockade

NSAID = non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; VAS = visual analog scale
South African Acute Pain Guidelines: Post-operative Pain

Towards end of surgical procedure
- Administer a longer-acting IV opioid (e.g., morphine, fentanyl)

Immediately post-op
- Titrate IV opioid (e.g., alfentanil, sufentanil)

At end of anaesthesia
- Administer IV non-steroidal analgesic

Postsurgery
- 5-day course of oral NSAIDs (coxibs generally preferred) is appropriate for most routine post-operative scenarios

Coxib = COX-2-specific inhibitor; IV = intravenous; NSAID = non-steroidal anti-inflammatory drug
### South African Acute Pain Guidelines: Acute Musculoskeletal Pain

| 1st 48 hours after musculoskeletal injury | Acetaminophen  
|                                         | Acetaminophen + codeine (for more severe pain)  
|                                         | Tramadol (for more severe injury) |

| After 48 hours post-injury* | NSAIDs  
|                            | Coxibs preferred:  
|                            | In elderly  
|                            | In those with history of gastrointestinal or other side effects following nsNSAID use**  
|                            | Where prolonged therapy is envisaged† |

*If assessment reveals clinical signs and symptoms of excessive inflammation; **Alternatively, acetaminophen can be continued;  
†In athletes, use of these agents is suggested for limited period (5 days).

Pharmacological Treatment of Acute Pain in the Middle East: Expert Panel Consensus

Acute pain due to:
- Sport injury
- Traumatic or inflammatory condition
- Musculoskeletal injury

Mild or moderate acute pain

Step 1: acetaminophen
(4 g/day maximum dose; 4 h minimum interval between each 1 g dose)

Step 2: coxib or nsNSAID
(make choice based on patient risk profile)

Step 3: add 1 of following:
- Acetaminophen/codeine
- Acetaminophen/tramadol
- Tramadol

Inadequate analgesia

Severe acute pain

Opioids
(refer patient to pain clinic or specialist)

Topical nsNSAID
(with or without combined oral acetaminophen, coxib or nsNSAID)

Inadequate analgesia

Inadequate analgesia

Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug
ESRA: Treatment Options in Relation to Intensity of Expected Post-operative Pain

Mild intensity pain (e.g., inguinal hernia, varices, laparoscopy)

- Acetaminophen + wound infiltration with local anesthetic
- NSAIDs (unless contraindicated)
- Regional block analgesia

Moderate intensity pain (e.g., hip replacement, hysterectomy, jaw surgery)

- Acetaminophen + wound infiltration with local anesthetic
- NSAIDs (unless contraindicated)
- Peripheral nerve block (single shot or continuous infusion) or opioid injection (IV PCA)

Severe intensity pain (e.g., thoracotomy, upper abdominal surgery, aortic surgery, knee replacement)

- Acetaminophen + wound infiltration with local anesthetic
- NSAIDs (unless contraindicated)
- Epidural local analgesia or major peripheral nerve or plexus block or opioid injection (IV PCA)

Add weak opioid or rescue analgesia with small increments of IV strong opioid if necessary

ESRA = European Society of Regional Anaesthesia and Pain Therapy; IV = intravenous; NSAID = non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia

ANZCA Guidelines: Management of Post-operative Pain after Short-Stay Surgery

- Infiltration of the wound with local anesthetic agents provides good and long-lasting analgesia

- Peripheral nerve blocks with long-acting local anesthetic agents provide long-lasting post-operative analgesia
  - Single-shot infraclavicular blocks provide effective analgesia and less nausea following hand and wrist surgery and earlier ambulation and hospital discharge compared with general anesthesia

- Continuous peripheral nerve blocks provide extended analgesia, leading to reduced opioid requirements, less sleep disturbance, earlier achievement of discharge criteria and improved rehabilitation
  - Continuous peripheral nerve blocks have been shown to be safe at home, if adequate resources and patient education are provided

ANZCA = Australian and New Zealand College of Anaesthetists
Recommendations for Management of Acute Pain

Acetaminophen

If ineffective
Add nsNSAIDs/coxibs

If ineffective
Add opioids
(preferably short-acting agents at regular intervals; ongoing need for such treatment requires reassessment)

Coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine.
Australian Guidelines: Pharmacologic Treatment of Acute Neck, Knee and Shoulder Pain

