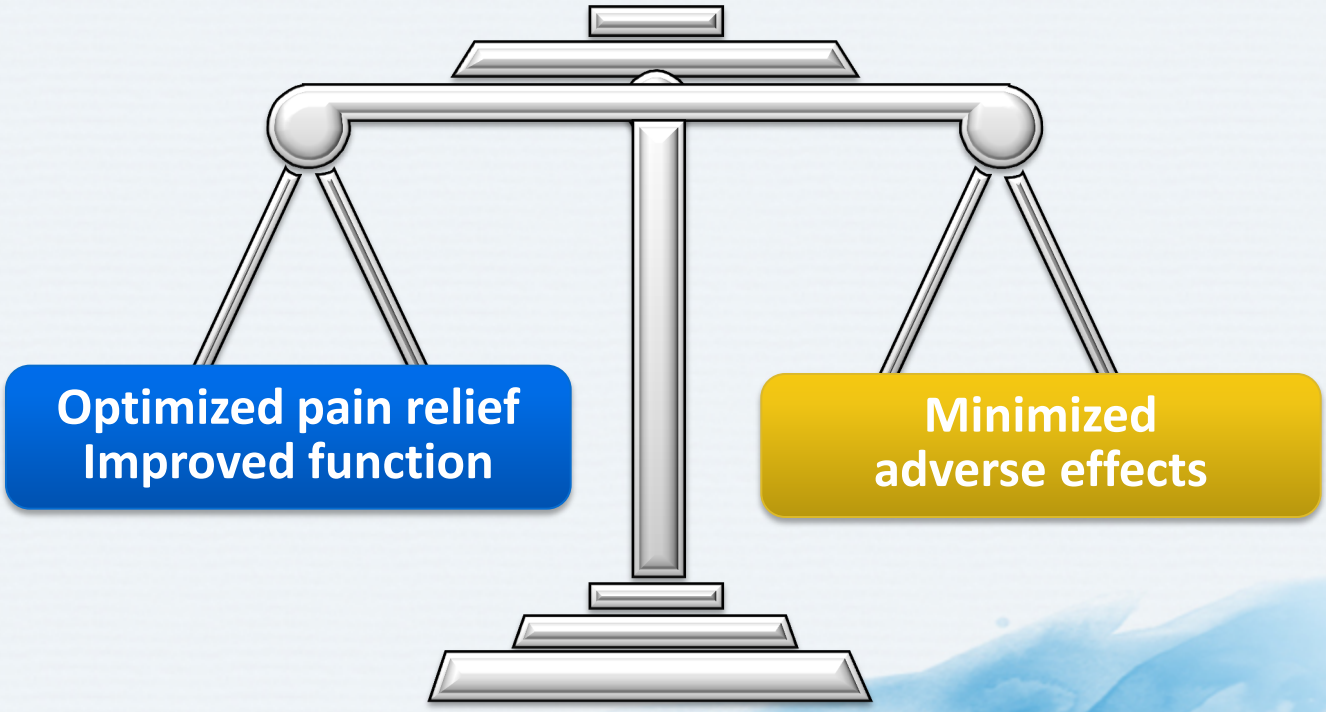
MANAGEMENT

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



Farrar JT *et al. Pain* 2001; 94(2):149-58; Gilron I *et al. CMAJ* 2006; 175(3):265-75.

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

Joshi GP *et al. Anesthesiol Clin N Am* 2005; 23(1):21-36; Kehlet H *et al. Lancet* 2006; 367(9522):1618-25.

Importance of Post-operative Pain Management

Consequences of the failure to adequately relieve pain:

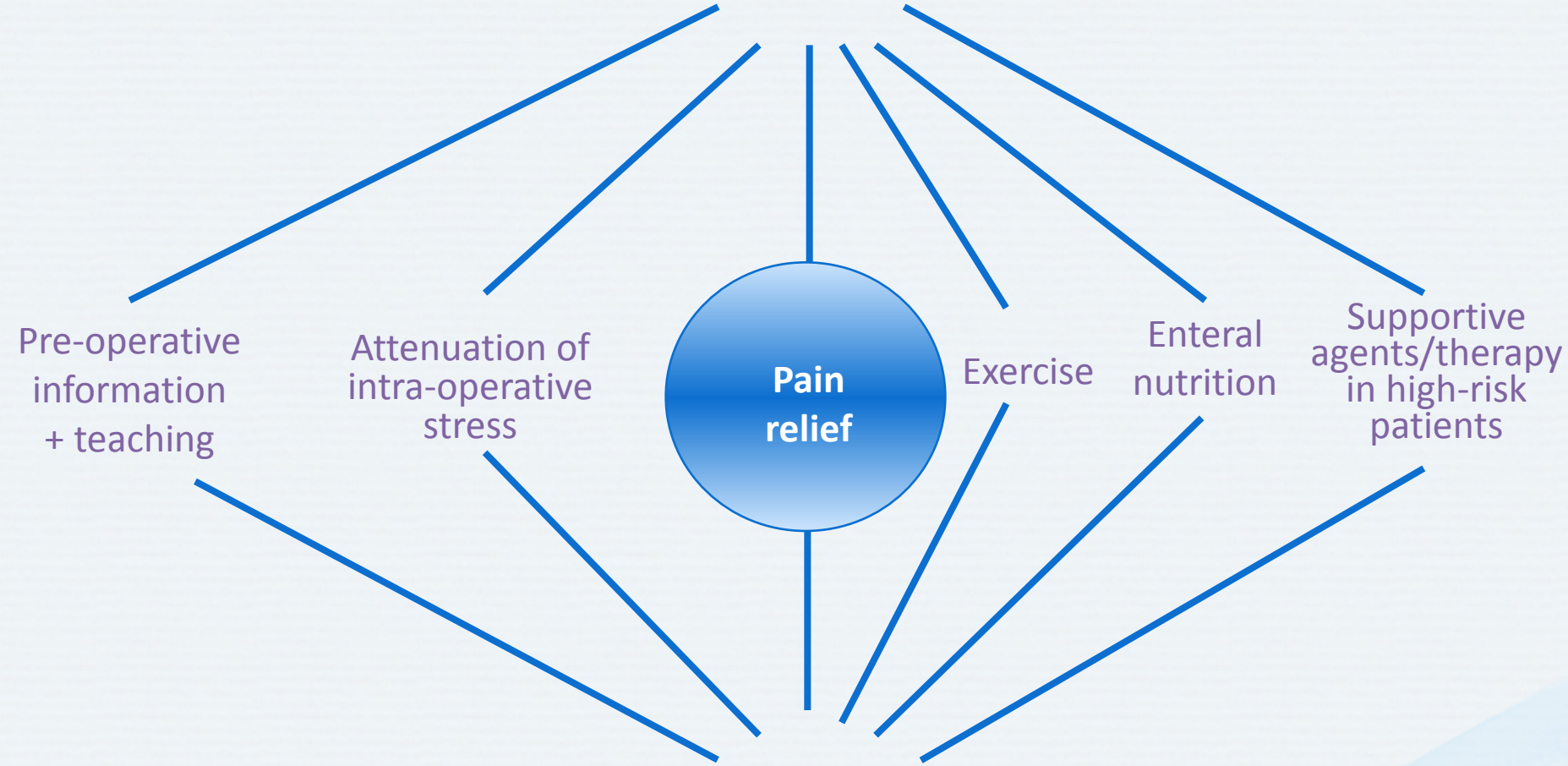
- Pneumonia
- Delayed readiness for discharge
- Increased patient monitoring/nursing time
- Delayed ambulation

Proper pain management may lead to:

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

Dunwoody CJ *et al. J Perianesth Nurs* 2008; 23(1 Suppl):S15-27; Joshi GP *et al*. *Anesthesiol Clin N Am* 2005; 23(1):21-36; Kehlet H *et al*. *Lancet* 2006; 367(9522):1618-25; Liu LL *et al. Drugs* 2003; 63(8):755-67; Shang AB *et al*. *Drugs* 2003; 63(9):855-67.

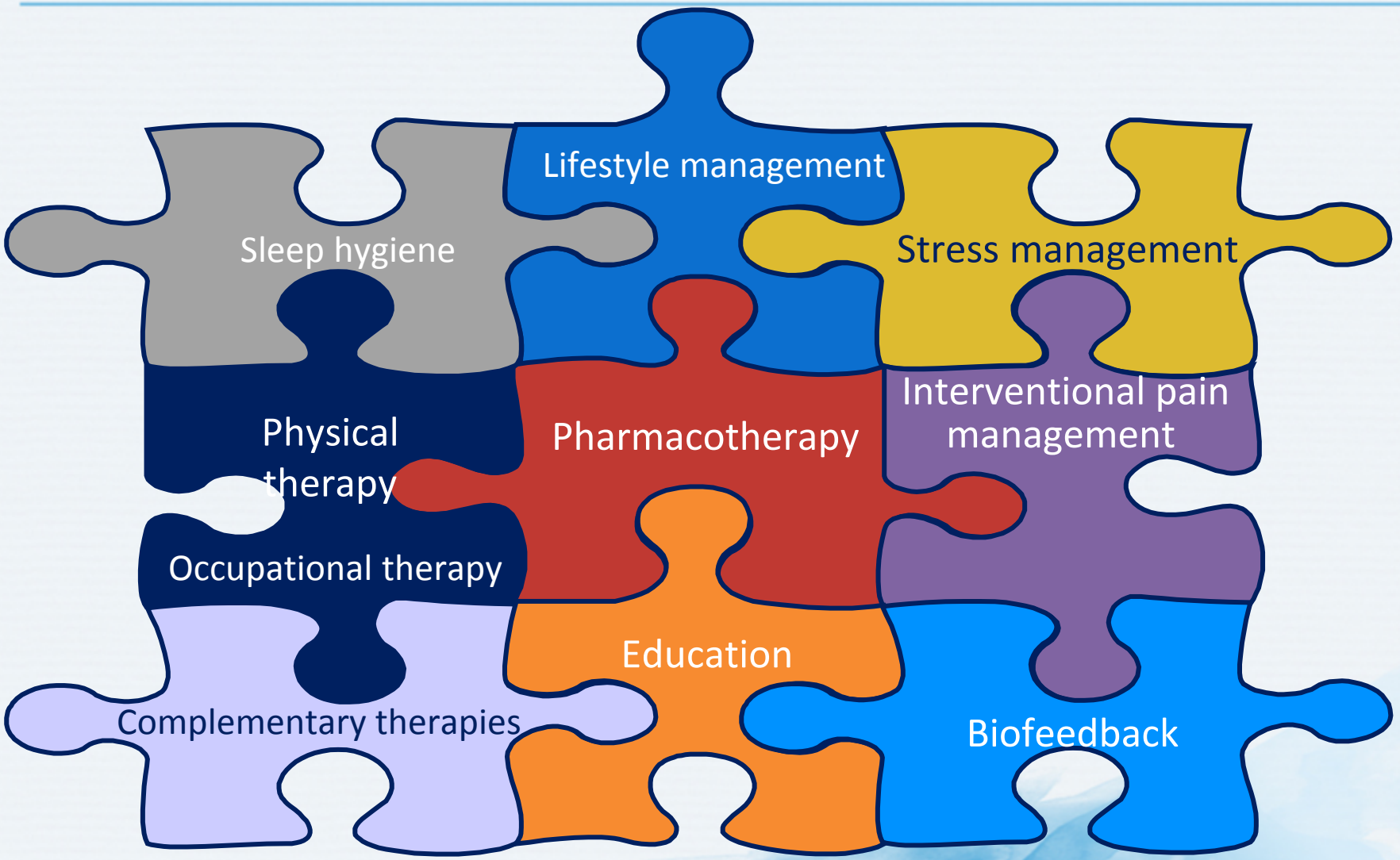
Controlling Post-operative Physiology



Reduced morbidity and accelerated convalescence

Kehlet H. *Br J Anaesth* 1997; 78(5):606-17.

Multimodal Treatment of Pain Based on Biopsychosocial Approach



Gatchel RJ *et al. Psychol Bull* 2007; 133(4):581-624; Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.*; National Academies Press; Washington, DC: 2011; Mayo Foundation for Medical Education and Research. *Comprehensive Pain Rehabilitation Center Program Guide.* Mayo Clinic; Rochester, MN: 2006.

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

Iverson RE *et al. Plast Reconstr Surg* 2006; 118(4):1060-9;
Miaskowski C *et al. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 6th ed. American Pain Society; Chicago, IL: 2008.

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

American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology* 2012; 116(2):248-73; Iverson RE *et al. Plast Reconstr Surg* 2006; 118(4):1060-9; Krenzischek DA *et al. J Perianesth Nurs* 2003; 18(4):228-36; Niraj G *et al. Br J Anaesth* 2011; 107(1):25-9; Miaskowski C *et al. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 6th ed. American Pain Society; Chicago, IL: 2008.

South African Acute Pain Guidelines: Cognitive Behavioral Interventions

Intervention	Potential utility
Reassurance and provision of information	• Reduces pain and distress after minor procedures • May improve pain relief after more major surgery • No significant benefit after non-surgical procedures
Relaxation training	• Not effective in the perioperative setting
Attentional techniques (e.g., imagery, distraction, music therapy)	• Distraction may reduce analgesic consumption in the perioperative phase • Music therapy is ineffective
Hypnosis	• Evidence that acute procedural pain for minor procedures can effectively be managed by hypnosis

South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

South African Acute Pain Guidelines: Physical Interventions

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

South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

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.

South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

Physical Interventions for Acute Pain

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

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine.
Acute Pain Management: Scientific Evidence. 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010.

Cognitive Behavioral Interventions for Acute Pain

Intervention	Potential utility
Reassurance and provision of information	• Evidence that information is effective in reducing procedure-related pain is tentatively supportive and not sufficient to make recommendations
Relaxation training	• Evidence is weak and inconsistent
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 and New Zealand College of Anaesthetists and Faculty of Pain Medicine.
Acute Pain Management: Scientific Evidence. 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010.

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 Acute Musculoskeletal Pain Guidelines Group. *Evidence-Based Management of Acute Musculoskeletal Pain. A Guide for Clinicians.* Australian Academic Press Pty. Lts; Bowen Hills, QLD: 2004.

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 Acute Musculoskeletal Pain Guidelines Group. *Evidence-Based Management of Acute Musculoskeletal Pain. A Guide for Clinicians.* Australian Academic Press Pty. Lts; Bowen Hills, QLD: 2004.

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

Australian Acute Musculoskeletal Pain Guidelines Group. *Evidence-Based Management of Acute Musculoskeletal Pain. A Guide for Clinicians.* Australian Academic Press Pty. Lts; Bowen Hills, QLD: 2004.

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

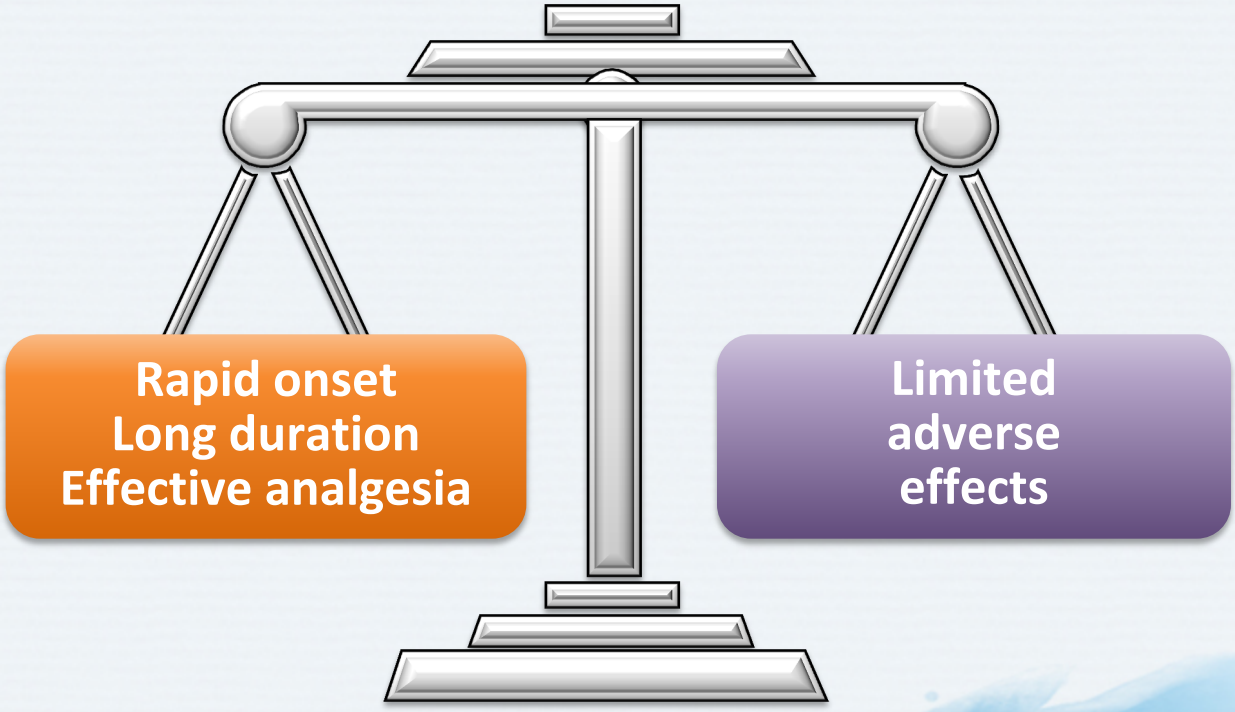
- No real consensus regarding non-pharmacological treatment modalities
- Pre-operative patient education may help management of post-operative pain

Australian Acute Musculoskeletal Pain Guidelines Group. *Evidence-Based Management of Acute Musculoskeletal Pain. A Guide for Clinicians.* Australian Academic Press Pty. Lts; Bowen Hills, QLD: 2004; Iverson RE *et al. Plast Reconstr Surg* 2006; 118(4):1060-9;
Miaskowski C *et al. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 6th ed. American Pain Society; Chicago, IL: 2008;
South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

Pharmacological Treatment

Ideal Characteristics for Acute Analgesic Therapy

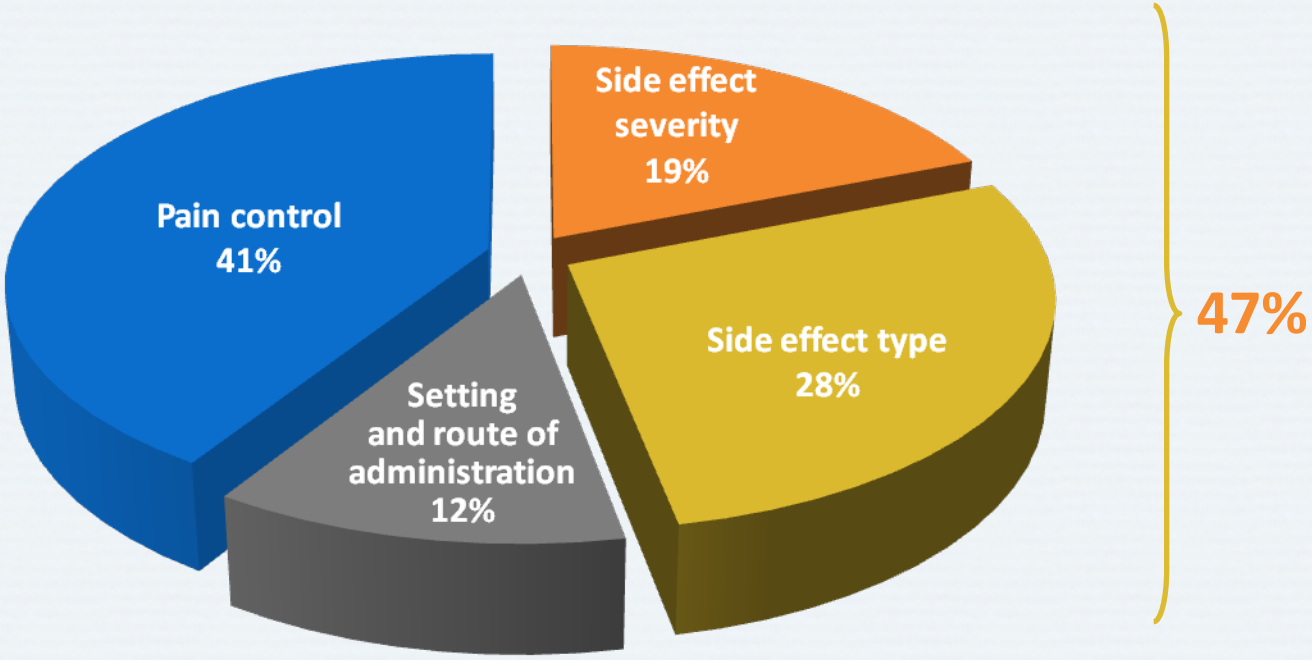
- Ideal drug characteristics for acute pain therapy:



Baumann TJ. In: DiPiro JT *et al* (eds). *Pharmacotherapy: A Pathophysiologic Approach.* 5th ed. McGraw-Hill; New York, NY: 2002.

Patients Prefer Avoiding Side Effects to Complete Pain Control

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



Gan TJ *et al. Br J Anaesth* 2004; 92(5):681-8.

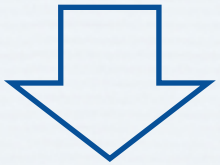
Proportion of Patients Experiencing Adverse Events

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

Gan TJ *et al. Br J Anaesth* 2004; 92(5):681-8.

So how do we treat acute pain?

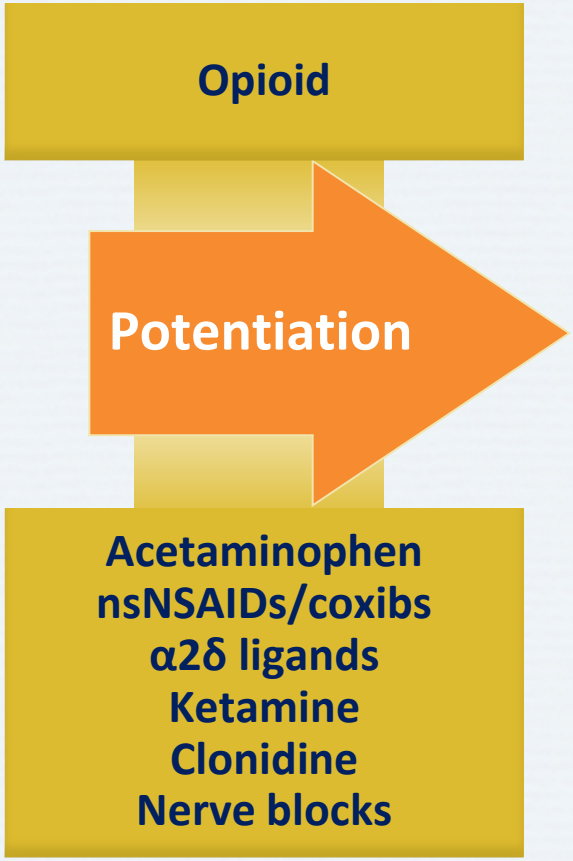
Treat according to pain mechanisms involved



Multimodal analgesia

Voscopoulos C, Lema M. *Br J Anaesth* 2010; 105(Suppl 1):i69-85.

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

Kehlet H, Dahl JB. *Anesth Analg* 1993; 77(5):1048-56.

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., dexamethatomidine)

NSAID = non-steroidal anti-inflammatory drug

Bader P *et al. Guidelines on Pain Management*. European Association of Urology; Arnhem, The Netherlands: 2010;
Kehlet H *et al. Acta Anaesthesiol Scand* 2010; 55(7):778-84; Paul S *et al*. Ceylon Med J 2010; 55(4):111-5; Robert B *et al. J Pain* 2010; 11(8):701-9;
Starks I *et al. ISRN Anesthesiology* 2011; 2011:742927; Vadivelu N *et al.* Yale J Biol Med 2010; 83(1):11-25.

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

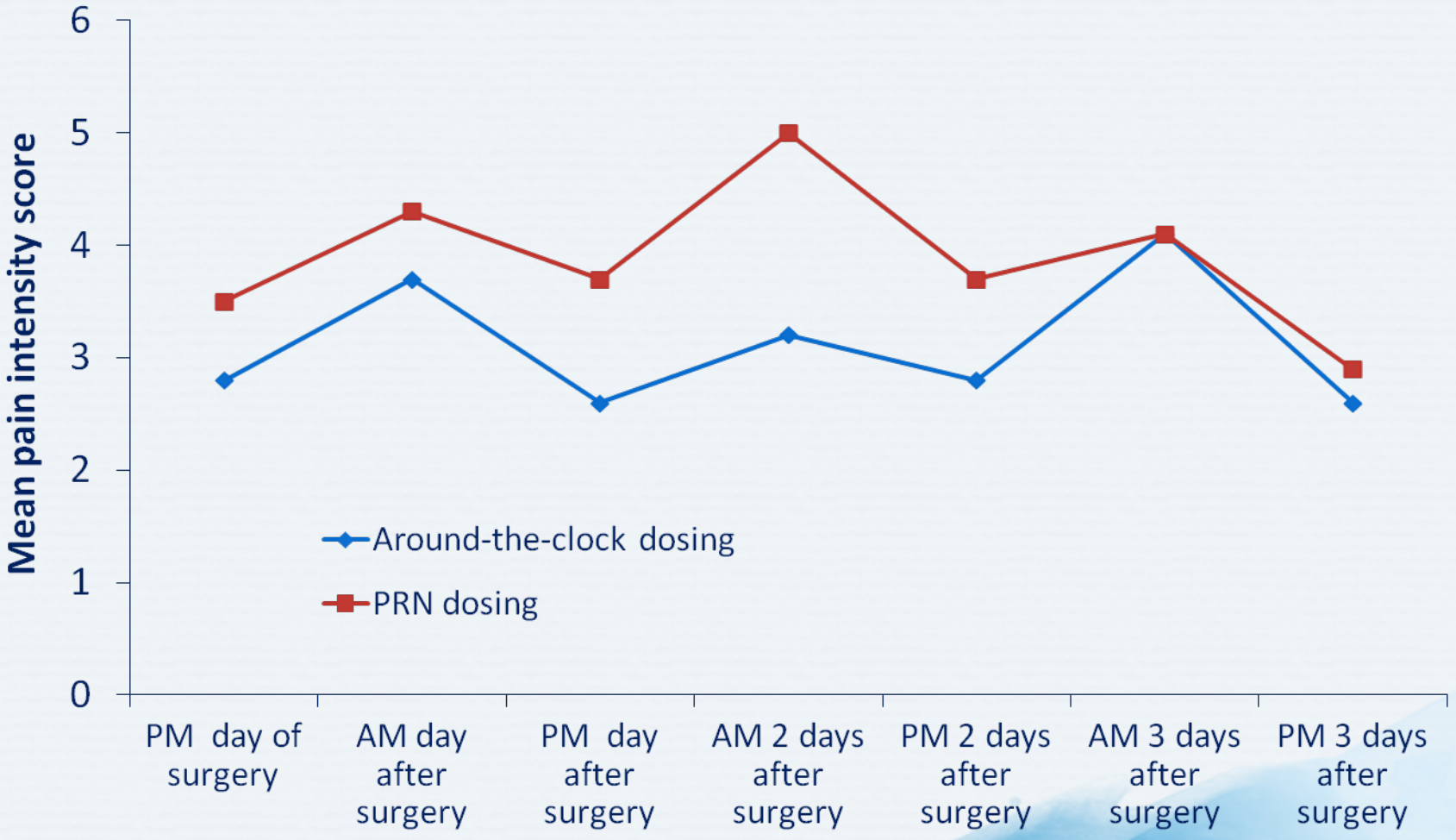
American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology* 2004; 100(6):1573-81.

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

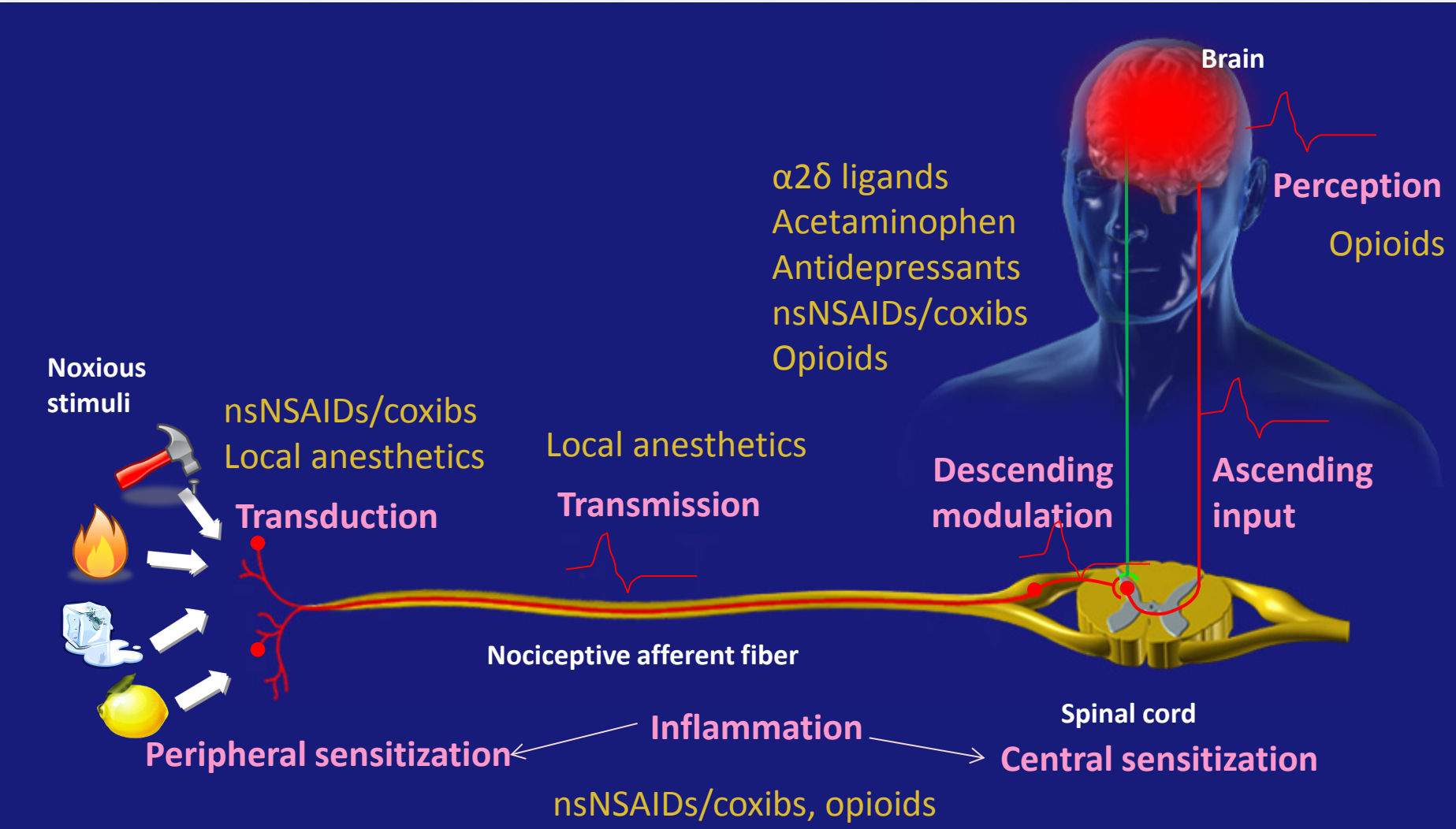
Kehlet H *et al*. *Br J Anaesth* 2001; 87(1):62-72.

Analgesics Should Be Given at Regular Intervals During Acute Pain Episodes



Sutters KA *et al. Clin J Pain* 2010; 26(2):95-103.

Mechanism-Based Pharmacological Treatment of Nociceptive/Inflammatory Pain



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

Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

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

Mattia A, Coluzzi F. *Minerva Anestesiol* 2009; 75(11):644-53.

What are NSAIDs (nsNSAIDs/coxibs)?

NSAID = Non-Steroidal Anti-Inflammatory Drug

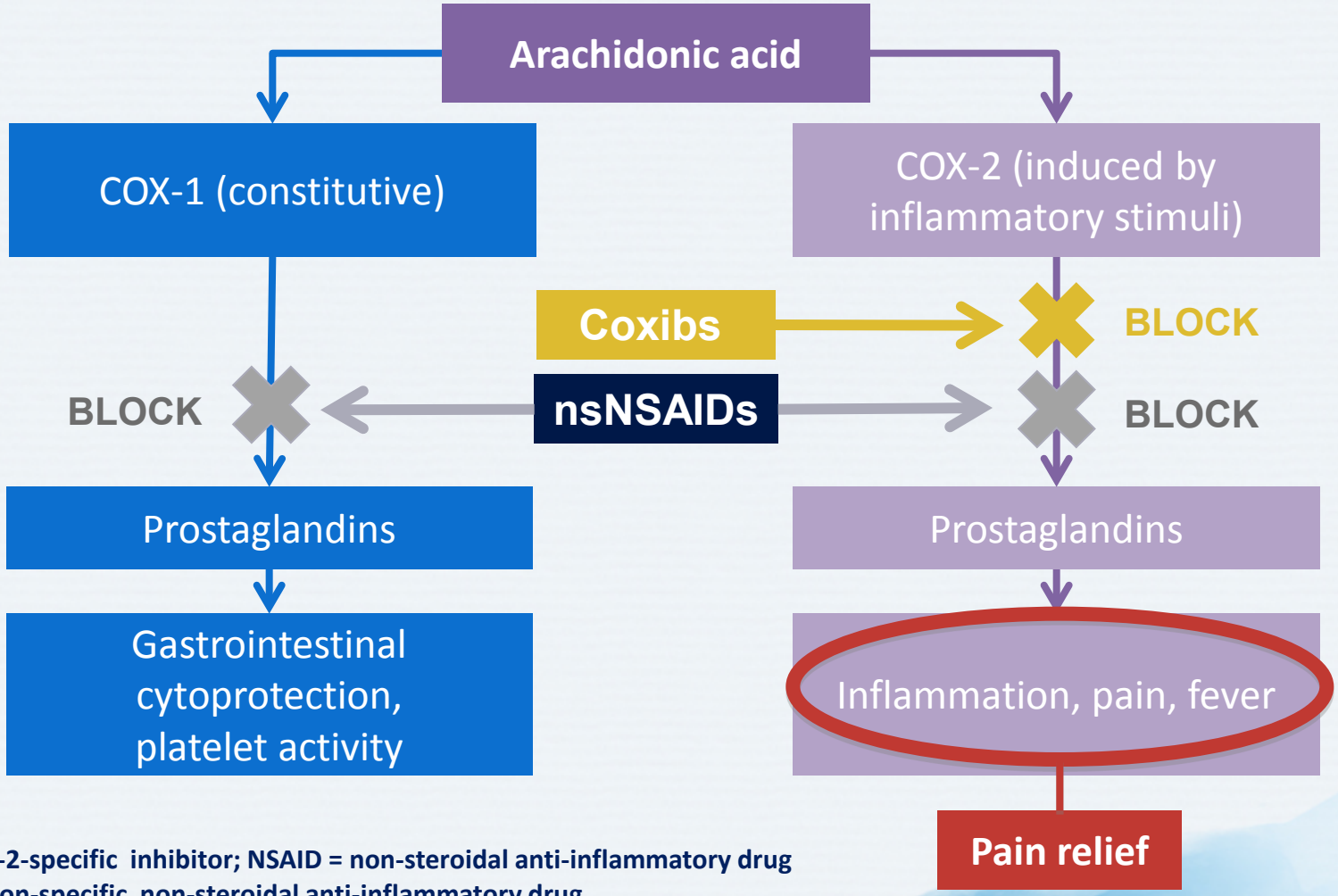
- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

Examples of nsNSAIDs:	*Examples of Coxibs:*
– Diclofenac	– Celecoxib
– Ibuprofen	– Etoricoxib
– Naproxen	– Parecoxib

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

Brune K. In: Kopf A *et al* (eds). *Guide to Pain Management in Low-Resource Settings.* International Association for the Study of Pain; Seattle, WA: 2010.

How do nsNSAIDs/coxibs work?



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

Gastrosource. *Non-steroidal Anti-inflammatory Drug (NSAID)-Associated Upper Gastrointestinal Side-Effects*. Available at: http://www.gastrosource.com/11674565?itemId=11674565. Accessed: December 4, 2010; Vane JR, Botting RM. *Inflamm Res* 1995;44(1):1-10.

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;
2. Ghilardi JR *et al. J Neurosci* 2004; 24(11):2727-32;
3. Samad TA *et al. Nature* 2001; 410(6827):471-5; 4. Smith CJ *et al*. *Proc Natl Acad Sci US* 1998; 95(22):13313-8.

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

Ahmadi S *et al. Nat Neurosci* 2002; 5(1):34-40; Baba H *et al. J Neurosci* 2001; 21(5):1750-6;
Samad TA *et al. Nature* 2001; 410(6827):471-5; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-9.

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

Ahmadi S *et al. Nat Neurosci* 2002; 5(1):34-40; Baba H *et al. J Neurosci* 2001; 21(5):1750-6;
Samad TA *et al. Nature* 2001; 410(6827):471-5; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-9.

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

Samad TA *et al. Nature* 2001; 410(6827):471-5; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-9.

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):

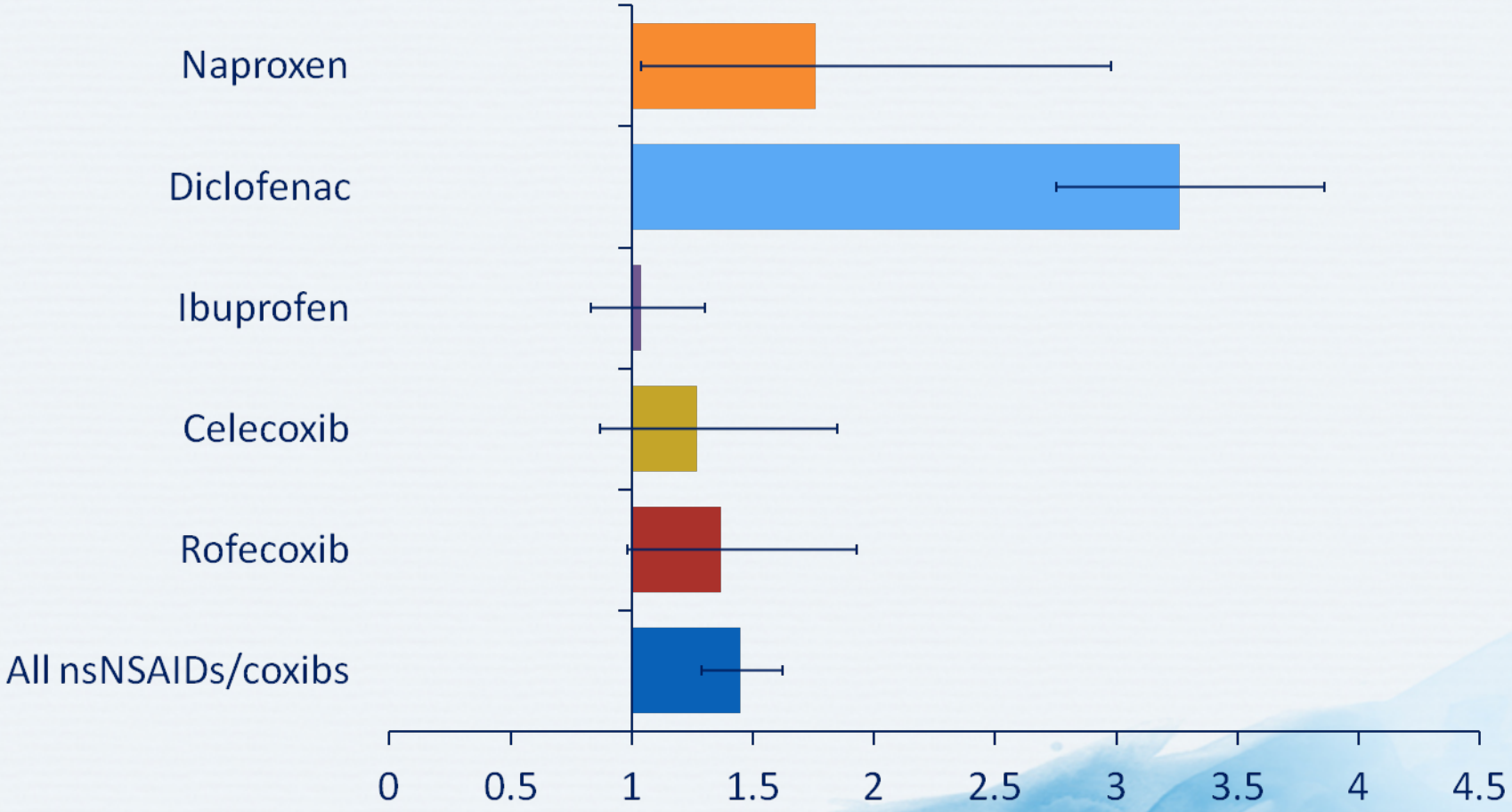
- Decreased platelet aggregation

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

Clemett D, Goa KL. *Drugs* 2000; 59(4):957-80; Grosser T *et al.* In: Brunton L *et al* (eds.). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

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

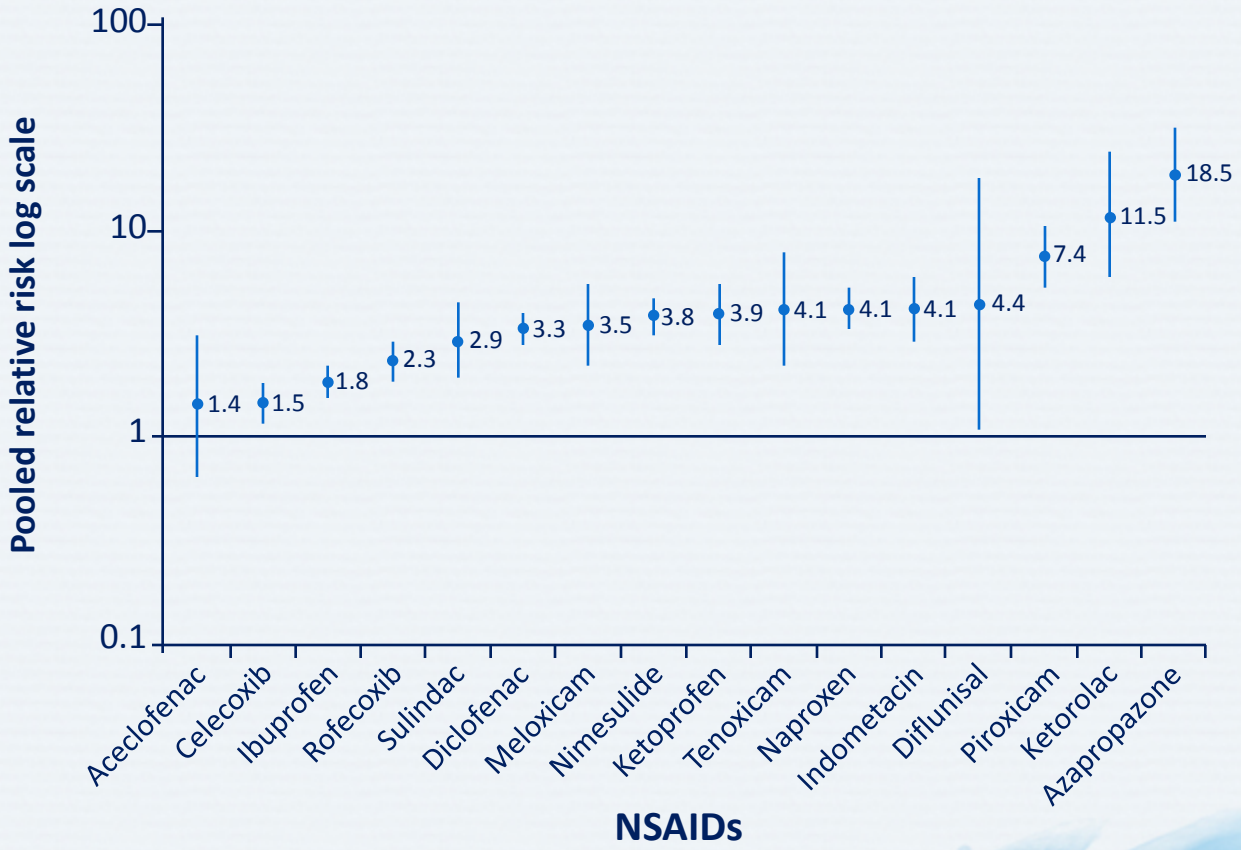


Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Schjerning Olsen AM *et al. Circulation* 2011; 123(20):2226-35.

Gastrointestinal Risk with nsNSAIDs/Coxibs

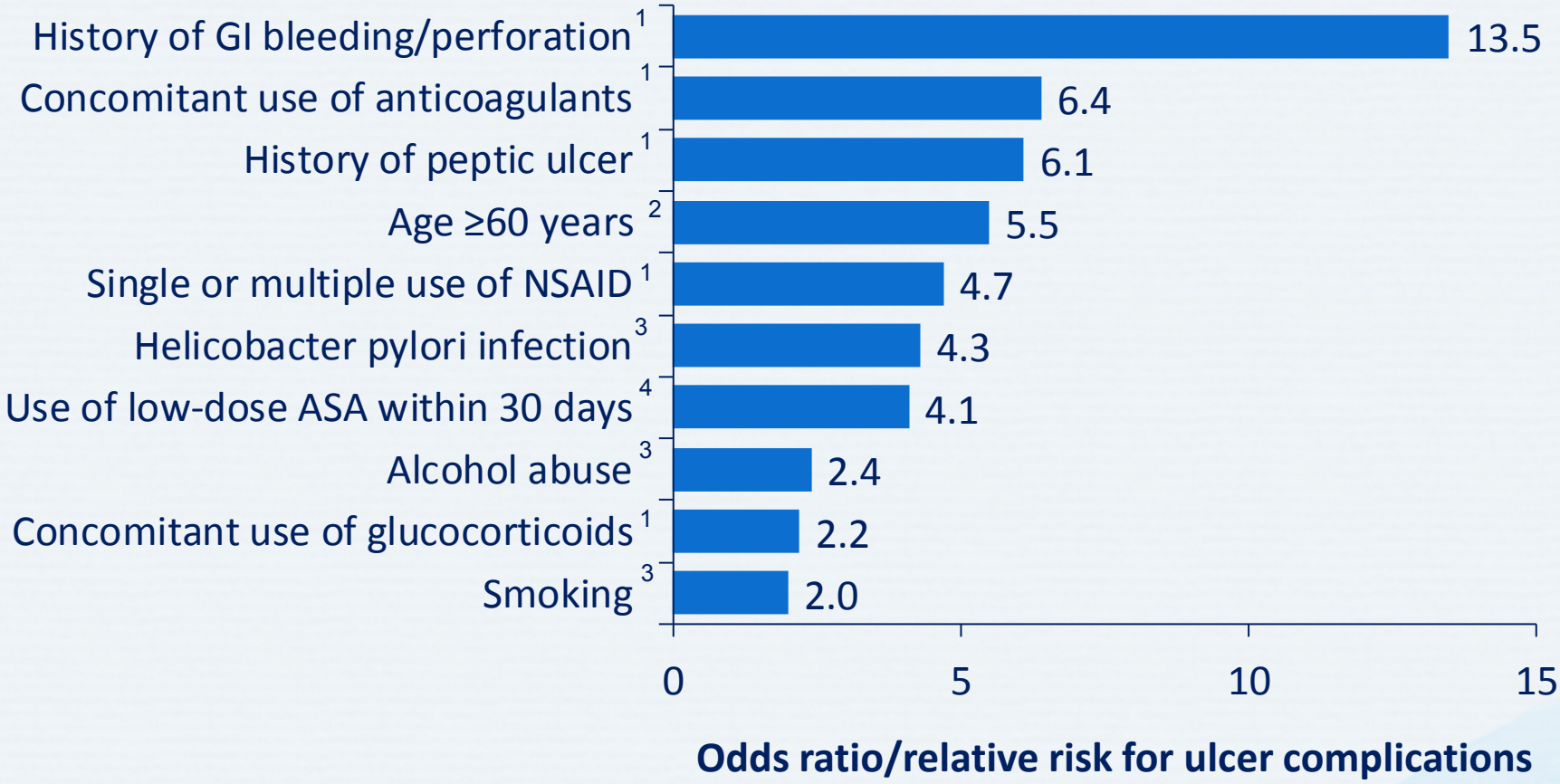
Pooled Relative Risks and 95% CIs of Upper Gastrointestinal Complications



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

Castellsague J *et al. Drug Saf* 2012; 35(12):1127-46.

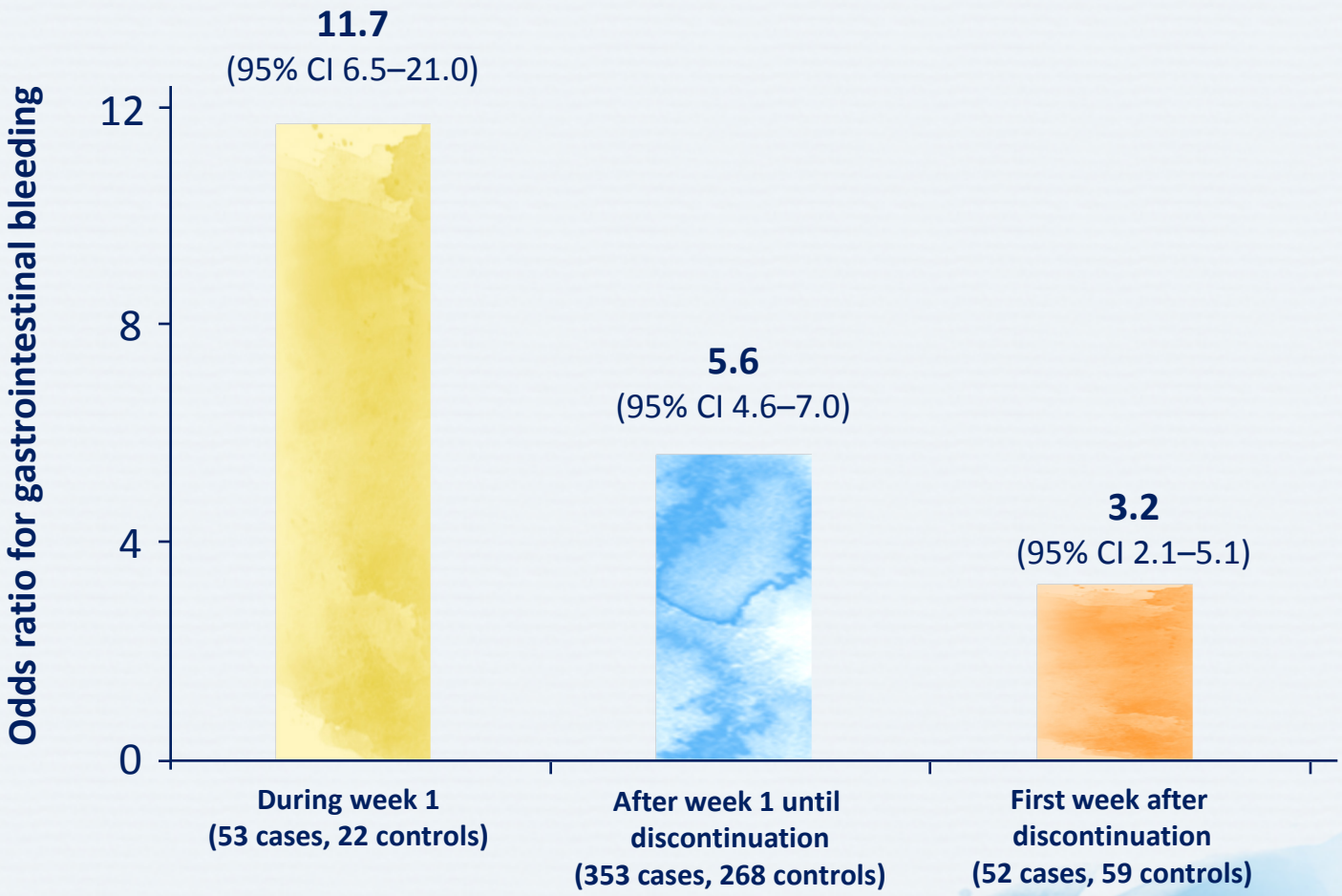
Risk Factors for Gastrointestinal Complications Associated with nsNSAIDs/Coxibs



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

1. Garcia Rodriguez LA, Jick H. *Lancet* 1994; 343(8900):769-72; 2. Gabriel SE *et al*. *Ann Intern Med* 1991; 115(10):787-96;
3. Bardou M. Barkun AN. *Joint Bone Spine* 2010; 77(1):6-12; 4. Garcia Rodríguez LA, Hernández-Díaz S. *Arthritis Res* 2001; 3(2):98-101.

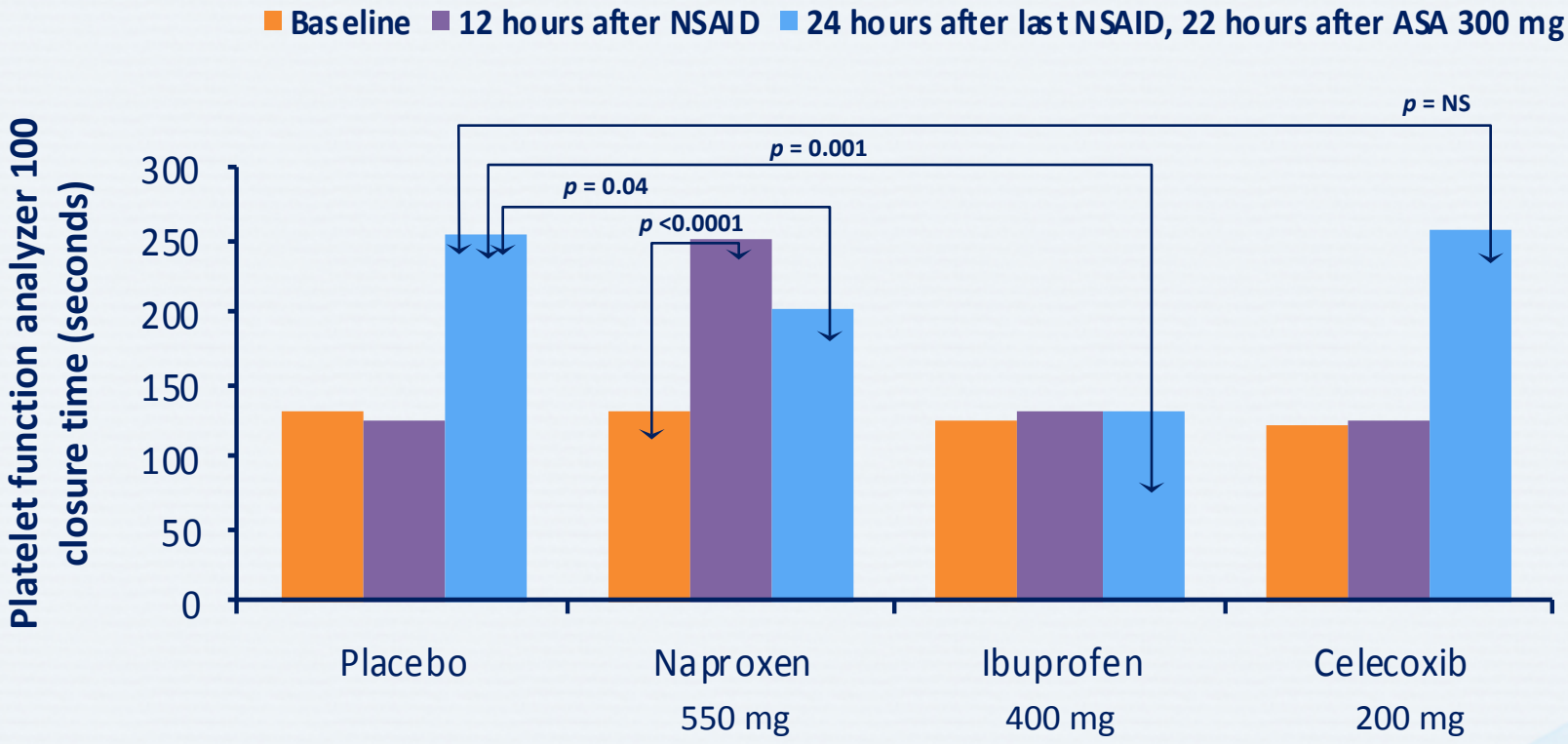
What is the gastrointestinal risk associated with the use of nsNSAIDs/coxibs in acute pain (i.e., for 7–10 days)?



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

Lewis SC *et al*. *Br J Clin Pharmacol* 2002; 54(3):320-6.

Effects of nsNSAIDs/Coxibs + ASA on Platelet Function



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
Gladding PA *et al. Am J Cardiol* 2008; 101(7):1060-3.

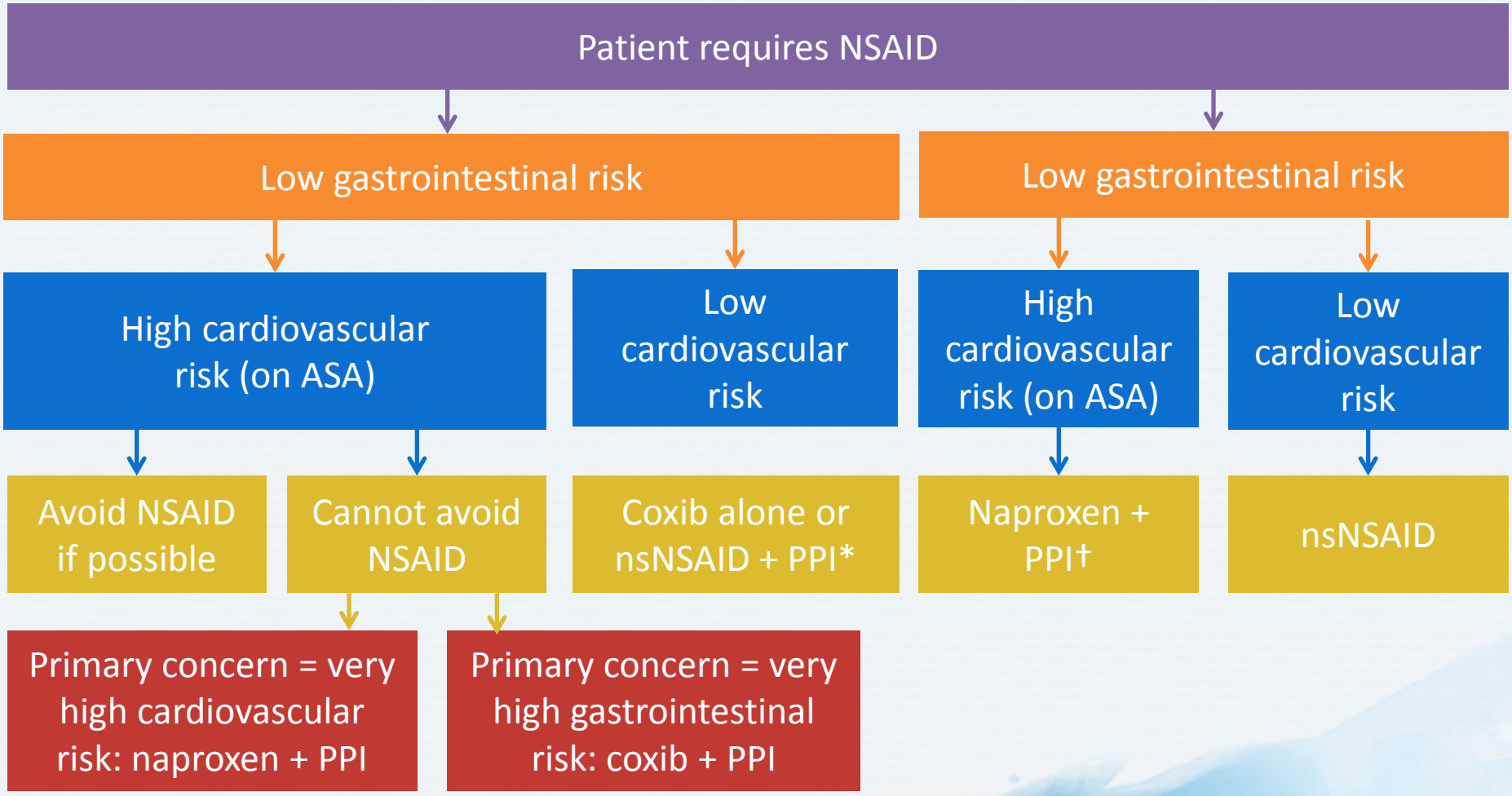
Guidelines Regarding ASA + NSAID Use

- 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

Bell AD *et al. Can J Cardiol* 2011; 123(20 Suppl A):S1-59.

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

Rostom A *et al. Aliment Pharmacol Ther* 2009; 29(5):481-96.

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

	Gastrointestinal risk	
	Not elevated	**Elevated**
Not on ASA	nsNSAID alone	Coxib nsNSAID + PPI
On ASA	Coxib + PPI nsNSAID + PPI	Coxib + PPI nsNSAID + PPI

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

Tannenbaum H *et al*. *J Rheumatol* 2006; 33(1):140-57.

Drug-Drug Interactions with nsNSAIDs/Coxibs

Interactions with nsNSAIDs/coxibs		
Drug	**Effect**	**Management**
Aminoglycoside antibiotics	Renal clearance inhibited	Monitor antibiotic concentration and adjust dose as necessary
Anticoagulants	Increased risk of bleeding	Monitor prothrombin time Avoid ASA use
Antihypertensive agents (with some NSAIDs)	Reduced antihypertensive effect Potential hyperkalemia with diuretics and ACE-Is	Monitor blood pressure, cardiac function and potassium concentration
Digoxin	Renal clearance inhibited	Monitor digoxin concentration and adjust dose as necessary

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

American Medical Association. *Table: Potential Drug Interactions with NSAID Analgesics.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_nsaids_interactions.htm. Accessed: September 5, 2013.

Drug-Drug Interactions with nsNSAIDs/Coxibs (cont'd)

Drug	Effect	Management
Lithium	Increased lithium concentration	Monitor lithium concentrations
Methotrexate	Increased methotrexate concentration	Monitor methotrexate concentration Avoid NSAIDs with high-dose methotrexate
Phenytoin (with ibuprofen)	Increased phenytoin levels	Monitor phenytoin concentration and adjust dose as necessary
Probenecid (with naproxen)	Reduced clearance of naproxen	Monitor for adverse effects

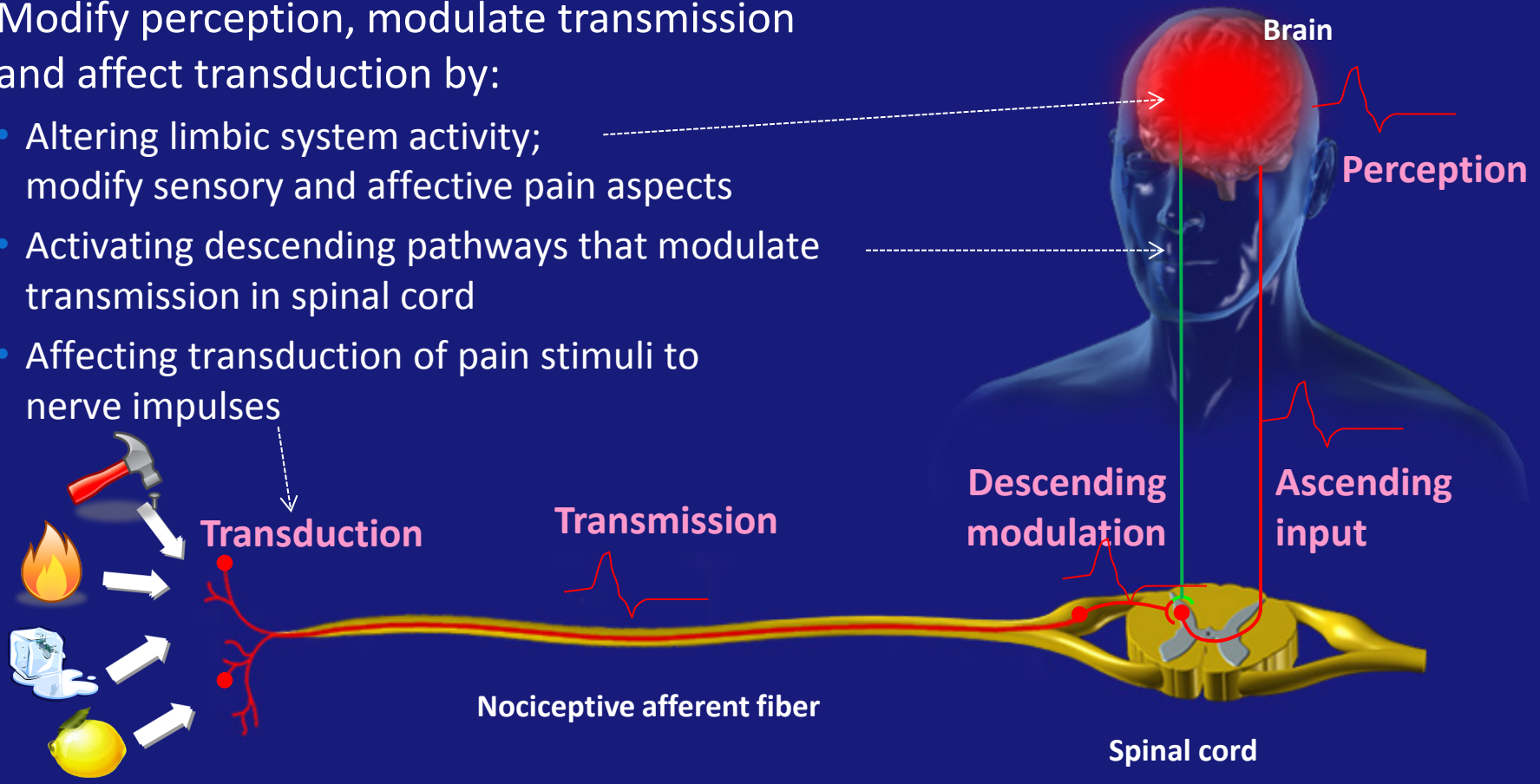
Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID

American Medical Association. *Table: Potential Drug Interactions with NSAID Analgesics.*
Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_nsaids_interactions.htm. Accessed: September 5, 2013.

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



Reisine T, Pasternak G. In: Hardman JG *et al* (eds). *Goodman and Gilman's: The Pharmacological Basics of Therapeutics.* 9th ed. McGraw-Hill; New York, NY: 1996; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7; Trescot AM *et al. Pain Physician* 2008; 11(2 Suppl):S133-53.

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

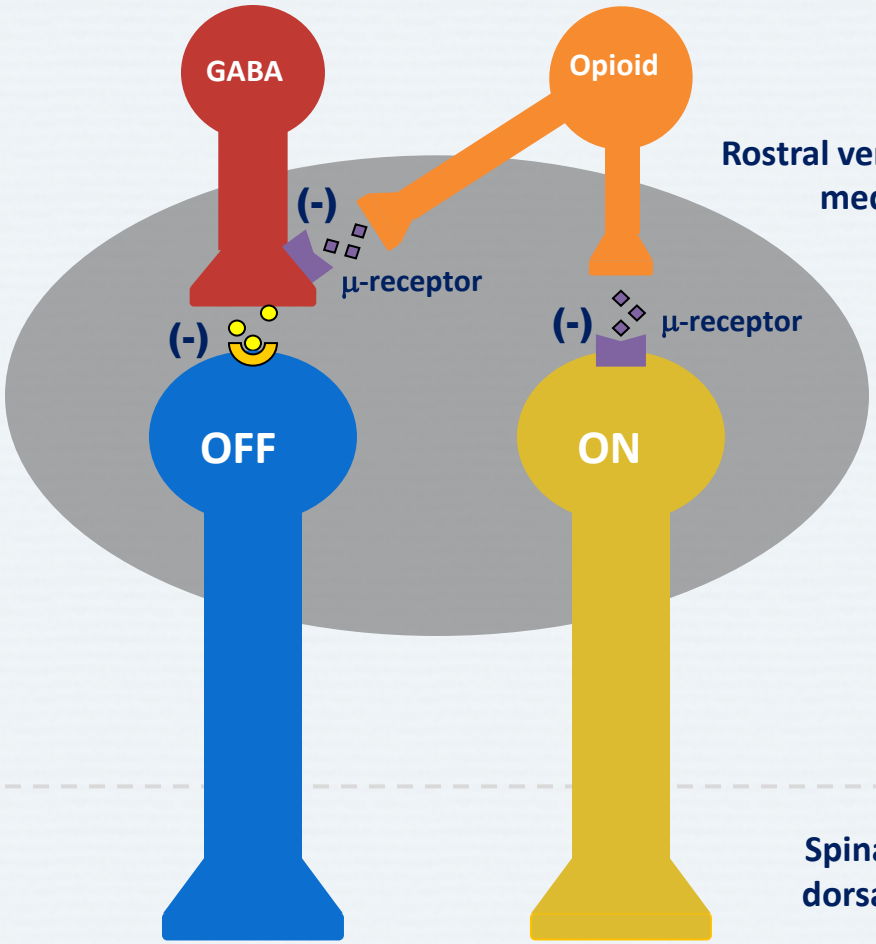
Moss J *et al. Mayo Clin Proc* 2008; 83(10):1116-30;
Tony L *et al*. In: Brunton L *et al* (eds). *Goodman and Gilman's The Pharmacological Basis of Therapeutics.* 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

Opioids and Pain Management

Opioid Receptor	Response
Mu	Supraspinal analgesia, respiratory depression, sedation, miosis, euphoria, cardiovascular effects, pruritis, nausea/vomiting, decreased gastrointestinal motility, dependence, tolerance
Delta	Analgesia, euphoria, dysphoria, psychotomimetic effects
Kappa	Spinal analgesia, dysphoria, psychotomimetic effects, miosis, respiratory depression, sedation

Gourlay GK. *Support Care Cancer* 2005; 13(3):153-9.;Reisine T *et al.* In: Hardman JG *et al* (eds). *Goodman and Gilman's: The Pharmacological Basics of Therapeutics.* 9th ed. McGraw-Hill; New York, NY: 1996.; Trescot AM *et al. Pain Physician* 2008; 11(2 Suppl):S133-53. Gourlay GK. *Supp Care Cancer*. 2005;13:153-9.

Opioids Modulate Control of "ON" and "OFF" Cells

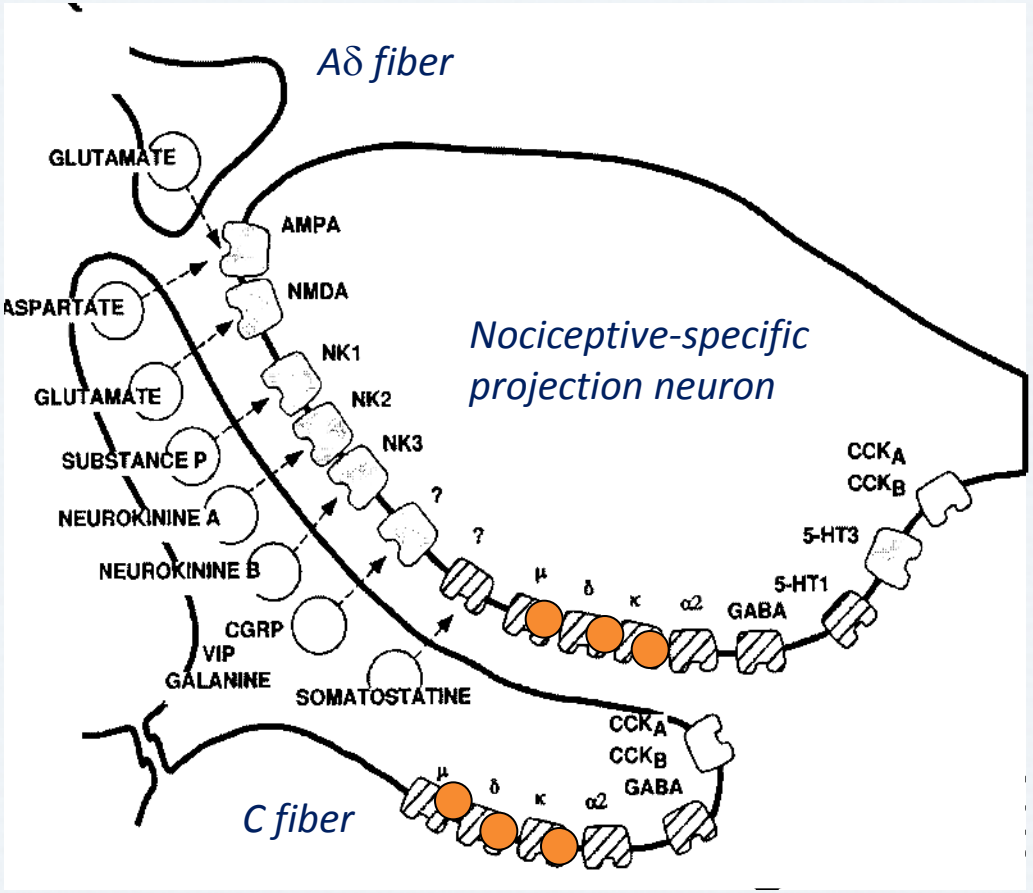


- **Opioid stimulation of mu-receptors on "ON" cells**
  - Reduced "ON" cell activity
  - Reduced facilitation of pain transmission at dorsal horn
  - **Less pain**
- **Opioid stimulation of mu-receptors on GABA-ergic interneurons innervating "OFF" cells**
  - Reduced GABA-ergic interneuron activity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

GABA = γ-aminobutyric acid

Fields HL *et al.* In: McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006.

Segmental Opioid Spinal Control



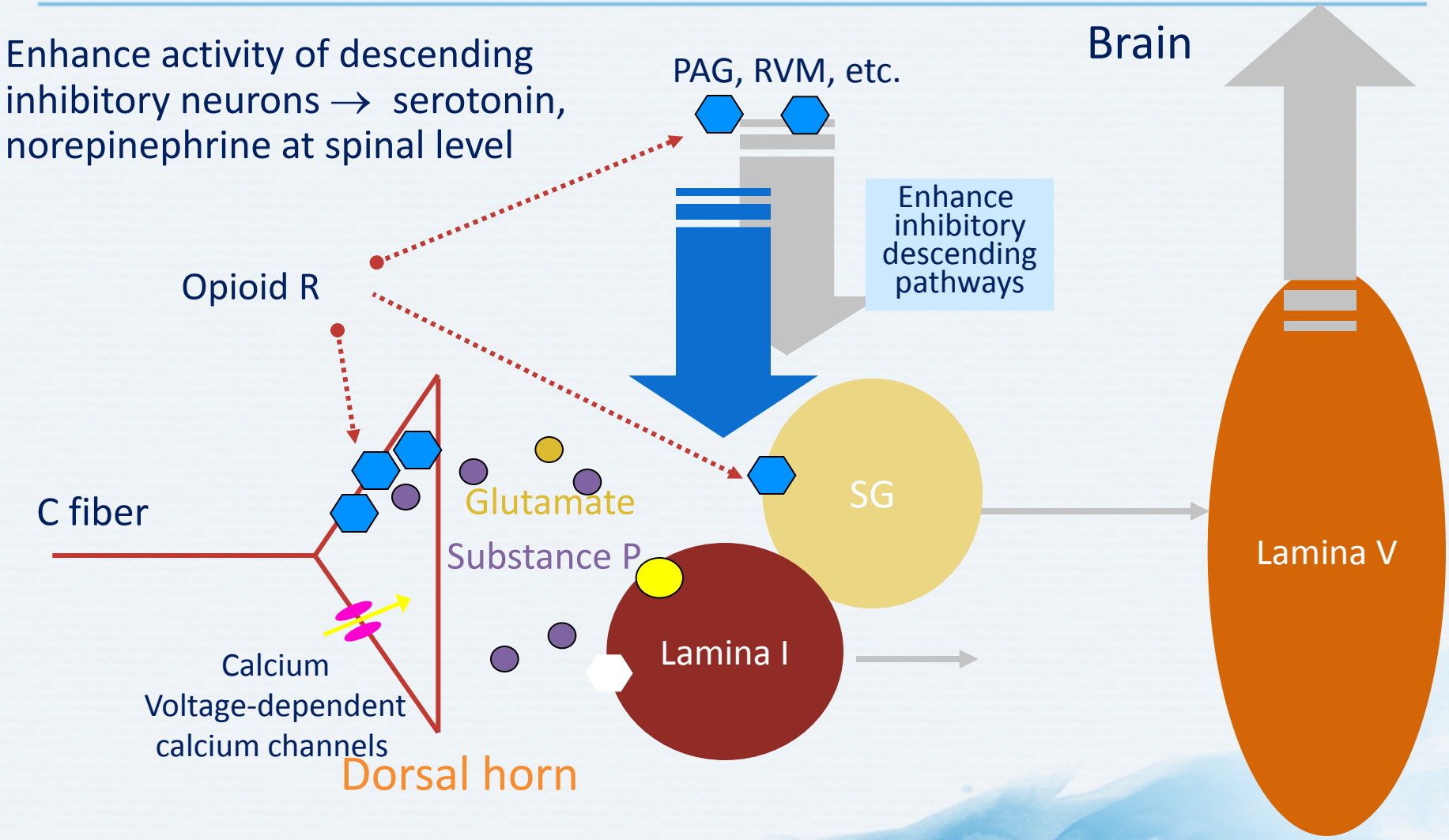
Endogenous opioid peptides:

- 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

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

Dickenson AH. *Behav Brain Sci* 1997; 20(3):392-403; Yaksh TL, Noueihed R. *Annu Rev Pharmacol Toxicol* 1985; 25:433-62.

Supraspinal Effect of Opioids

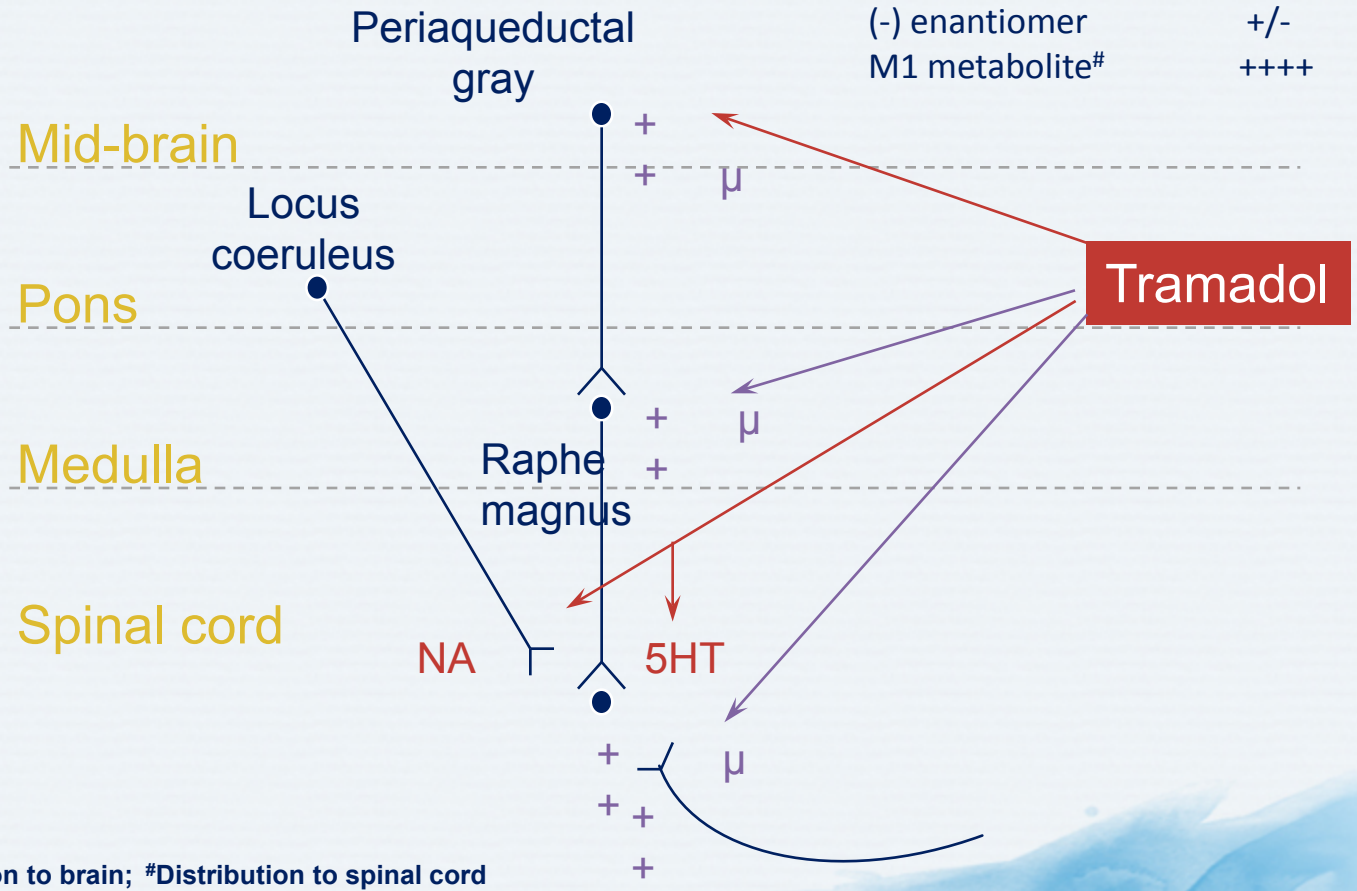


PAG = periaqueductal gray; RVM = rostral ventromedial medulla; SG = substantia gelatinosa

Dickenson A. *Br J Anaesth* 1995; 75(2):193-200.

Activity of Tramadol, Enantiomers and M1 Metabolite

	Uptake Inhibition		
	Mu-opioid	5HT	NA
Tramadol*	++	+	+
(+) enantiomer	+++	+ +	+/-
(-) enantiomer	+/-	+/-	++
M1 metabolite#	++++	+/-	+/-



***Distribution to brain; #Distribution to spinal cord**
5HT = serotonin; NA = noradrenaline

Vickers MD *et al. Anaesthesia* 1992; 47(4): 291-6.

Opioids Can Induce Hyperalgesia

- Primary hyperalgesia
  - Sensitization of primary neurons → 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

Dolan S, Nolan AM. *Neuroreport* 1999; 10(3):449-52; Raja SN *et al.* In: Wall PB, Melzack R (eds). *Textbook of Pain*. 4th ed. Churchhill Linvingstone; London, UK: 1999; Woolf CJ. *Drugs* 1994; 47(Suppl 5):1-9.

Opioids Can Induce Allodynia

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

NMDA = N-methyl-D-aspartate

Dolan S, Nolan AM. *Neuroreport* 1999; 10(3):449-52; Raja SN *et al.* In: Wall PB, Melzack R (eds). *Textbook of Pain*. 4th ed. Churchhill Linvingstone; London, UK: 1999; Woolf CJ. *Drugs* 1994; 47(Suppl 5):1-9.

Adverse Effects of Opioids

System	Adverse effects
Gastrointestinal	Nausea, vomiting, constipation
CNS	Cognitive impairment, sedation, lightheadedness, dizziness
Respiratory	Respiratory depression
Cardiovascular	Orthostatic hypotension, fainting
Other	Urticaria, miosis, sweating, urinary retention

CNS = central nervous system

Moreland LW, St Clair EW. *Rheum Dis Clin North Am* 1999; 25(1):153-91; Yaksh TL, Wallace MS. In*:* Brunton L *et al* (eds). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

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**

Oderda GM *et al*. *J Pain Symptom Manage* 2003; 25(3):276-83.

Additional Opioid Use Concerns

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

World Health Organization. *Understanding Health Professionals' Fear of Opioids.*
Available at: http://www.whocancerpain.wisc.edu/?q=node/332. Accessed: October 17, 2013.

Drug-Drug Interactions with Opioids

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

American Medical Association. *Table: Important Opioid Drug Interactions.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_opioid_interactions.htm. Accessed: September 5, 2013; Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute Pain Management: Scientific Evidence. 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010; South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

Drug-Drug Interactions with Opioids (cont'd)

Drug0	Opioid(s)	Effect
Butyrophenones	All	Increased sedation
Carbamazepine	Methadone Propoxyphene	Increased opioid metabolism (may induce withdrawal) Increased carbamazepine levels, potential toxicity
Cimetidine	Meperidine, morphine	Increased opioid effects
Desipramine	Methadone, morphine	Possible toxicity due to inhibition of desipramine metabolism
Doxepin	Propoxyphene	Possible toxicity due to increased doxepin levels
Erythromycin	Methadone	Increased opioid metabolism (may induce withdrawal)
MAOIs	Meperidine	Excitatory response (includes seizures, arrhythmia, hyperpyrexia)
Phenytoin	Methadone	Increased opioid metabolism (may induce withdrawal)
Quinidine	Codeine	Decreased analgesia
TCAs	All	Increased sedation

MAOI = monoamine oxidase inhibitor; TCA = tricyclic antidepressant

American Medical Association. *Table: Important Opioid Drug Interactions.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_opioid_interactions.htm. Accessed: September 5, 2013.

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

Achneck HE *et al. Circulation* 2010; 122(20):2068-77; Cheetham TC *et al*. *Ann Pharmacother* 2009; 43(11):1765-73; Fisher WD. *Can J Surg* 2011; 54(5):344-51; Kwong LM *et al. Ann Pharmacother* 2012; 46(9):1232-8.

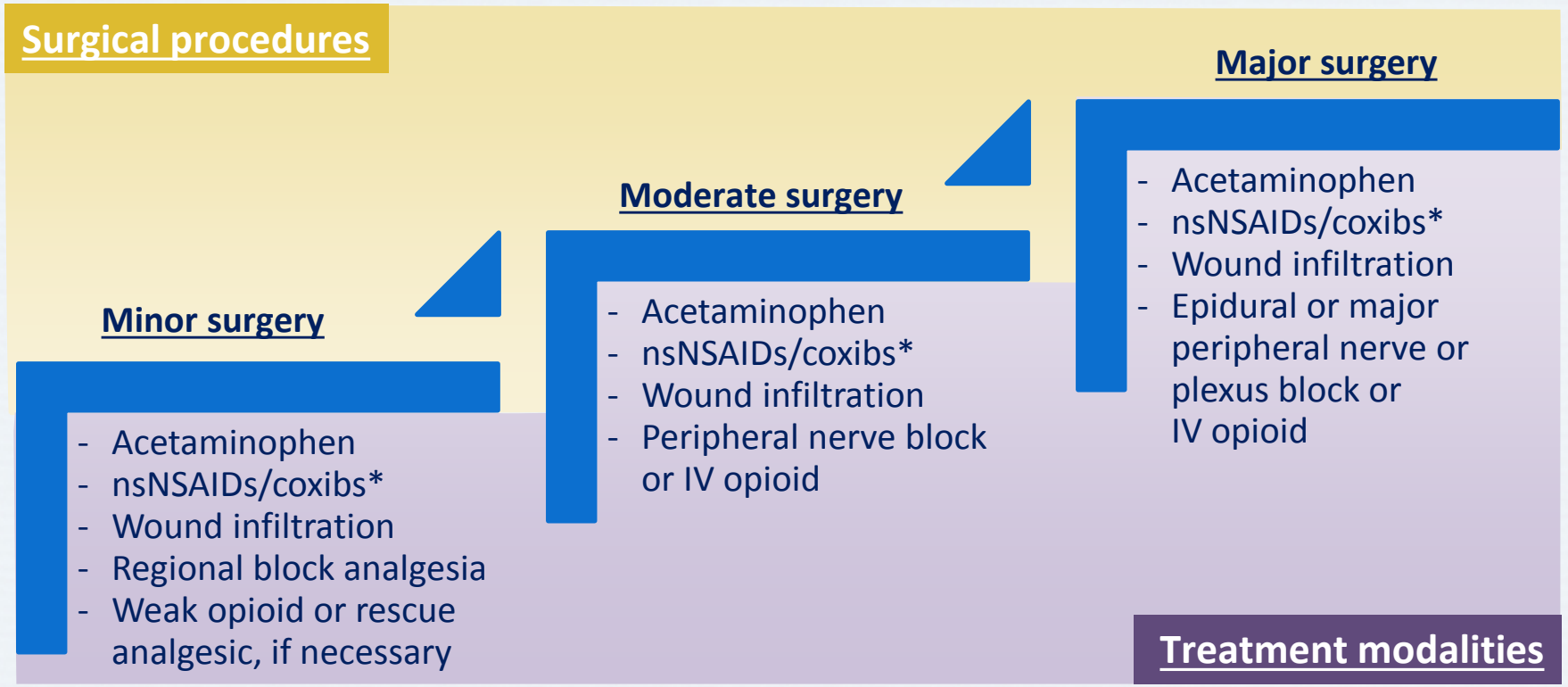
Special Considerations for Post-operative Management in the Elderly

- 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

Hallingbye T *et al*. *Aging Health* 2011; 7(6):813-28; Herr KA *et al*. *Clin Geriatr Med* 2001; 17(3):457-78; Rakel B *et al*. *J Perianesth Nurs* 2004; 19(3):194-208. American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. *J Am Geriatr Soc* 2009; 57(8):1331-46.

Analgesia for Post-operative Pain Based on Type of Surgery



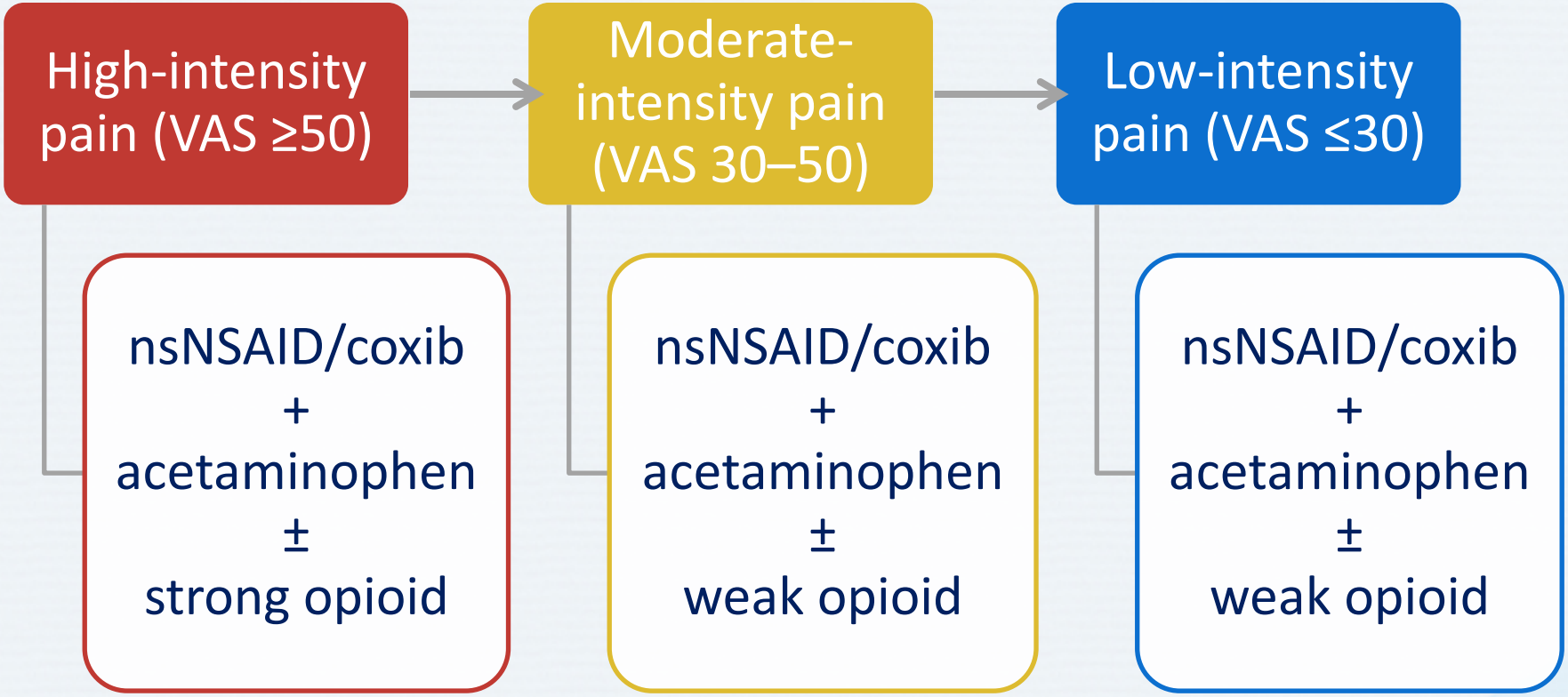
***Unless contraindicated**

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

Sivrikaya GU. In: Racz G (ed). *Pain Management – Current Issues and Opinions.* InTech; Rijeka, Croatia: 2012.

PROSPECT Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

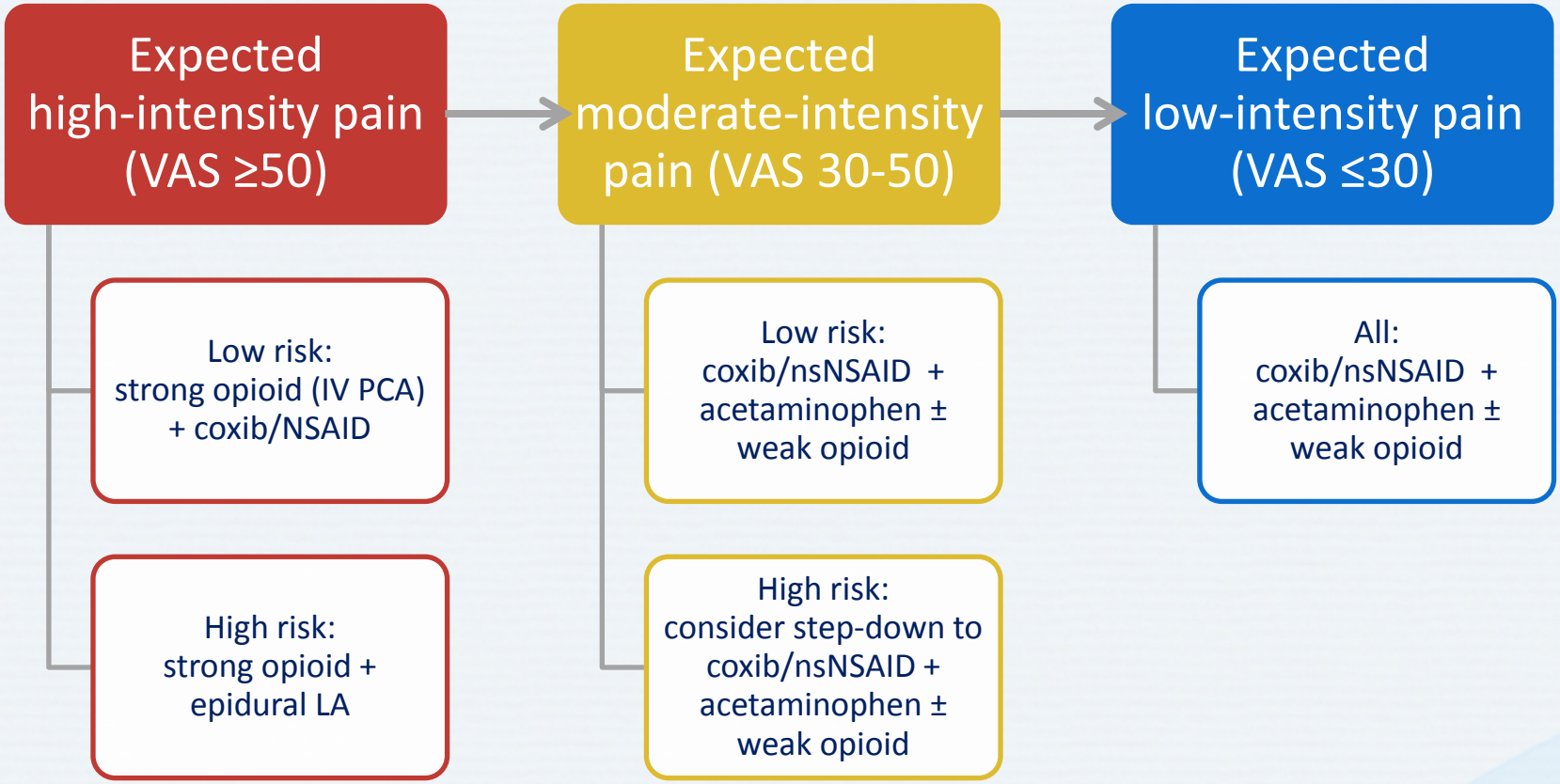
PROSPECT: Management of Post-operative Pain*



***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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

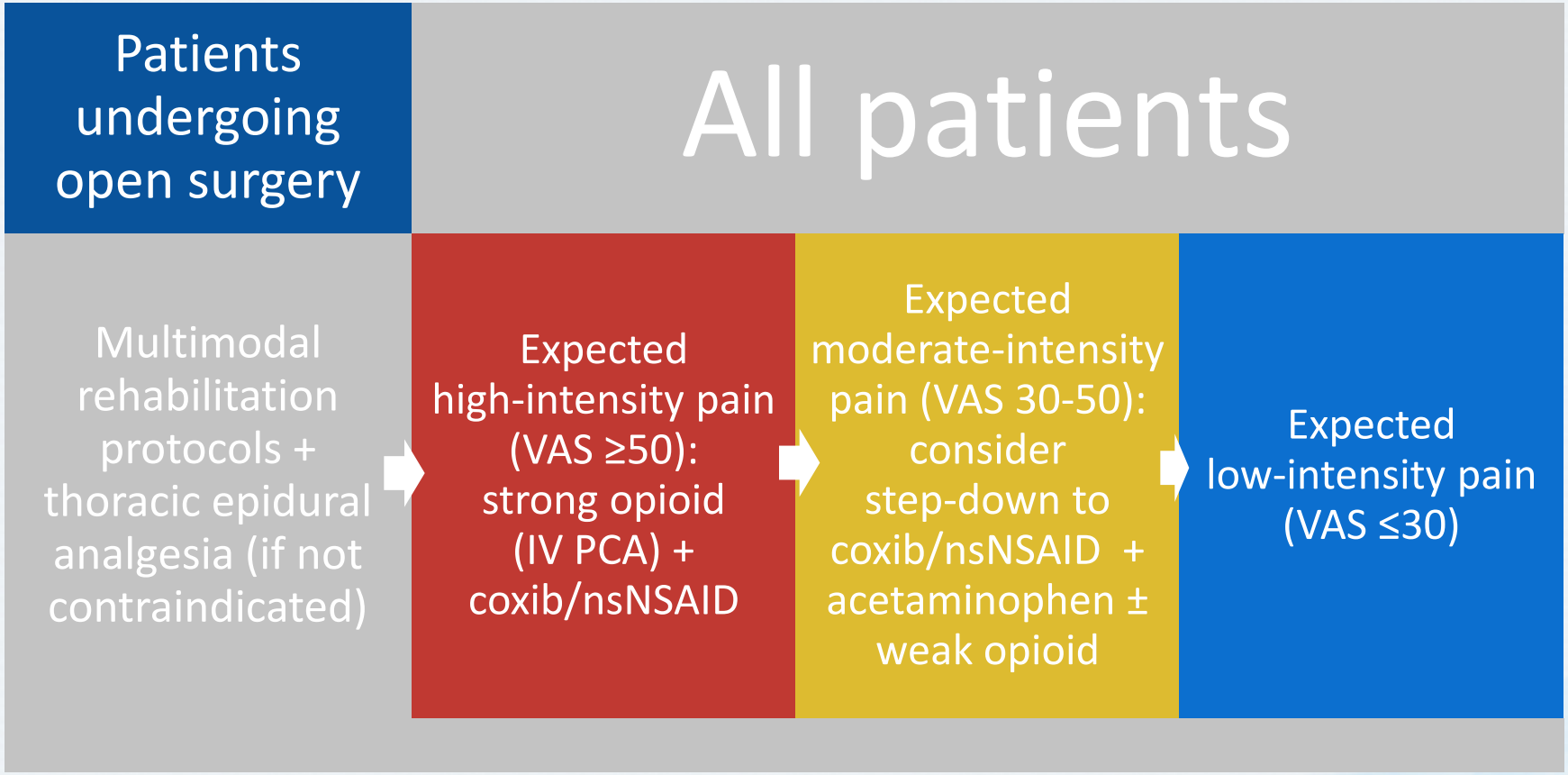
PROSPECT: Management of Abdominal Hysterectomy Postoperative Pain



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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

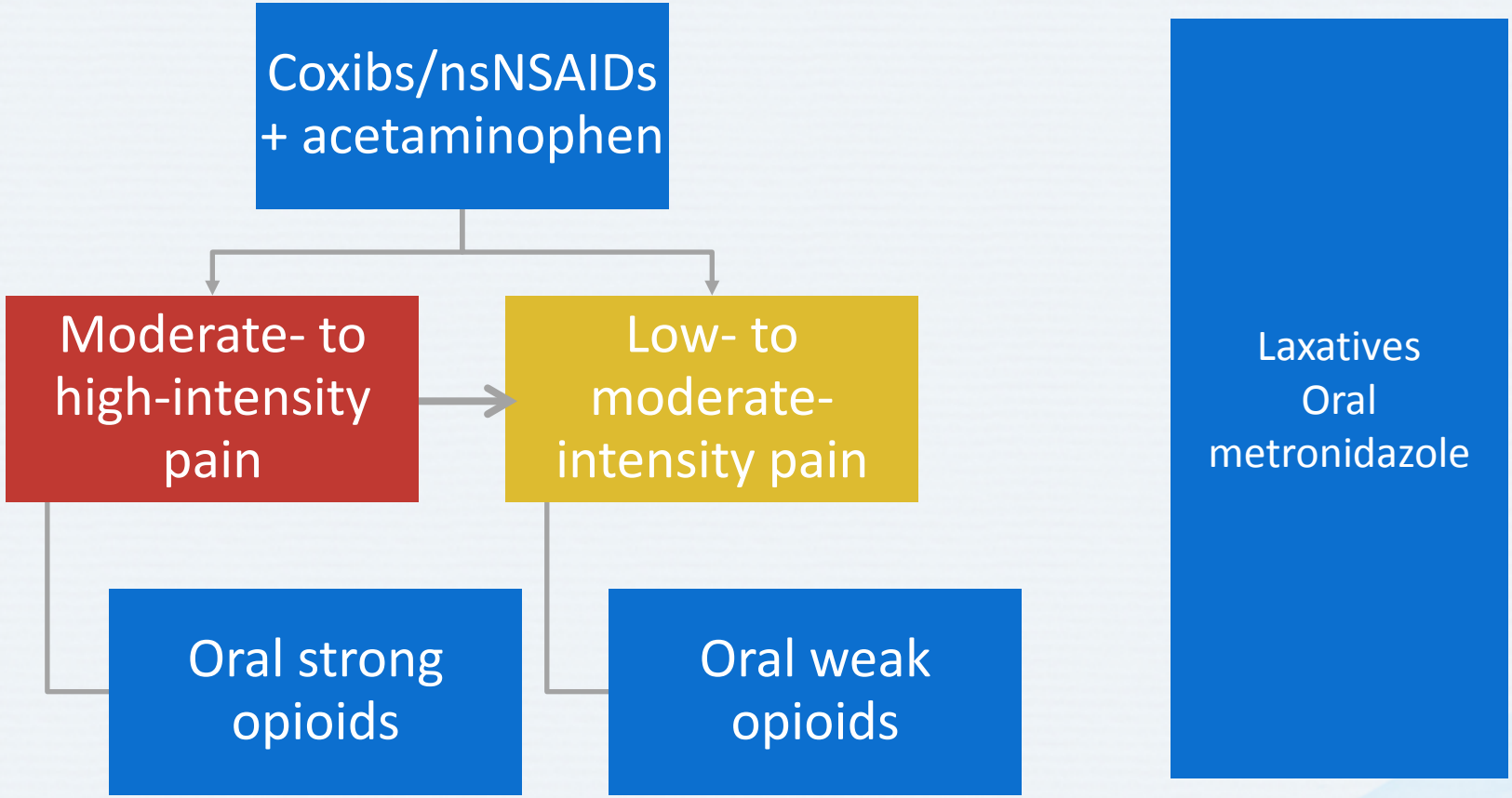
PROSPECT: Management of Colonic Resection Post-operative Pain



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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

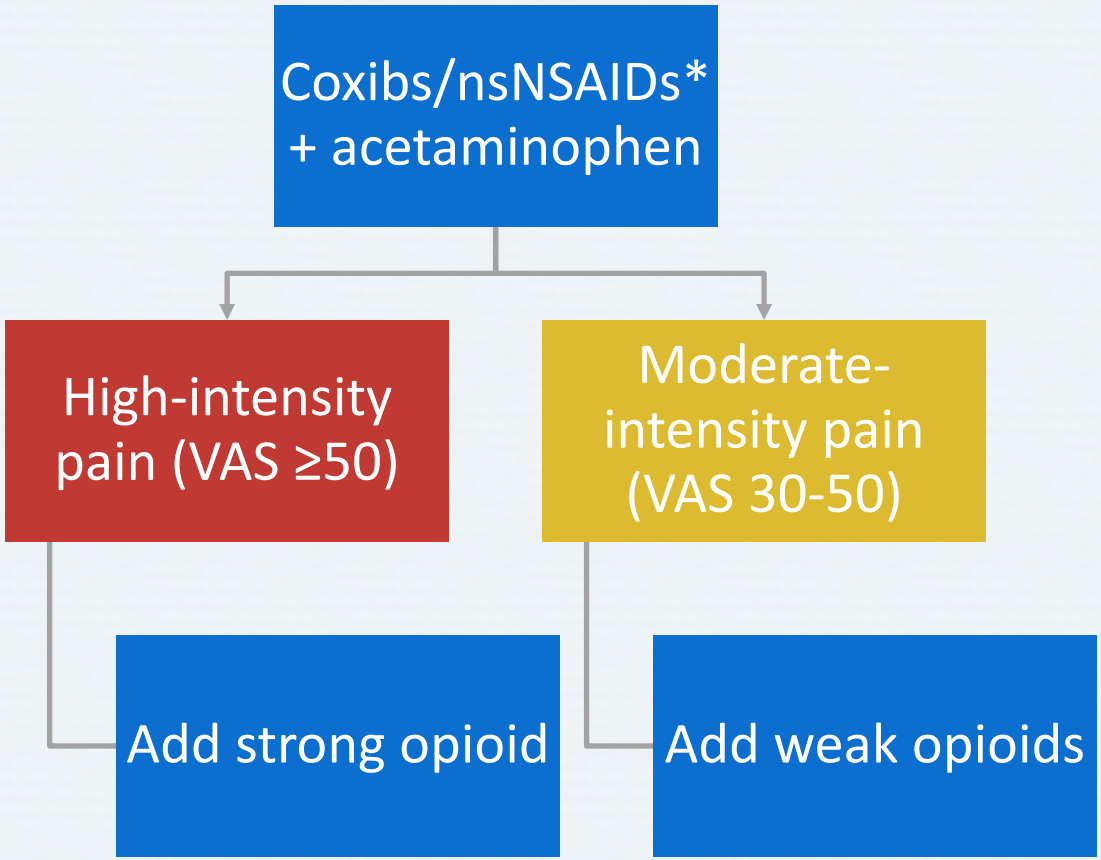
PROSPECT: Management of Hemorrhoid Surgery Post-operative Pain



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

PROSPECT Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

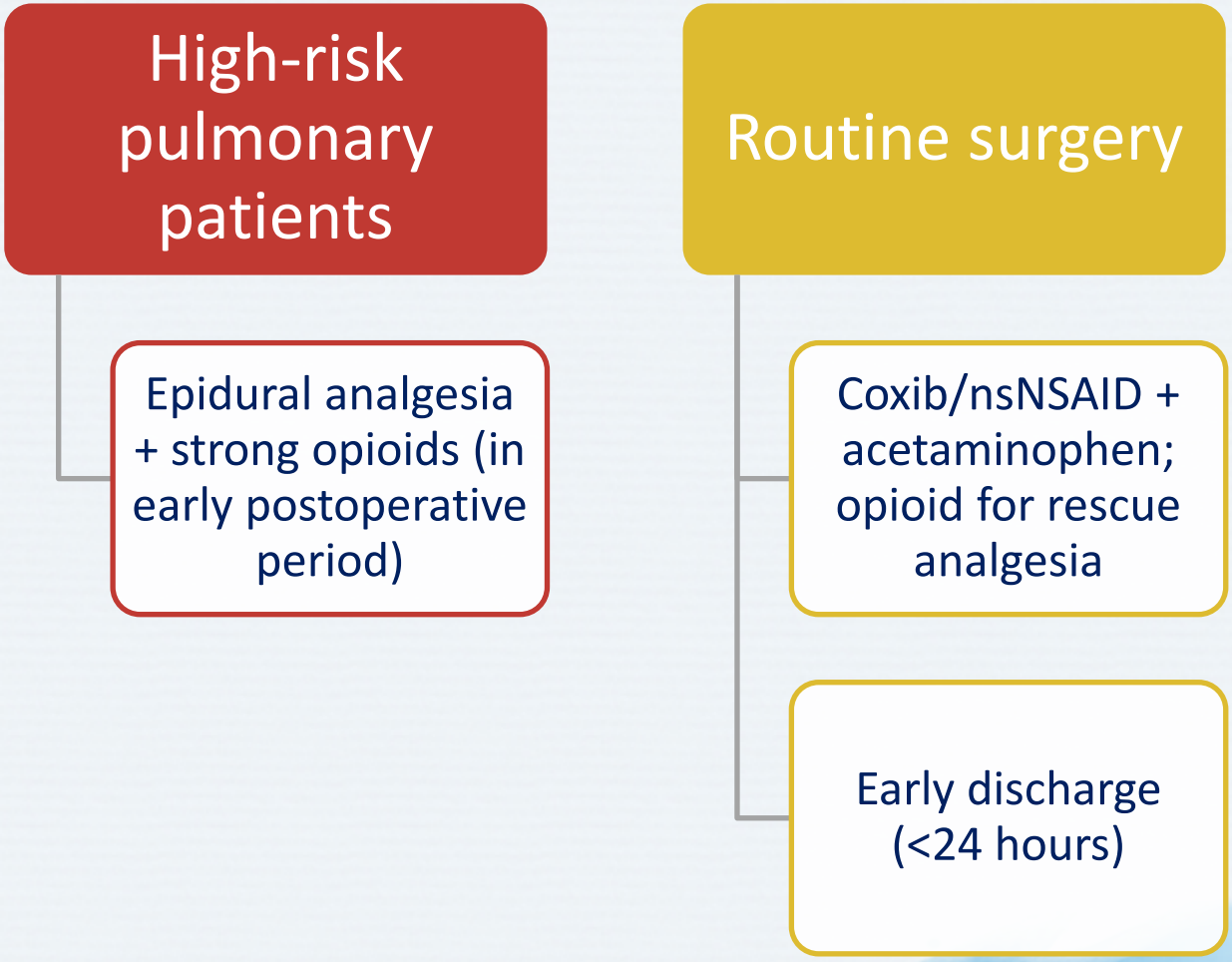
PROSPECT: Management of Herniorrhaphy Post-operative Pain



***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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

PROSPECT: Management of Laparoscopic Cholecystectomy Post-operative Pain



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

PROSPECT Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

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

PROSPECT Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

PROSPECT: Management of Radical Prostatectomy Post-operative Pain

High-intensity pain (VAS ≥50)

→ Coxib + acetaminophen ± $\alpha_2\delta$ ligands + IV PCA opioid

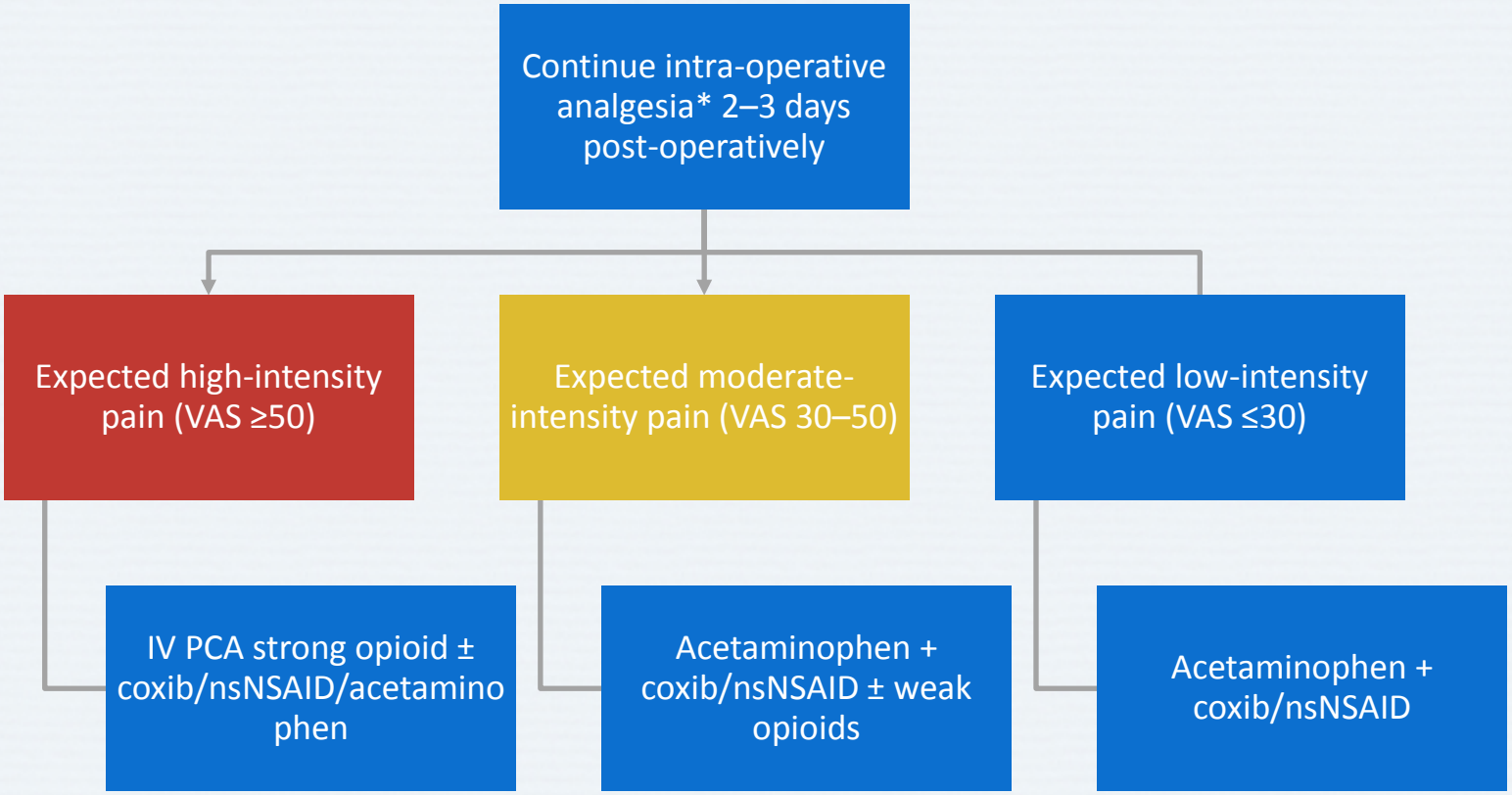
Moderate or low-intensity pain (VAS <50)

→ Coxib + acetaminophen ± $\alpha_2\delta$ ligands ± weak opioid

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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

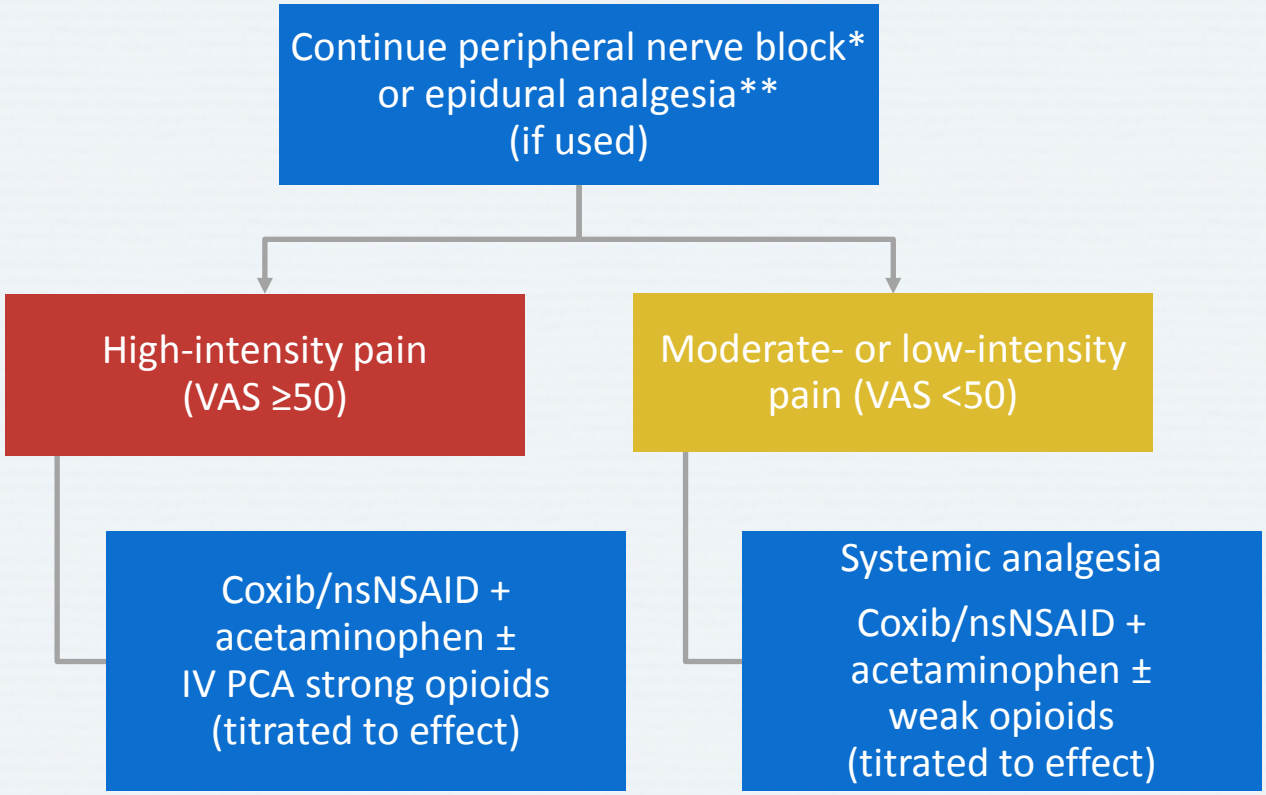
PROSPECT: Management of Thoracotomy Post-operative Pain



***Either thoracic epidural LA + opioid + epinephrine or paravertebral block with LA is recommended as the primary analgesic approach**
Coxib = COX-2-specific inhibitor; IV = intravenous; LA = local anesthetic; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PROSPECT = Procedure Specific Postoperative Pain Management; VAS = visual analog scale

PROSPECT Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

PROSPECT: Management of Total Hip Arthroplasty Post-operative Pain

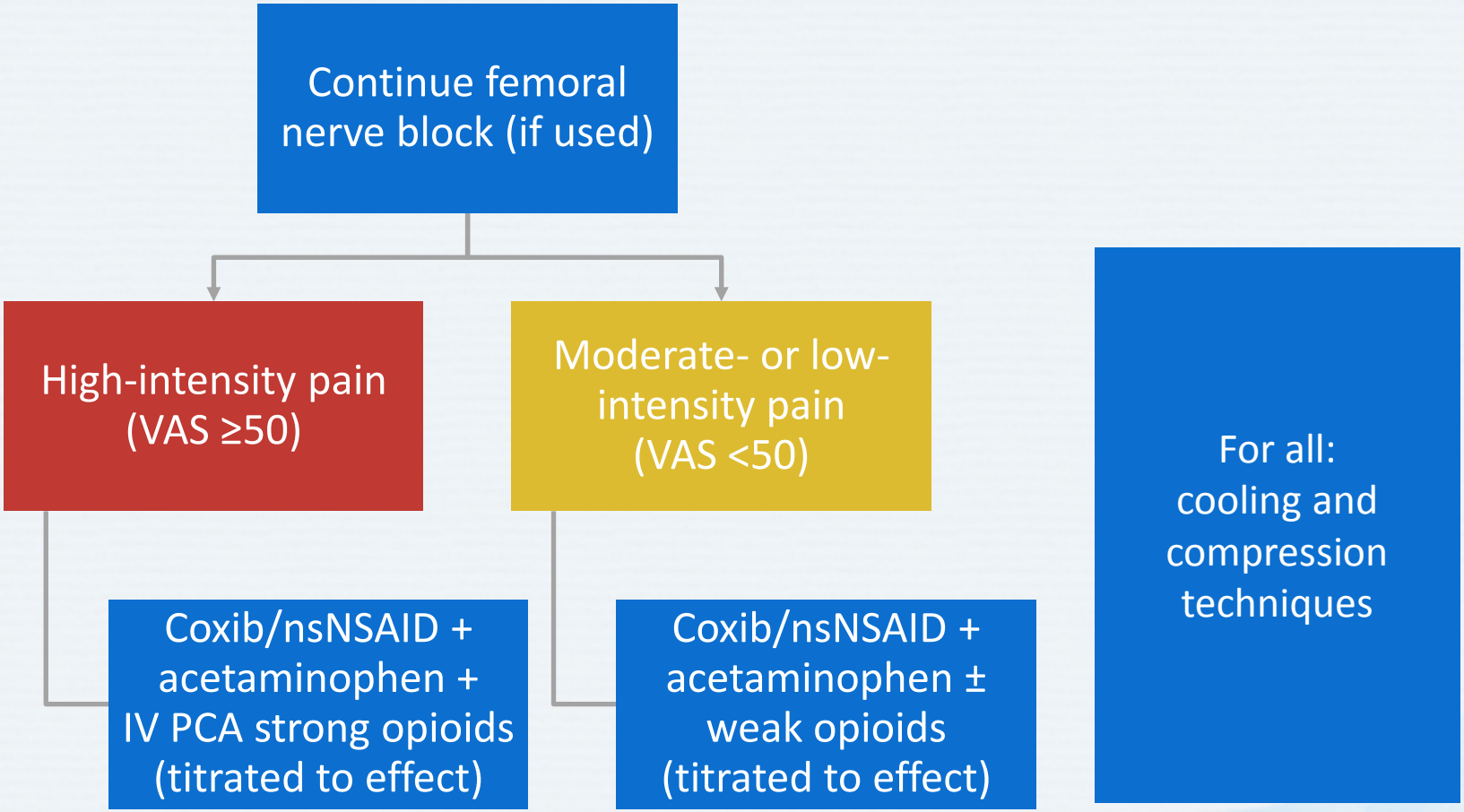


***By cathether techniques, using patient-controlled regional analgesia; **Establish epidural infusion as the nerve block regresses using patient-controlled epidural analgesia**

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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

PROSPECT: Management of Total Knee Arthroplasty Post-operative Pain



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 Working Group. *Procedure Specific Postoperative Pain Management.* Available at: http://www.postoppain.org/frameset.htm. Accessed: July 24, 2013.

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 Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

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 Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

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 Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

South African Acute Pain Guidelines: Acute Musculoskeletal Pain

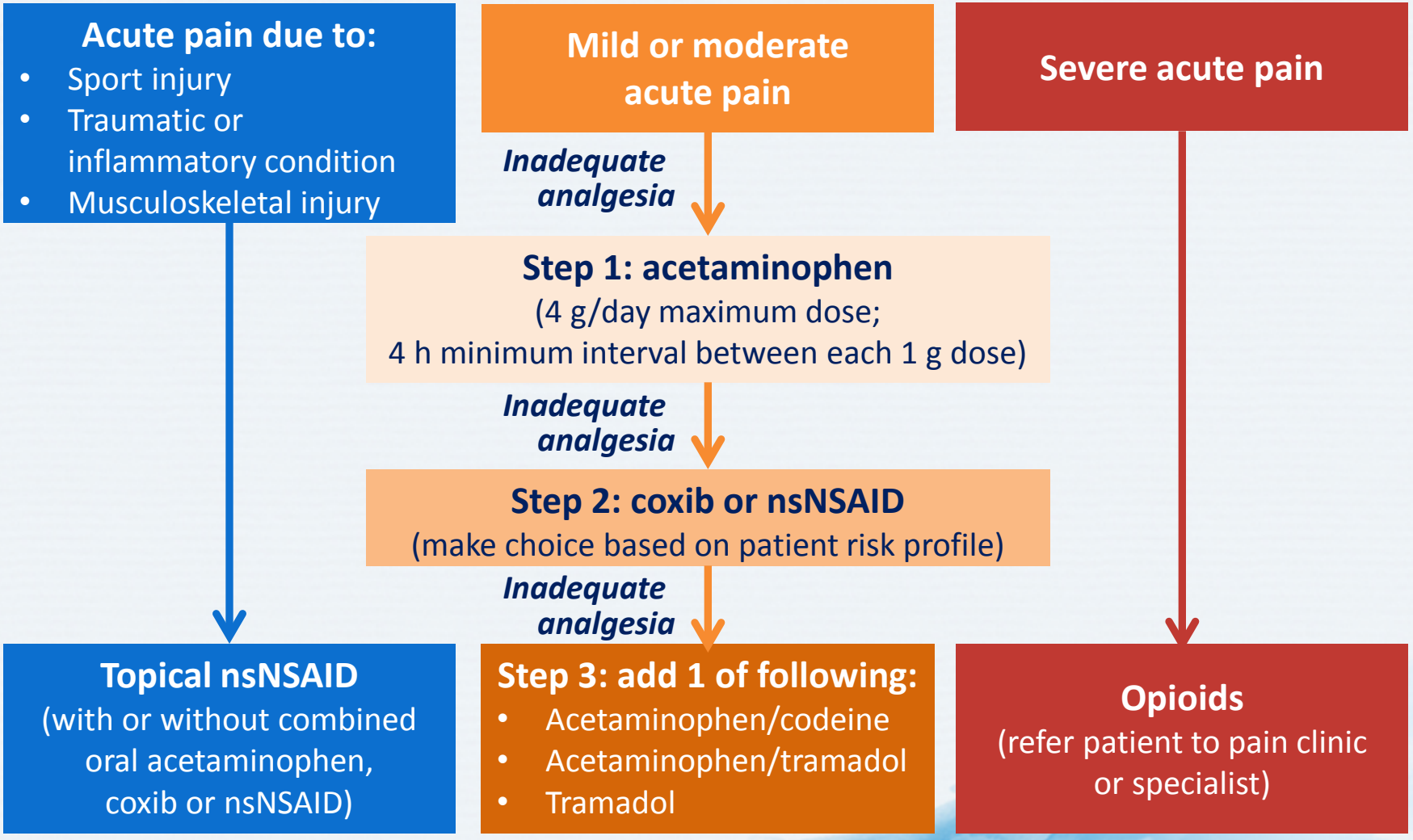
1st 48 hours after musculoskeletal injury	• Acetaminophen • Acetaminophen + codeine (for more severe pain) • Tramadol (for more severe injury)

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

South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

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



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

Ayad AE *et al. J Int Med Red* 2011; 39(4):1123-41.

ESRA: Treatment Options in Relation to Intensity of Expected Post-operative Pain

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

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

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

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

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

(i) Acetaminophen + wound infiltration with local anesthetic
(ii) NSAIDs (unless contraindicated)
(iii) Regional block analgesia
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

Rawal N *et al. Postoperative Pain Management – Good Clinical Practice.* AstraZeneca: Södertälje, Sweden.0000

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

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. *Acute Pain Management: Scientific Evidence.* 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010.

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.
Acute Pain Management: Scientific Evidence. 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010.

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

Australian Acute Musculoskeletal Pain Guidelines Group. *Evidence-Based Management of Acute Musculoskeletal Pain. A Guide for Clinicians.* Australian Academic Press Pty. Lts; Bowen Hills, QLD: 2004.

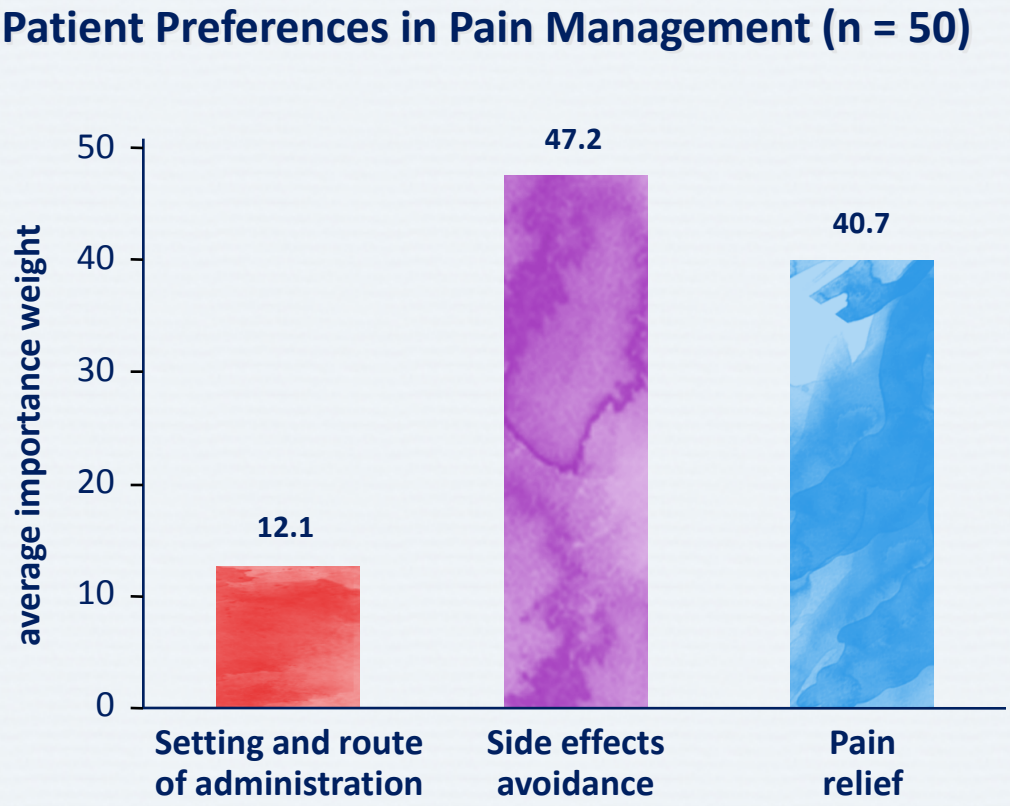
Adherence

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

Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* The National Academies Press; Washington, DC: 2011; Sinatra R. *Pain Medicine* 2010; 11(12):1859-71.

Surgical Patients Prefer Avoidance of Opioid Side Effects over Pain Control



Gan TJ *et al. Br. J Anaesth* 2004; 92(5):681-8.

Many Patient Do Not Take Analgesics at Home Following Surgery

Percent of Patients* Who Took Analgesic Medication at Home

	24 h	48 h	Days 3–6	Day 7
Mild opioids	58%	43%	43%	7%
Acetaminophen	15%	9%	10%	2%
NSAIDs	3%	3%	5%	1%
None	32%	51%	61%	90%

Beauregard L *et al. Can J Anaesth* 1998; 45(4):304-11.

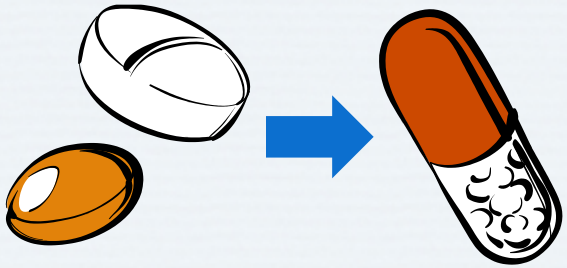
Strategies to Improve Adherence

- **S**implify regimen
- **I**mpart knowledge
- **M**odify patient beliefs and human behavior
- **P**rovide communication and trust
- **L**eave the bias
- **E**valuate adherence

Atreja A *et al*. *Medacapt Gen Med* 2005; 7(1):4.

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

American College of Preventive Medicine. *Medication Adherence Clinical Reference.* Available at: http://www.acpm.org/?MedAdherTT_ClinRef. Accessed: October 8, 2013; van Dulmen S *et al. BMC Health Serv Res* 2008; 8:47.

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

American College of Preventive Medicine. *Medication Adherence Clinical Reference.* Available at: http://www.acpm.org/?MedAdherTT_ClinRef. Accessed: October 8, 2013.

Modifying Patient Beliefs and Behaviors: Motivational Interviewing Technique

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

Bisono A *et al.* In: O'Donoghue WT, Levensky ER (eds). *Promoting Treatment Adherence: A Practical Handbook for Health Care Providers.* SAGE Publications, Inc.; London, UK: 2006.

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

Acknowledge biases

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

American College of Preventive Medicine. *Medication Adherence Clinical Reference.* Available at: http://www.acpm.org/?MedAdherTT_ClinRef. Accessed: October 8, 2013.

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

Hahn S, Budenz DL. *Adv Stud Ophthalmol* 2008; 5(2):44-9.

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