• nsNSAIDs/coxibs and corticosteroid injection are recommended for acute shoulder pain
• Insufficient evidence was found to provide clear recommendations for acute neck and knee pain

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug
Adherence
Causes of Inadequate Pain Management

- Lack of knowledge/training on analgesic therapy
- Unrealistic patient expectations or beliefs
- Patient stoicism or reluctance to report pain
- Prejudice or social stigma against the use of analgesics
- Practitioner and patient concerns of addiction
- **Patient non-adherence (often due to side effects)**
- Regulatory barriers create concerns about prosecution
- Failure to address multiple physical, mental, emotional, and social dimensions of pain

Surgical Patients Prefer Avoidance of Opioid Side Effects over Pain Control

**Patient Preferences in Pain Management (n = 50)**

- **Setting and route of administration**: 12.1
- **Side effects avoidance**: 47.2
- **Pain relief**: 40.7

Many Patient Do Not Take Analgesics at Home Following Surgery

Percent of Patients* Who Took Analgesic Medication at Home

<table>
<thead>
<tr>
<th></th>
<th>24 h</th>
<th>48 h</th>
<th>Days 3–6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild opioids</td>
<td>58%</td>
<td>43%</td>
<td>43%</td>
<td>7%</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>15%</td>
<td>9%</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>3%</td>
<td>3%</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>None</td>
<td>32%</td>
<td>51%</td>
<td>61%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Strategies to Improve Adherence

- Simplify regimen
- Impart knowledge
- Modify patient beliefs and human behavior
- Provide communication and trust
- Leave the bias
- Evaluate adherence
Simplifying Medication Regimen

• If possible, adjust regimen to minimize:
  – Number of pills taken
  – Number of doses per day
  – Special requirements (e.g., bedtime dosing, avoiding taking medication with food, etc.)

• Recommend all medications be taken at the same time of day (if possible)

• Link taking medication to daily activities, such as brushing teeth or eating

• Encourage use of adherence aids such as medication organizers and alarms

Imparting Knowledge

• Provide clear, concise instructions (written and verbal) for each prescription
• Be sure to provide information at a level the patient can understand
• Involve family members if possible
• Provide handouts and/or reliable websites for patients to access information on their condition
• Provide concrete advice on how to cope with medication costs

### Modifying Patient Beliefs and Behaviors: Motivational Interviewing Technique

<table>
<thead>
<tr>
<th>Techniques</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Express empathy</td>
<td>• “It’s normal to worry about medication side effects”</td>
</tr>
<tr>
<td>• Develop discrepancy</td>
<td>• “You obviously care about your health; how do you think not taking your pills is affecting it?”</td>
</tr>
<tr>
<td>• Roll with resistance</td>
<td>• “I understand that you have a lot of other things besides taking pills to worry about”</td>
</tr>
<tr>
<td>• Support self efficacy</td>
<td>• “It sounds like you have made impressive efforts to work your new medication into your daily routine”</td>
</tr>
</tbody>
</table>

Providing Communication and Trust: Communication Tips

- Be an active listener
  - Focus on the patient
  - Nod and smile to show you understand
- Make eye contact
- Be aware of your own body language
  - Face the patient
  - Keep arms uncrossed
  - Remove hands from pockets
- Recognize and interpret non-verbal cues

McDonough RP, Bennett MS. Am J Pharm Educ 2006; 70(3):58;
Srnka QM, Ryan MR. Am Pharm 1993; NS33(9):43-6.
Leaving the Bias

Learn more about how low health literacy can affect patient outcomes

Specifically ask about attitudes, beliefs and cultural norms with regards to medication

Tailor communication to patient’s beliefs and level of understanding

Acknowledging biases

Evaluating Adherence: 4-Step Strategy for Detecting Non-adherence

1. Ask an open-ended question about taking medicine
2. Normalize and universalize non-adherence to reverse the judgmental environment
3. Make the role of accurate information about adherence in medical decision-making explicit
4. Don’t ask about “forgetting” or “missed” doses until the first 3 steps have set the stage

Summary
Management of Acute Pain: Summary

- Pharmacotherapy remains the mainstay of most acute pain conditions
  - However, analgesics, including opioids and nsNSAIDs/cpxobs, can be associated with adverse effects
  - Individual patient risk profile should be considered when selecting pain management therapies
- Agents with different mechanisms of action can potentially have additive or synergistic effects
  - Multimodal therapy is generally recommended for acute pain conditions

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug