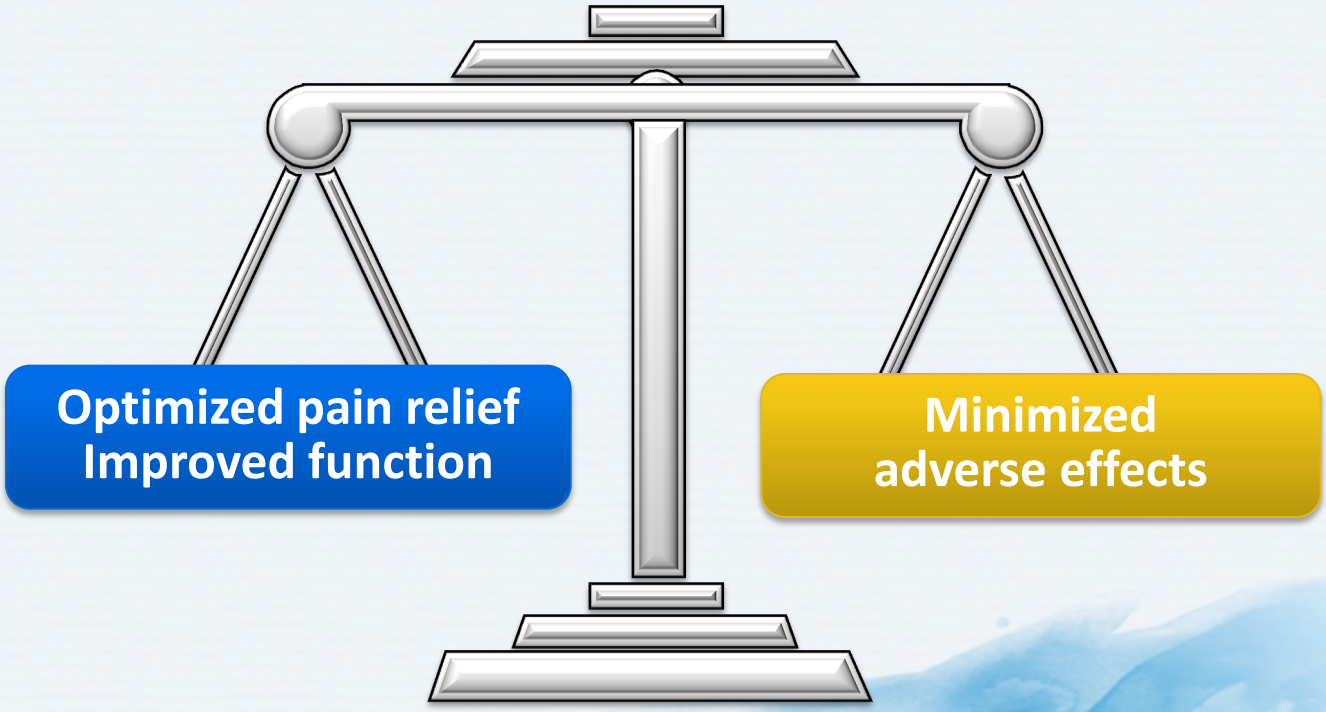
MANAGEMENT

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.

Pain Should Be Treated in a Timely Manner

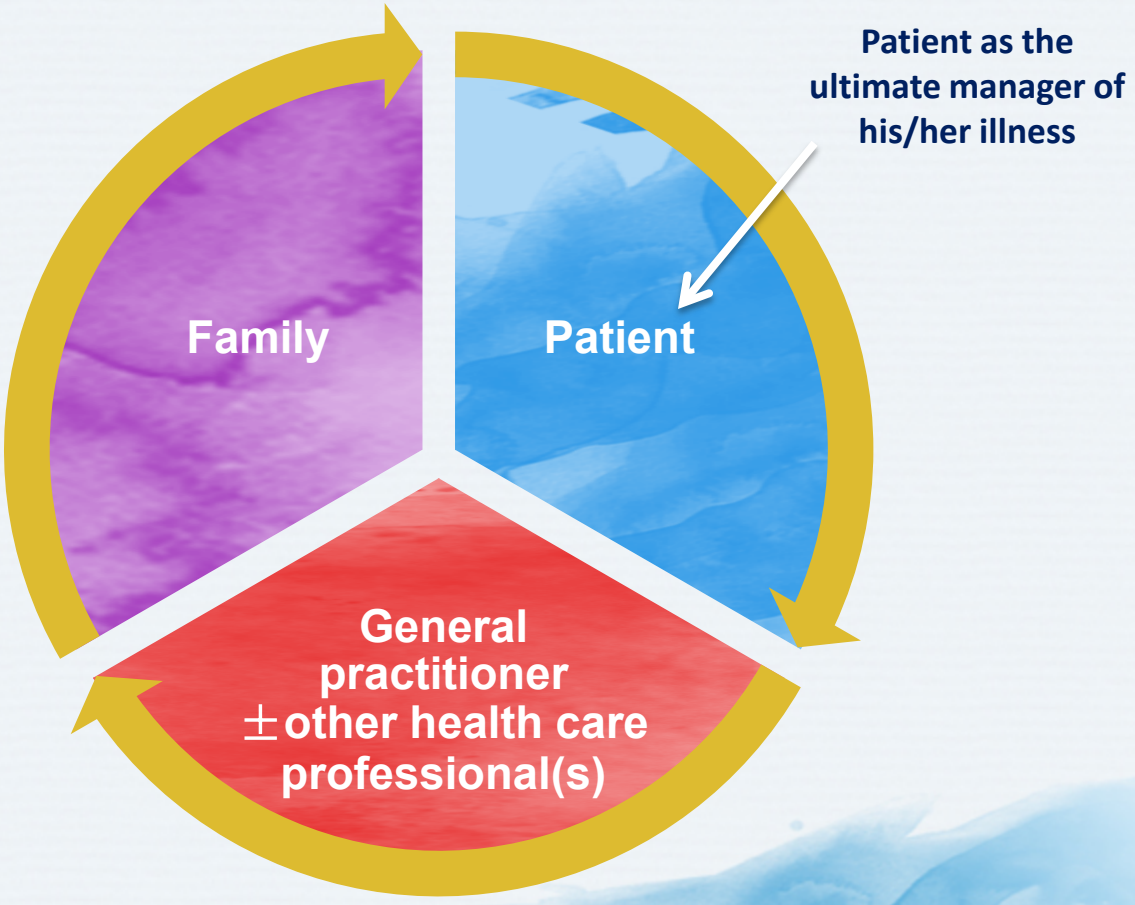
IASP Recommendations for Wait Times	
Wait time	**Condition**
Treat immediately	• Acute painful conditions
1 week (most urgent)	• Painful severe condition with risk of deterioration or chronicity • Pain in children • Pain related to cancer or terminal or end-stage illness
1 month (urgent or semi-urgent)	• Severe undiagnosed or progressive pain with risk of increasing functional impairment, generally of 6 months' duration or less
8 weeks (routine or regular)	• Persistent long-term pain without significant progression

IASP = International Association for the Study of Pain

International Association for the Study of Pain Task Force on Wait-Times. *Summary and Recommendations*. Available at: http://www.iasppain.org/AM/Template.cfm?Section=Wait_Times&Template=/CM/ContentDisplay.cfm&ContentID=13107. Accessed: August 28, 2013.

Deciding on the Best Course of Treatment for the Patient

Collaborative Care



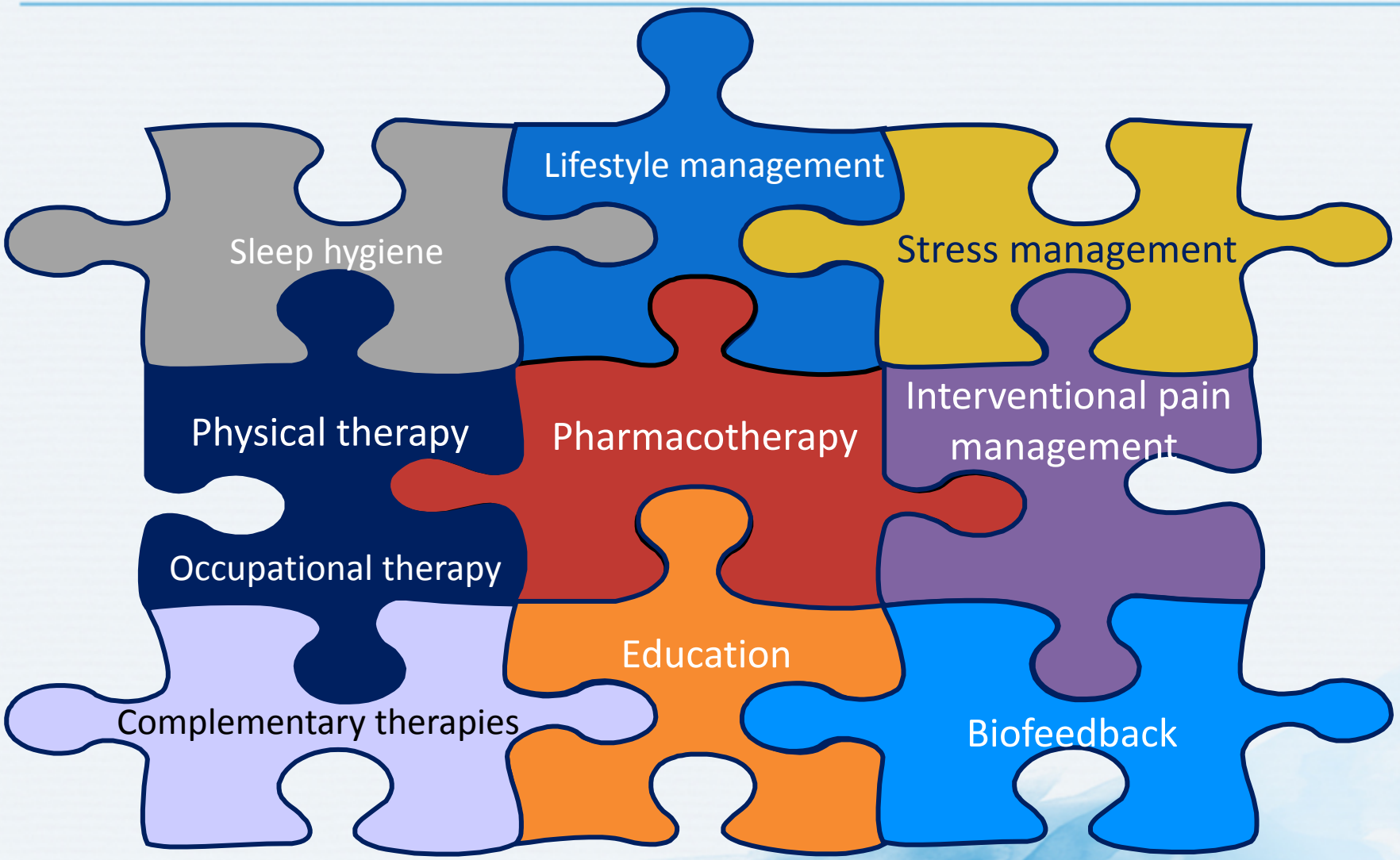
Ayad AE *et al. J Int Med Res* 2011; 39(4):1123-41; Saltman D *et al. Med J Aust* 2001; 175(Suppl):S92-6.

Treatments for Pain

- Medications
- Regional anesthetic interventions
- Surgery
- Psychological therapies
- Rehabilitative/physical therapies
- Complementary and alternative medicine

Institute of Medicine. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. The National Academies Press; Washington, DC: 2011.

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

Non-pharmacological Interventions

- Non-pharmacological interventions are commonly used in clinical practice
- Establishing reliable evidence of efficacy and effectiveness can be challenging in terms of design and interpretation of studies

Type of therapy	Examples
Psychological	• Hypnosis • Relaxation • Cognitive behavioral therapy
Physical	• Acupuncture • Transcutaneous electrical nerve stimulation • Healing touch and massage • Occupational therapy
Clinical process	• Pain assessment • Physician advice and communication • Education

Bennett MI, Closs SJ. *Pain Clinical Updates* 2010; 18(2):1-6.

Psychological Therapies

- Individual and group counseling
- Biofeedback
- Relaxation techniques
- Self-hypnosis
- Visual imaging
- Learning or conditioning techniques
- Behavioral techniques
- Cognitive techniques
- Psychotherapy

American Academy of Pain Management. *Essential Tools for Treating the Patient in Pain*. Available at: http://www.painmed.org/annualmeeting/2012-essential-tools-course-information/. Accessed: June 12, 2012;
Kerns RD *et al. Annu Rev Clin Psychol* 2011; 7:411-34.

Rehabilitative/Physical Therapies

- Heat
- Deep heat (ultrasound)
- Cryotherapy
- Aquatic therapy
- Transcutaneous electrical nerve stimulation
- Iontophoresis and phonophoresis
- Traction
- Exercise
- Manual therapy
- McKenzie method
- Core stabilization

American Academy of Pain Management. *Essential Tools for Treating the Patient in Pain*. Available at: http://www.painmed.org/annualmeeting/2012-essential-tools-course-information/. Accessed: June 12, 2012.

What is complementary and alternative medicine?

A group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine.

– NCCAM definition

NCCAM = National Center for Complementary and Alternative Medicine

National Institutes of Health. *Complementary, Alternative, or Integrative Health: What`s in a name?* Available at: http://nccam.nih.gov/health/whatiscam/#definingcam. Accessed: July 12, 2013.

Evidence of Potential Benefits of Complementary and Alternative Medicine

	Arthritis	Headache	Low back pain	Neck pain
Acupuncture	√	√	√	X
Balneotherapy (mineral baths)	X			
Feverfew		X		
Gamma linoleic acid	X			
Glucosamine/chondroitin	X			
Herbal remedies	X		X	
Massage			√	
Spinal manipulation		√	√	X
Progressive relaxation			√	
Prolotherapy			X	
Tai chi	X			
Yoga			√	

√ = promising evidence of potential benefit; X = limited, mixed or no evidence to support use

National institutes of Health. *Chronic Pain and CAM: At a Glance. A*vailable at: http://nccam.nih.gov/health/pain/chronic.htm. Accessed: July 29, 2013.

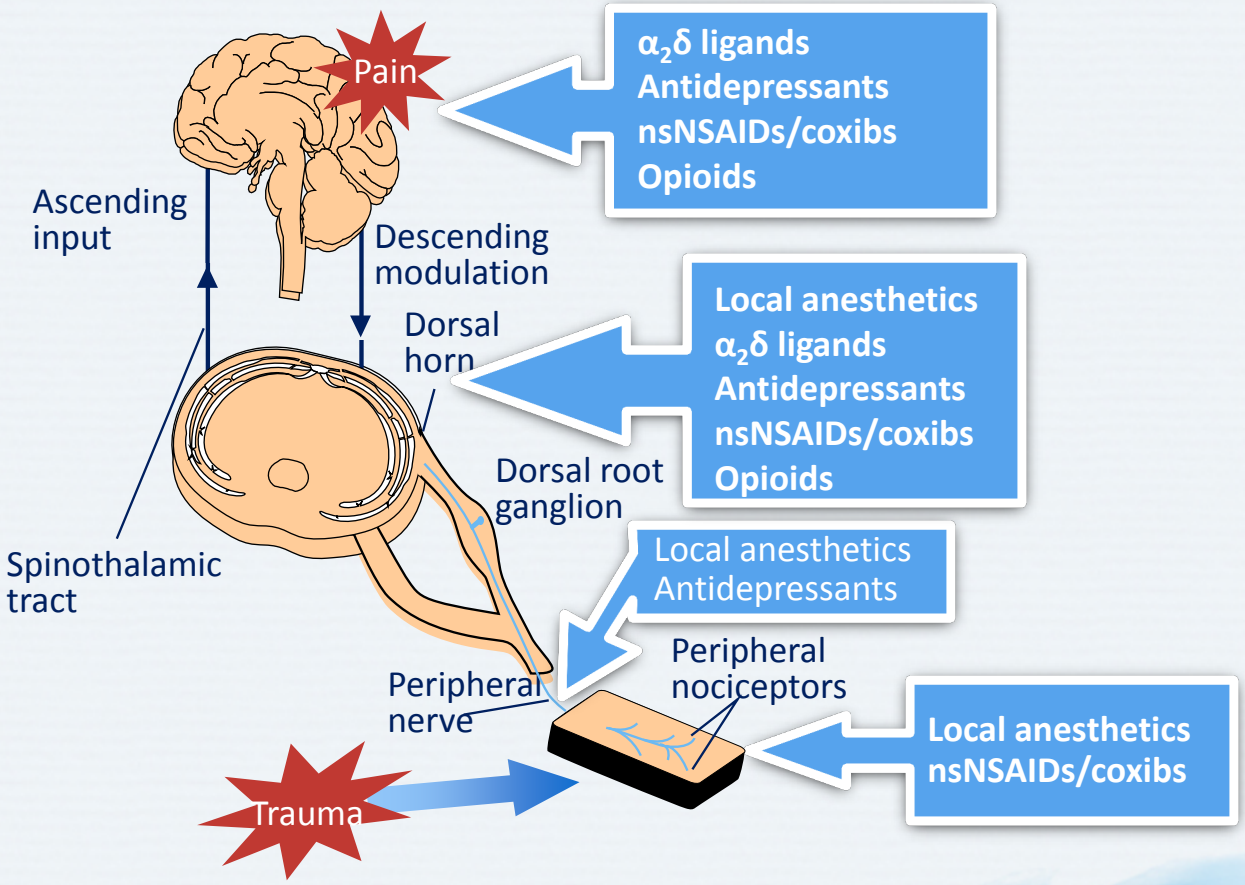
Treating Pain: Use a Mind-Body Approach

- Biopsychosocial approach to assessing and treating chronic pain offers a uniquely valuable clinical perspective
- Mind-body perspective now generally accepted by pain researchers
- Found to be useful by clinicians in various disciplines, such as osteopathic medicine, rheumatology, and physiotherapy

Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* The National Academies Press; Washington, DC: 2011.

Pharmacological Treatment

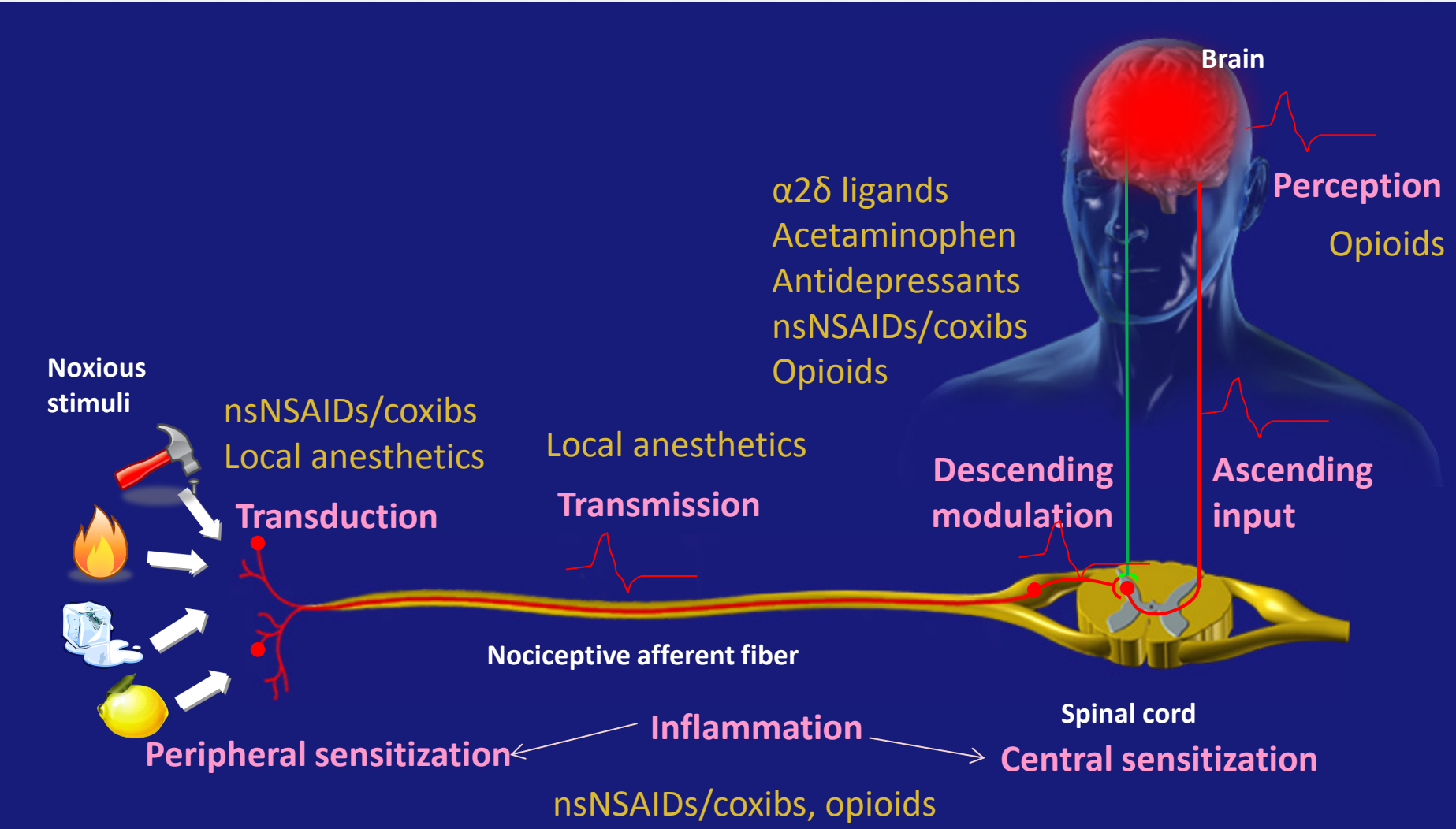
Analgesics Affect Different Parts of the Pain Pathway



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

Adapted from: Gottschalk A *et al. Am Fam Physician* 2001; 63(10):1979-84; Verdu B *et al. Drugs* 2008; 68(18):2611-32.

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

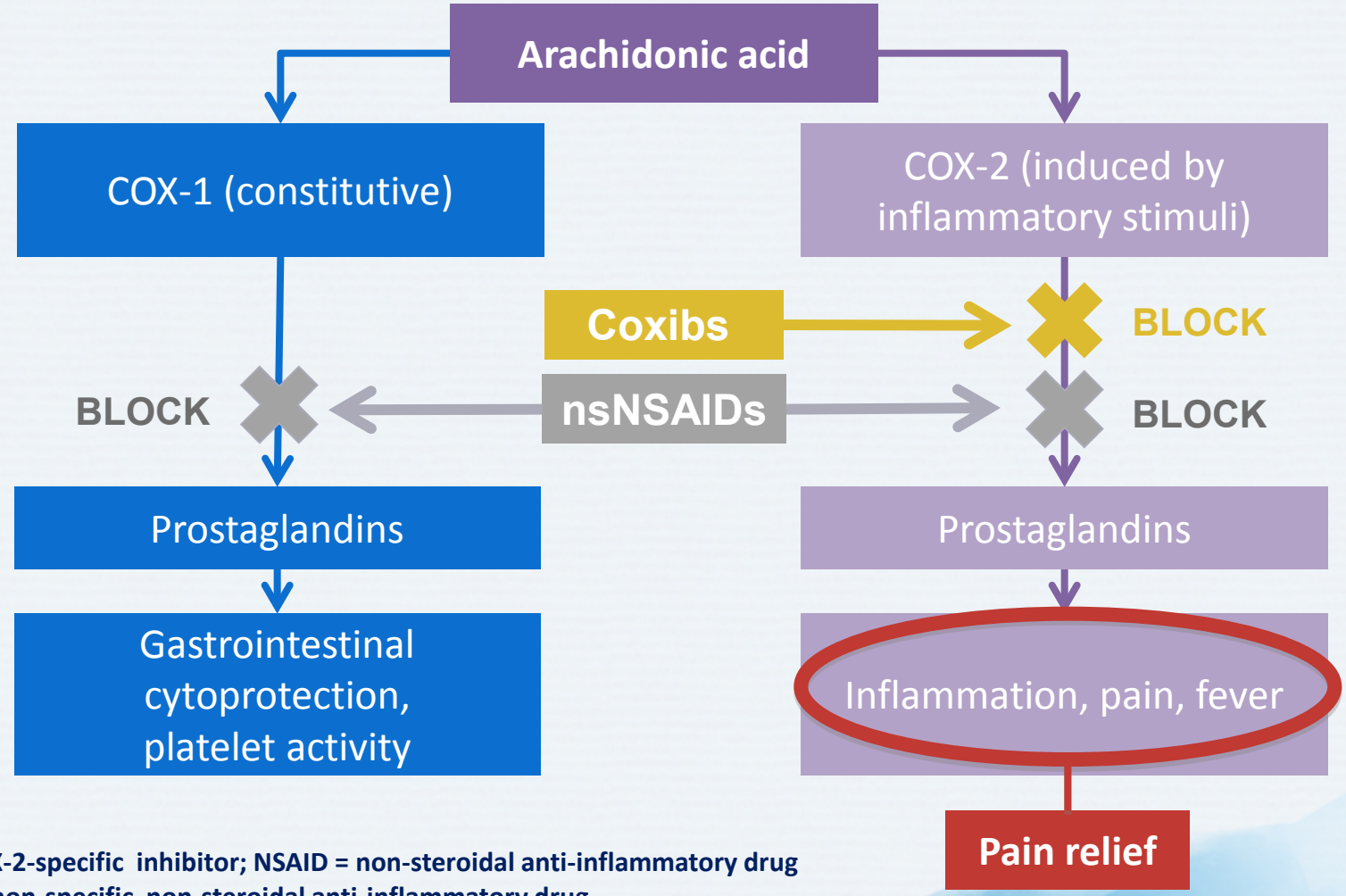
- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

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

ASA = acetylsalicylic acid; 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-2[2]
  - 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

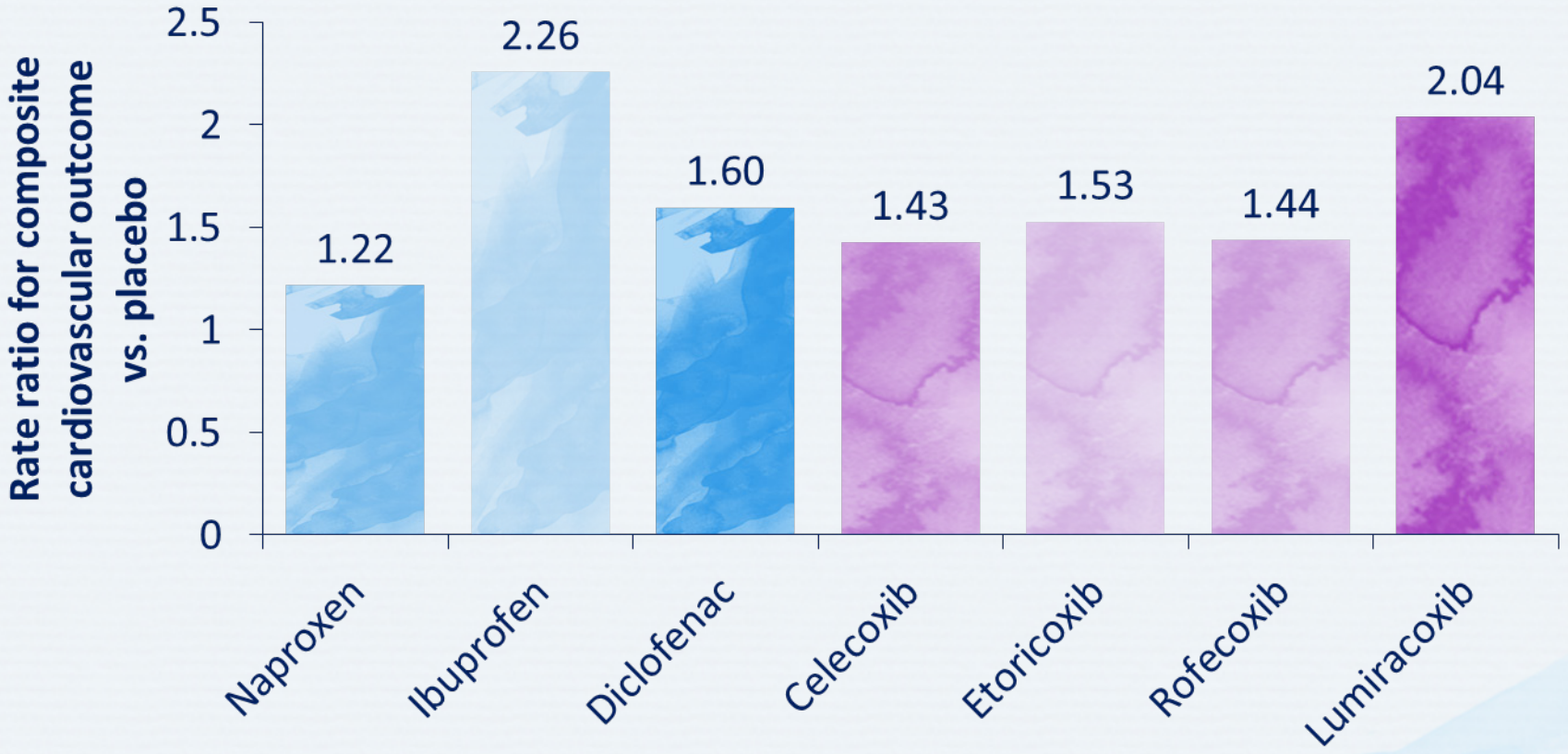
Cox-1-mediated NSAIDs (nsNSAIDs):

- 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.

nsNSAIDs/Coxibs and Cardiovascular Risk

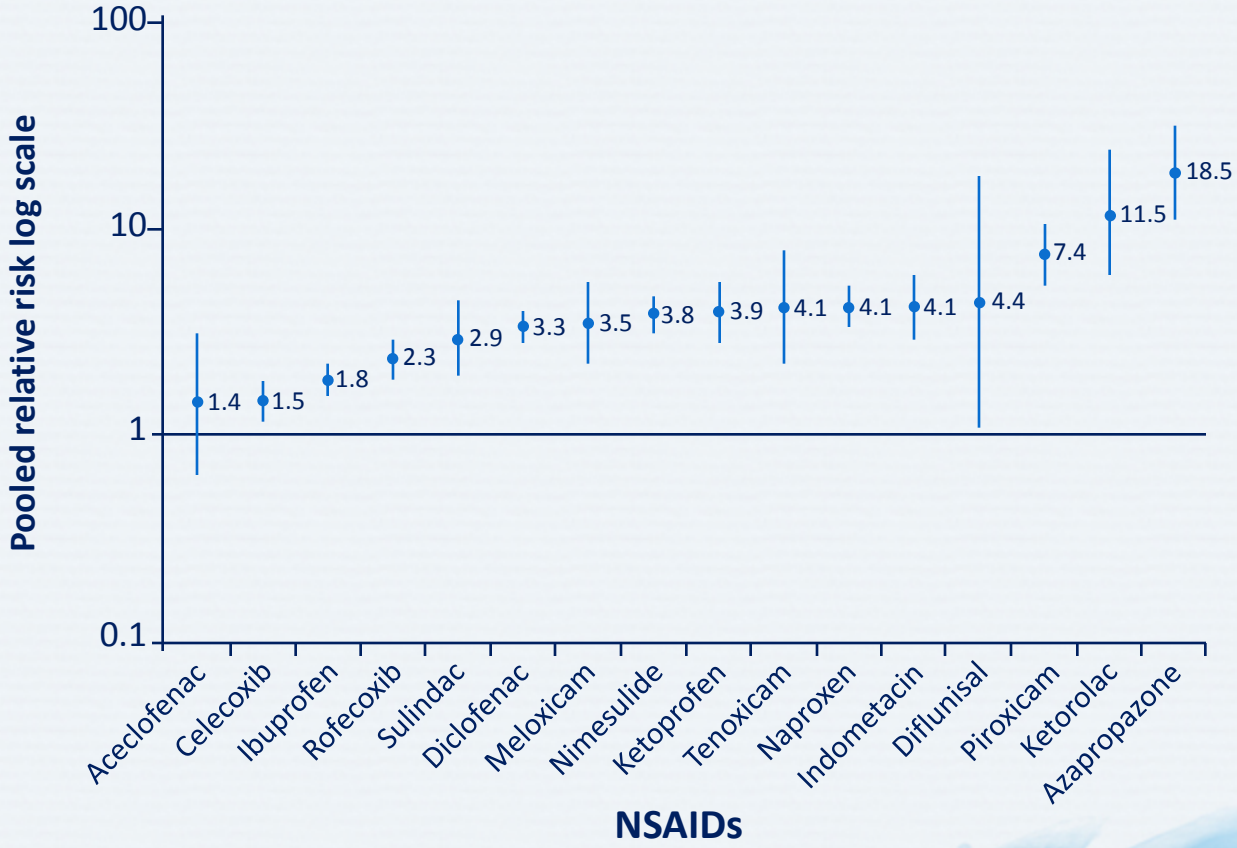


Composite includes non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death compared with placebo; chart based on network meta-analysis involving 30 trials and over 100,000 patients.
Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Trelle S *et al. BMJ* 2011; 342:c7086.

Gastrointestinal Risk with nsNSAIDs/Coxibs

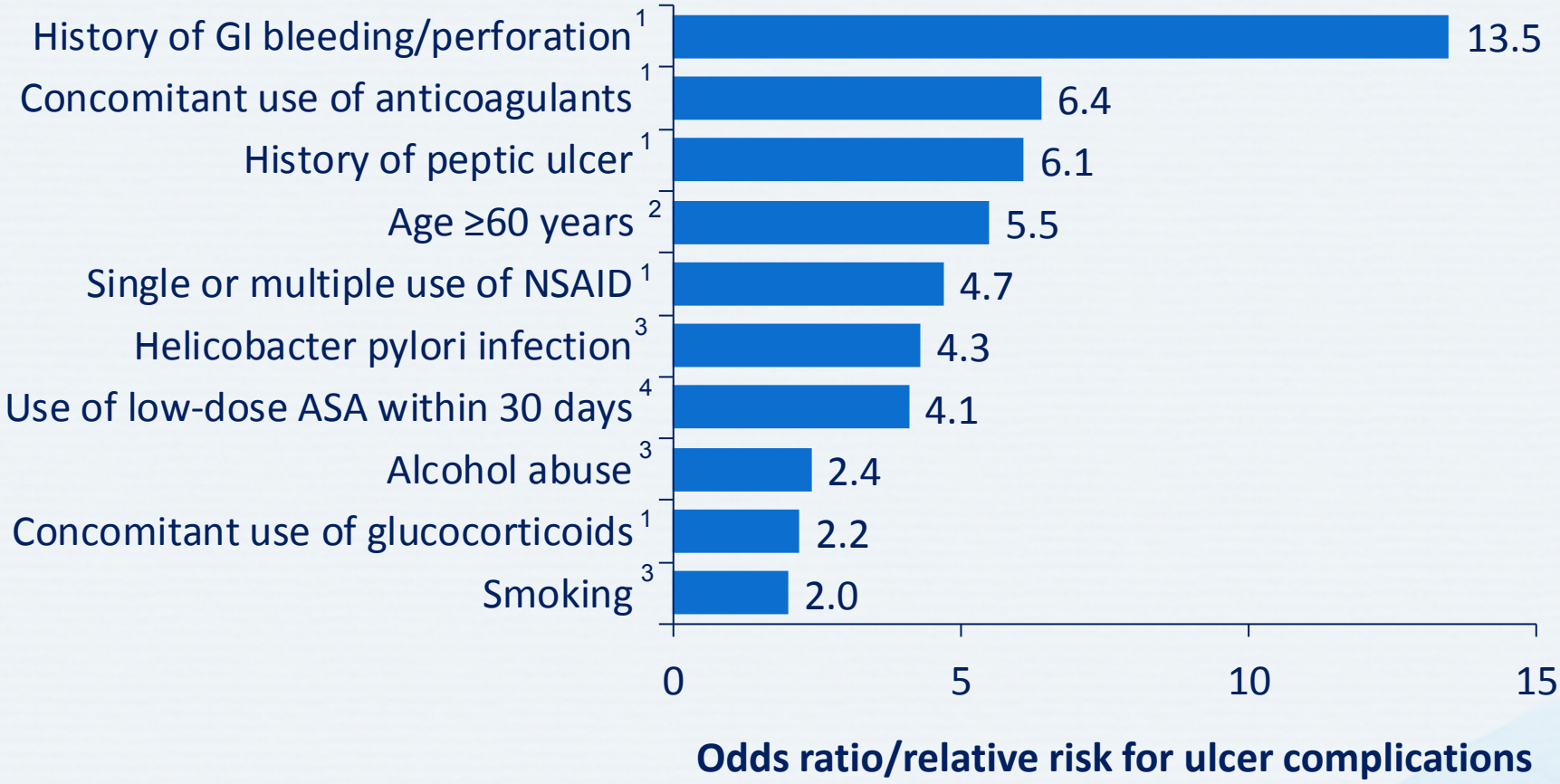
Pooled Relative Risks and 95% CIs of Upper Gastrointestinal Complications



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.

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

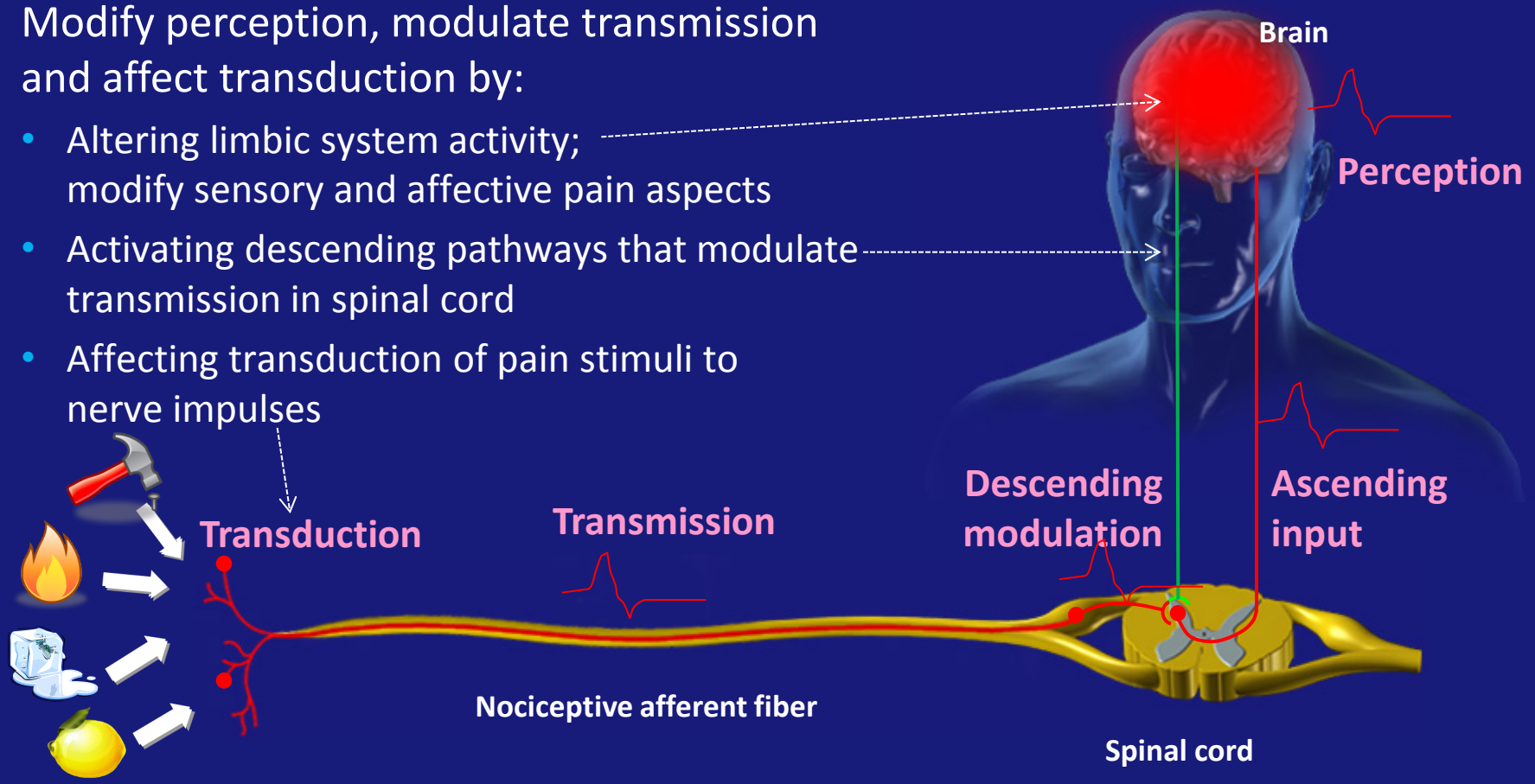
ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor;
nsNSAID = non-selective non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor

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

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



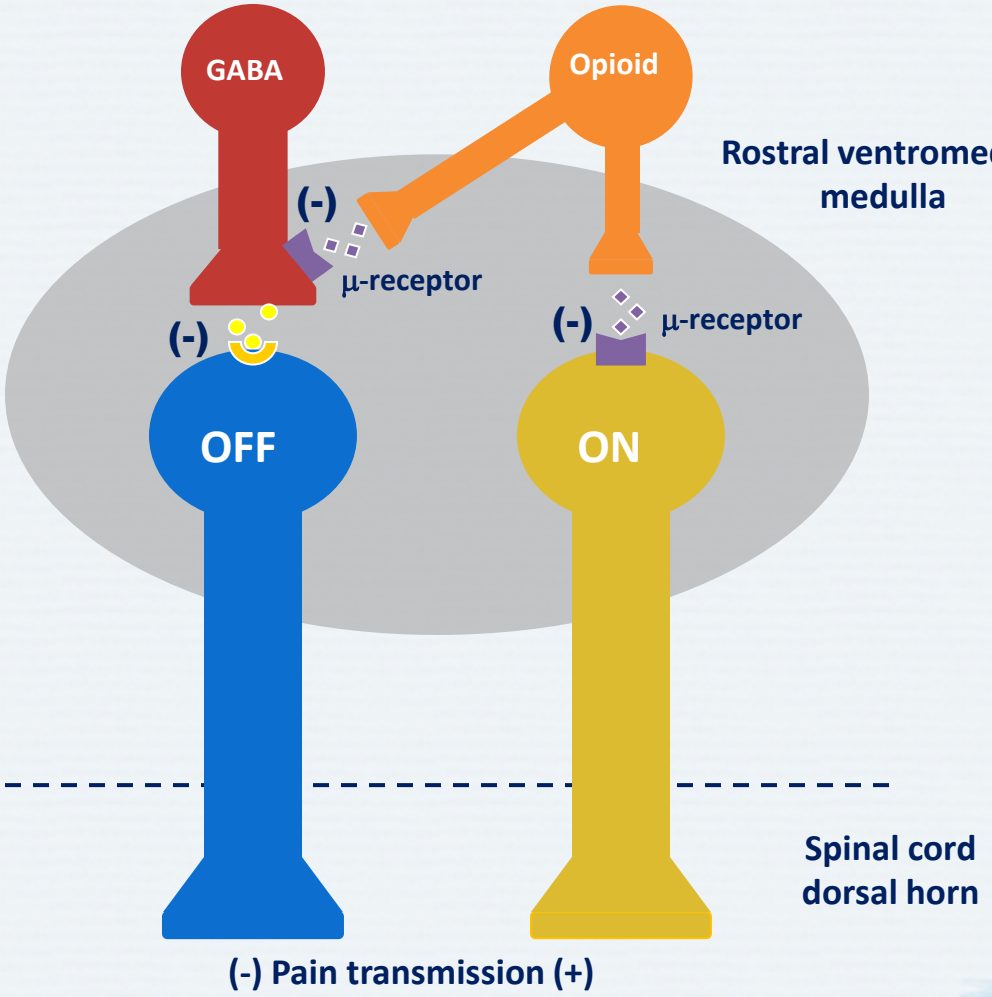
Reisine T, Pasternak G. In: Hardman JG *et al* (eds). *Goodman and Gilman's: The Pharmacological Basics of Therapeutics.* 9th ed. McGraw-Hill; New York, NY: 1996; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7; Trescot AM *et al. Pain Physician* 2008; 11(2 Suppl):S133-53.

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.

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.

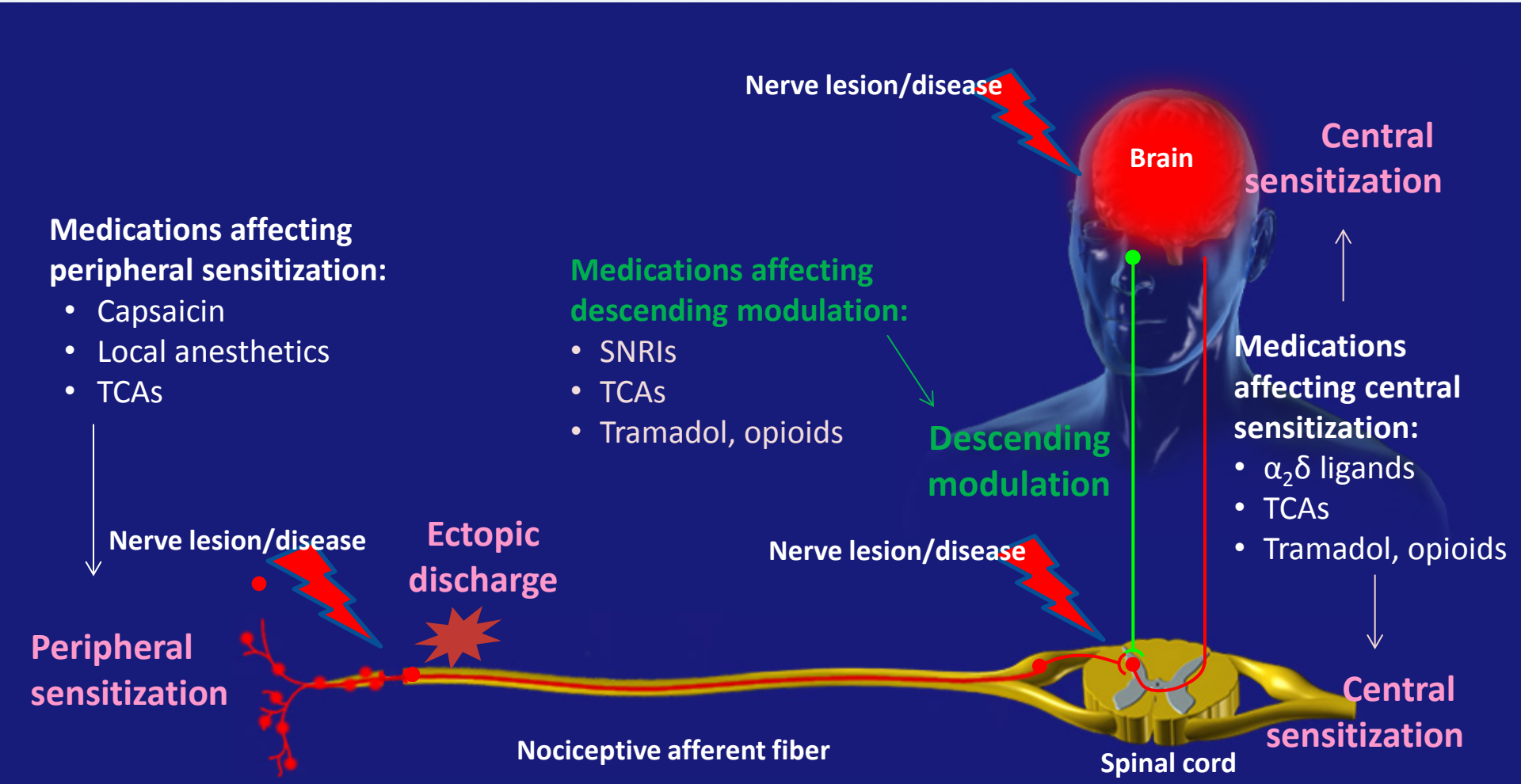
Adverse Effects of Opioids

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.

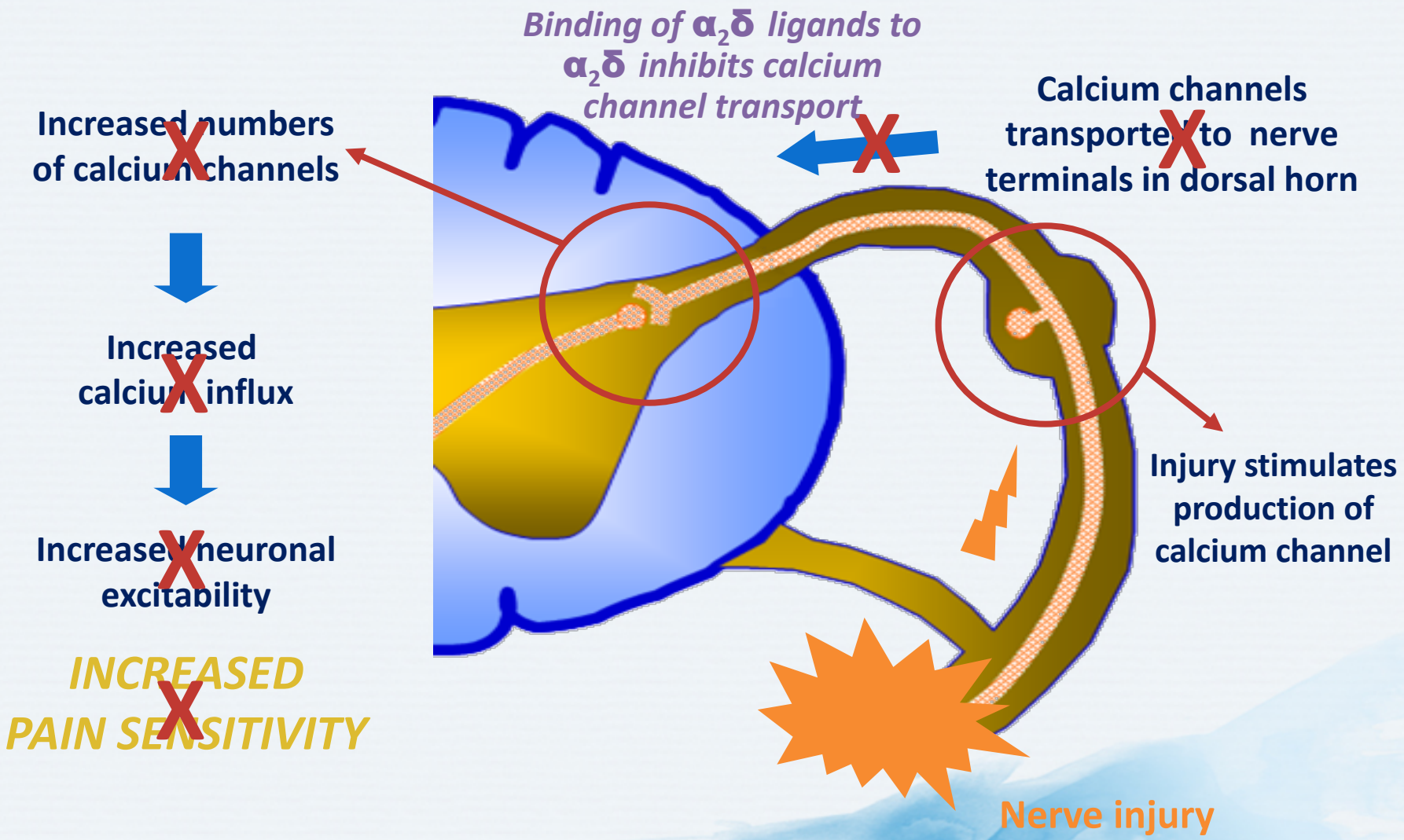
Mechanism-Based Pharmacological Treatment of Neuropathic Pain



SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Adapted from: Attal N *et al. Eur J Neurol* 2010; 17(9):1113-e88; Beydoun A, Backonja MM. *J Pain Symptom Manage* 2003; 25(5 Suppl):S18-30; Jarvis MF, Boyce-Rustay JM. *Curr Pharm Des* 2009; 15(15):1711-6; Gilron I *et al. CMAJ* 2006; 175(3):265-75; Moisset X, Bouhassira D. NeuroImage 2007; 37(Suppl 1):S80-8; Morlion B. Curr Med Res Opin 2011; 27(1):11-33; Scholz J, Woolf CJ. Nat Neurosci 2002; 5(Suppl):1062-7.

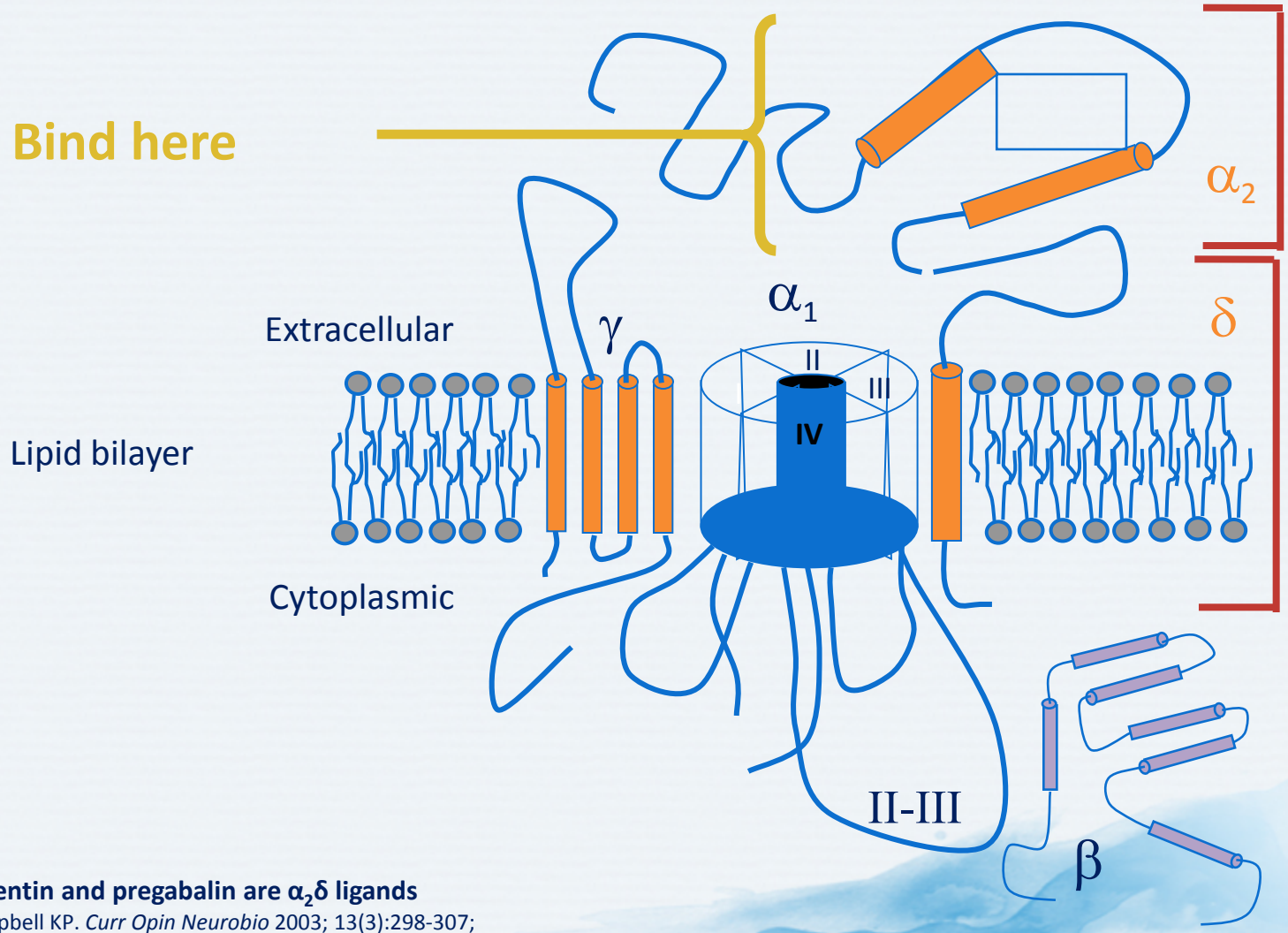
Role of $\alpha_2\delta$-Linked Calcium Channels in Neuropathic Pain



Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands

Bauer CS *et al. J Neurosci* 2009; 29(13):4076-88.

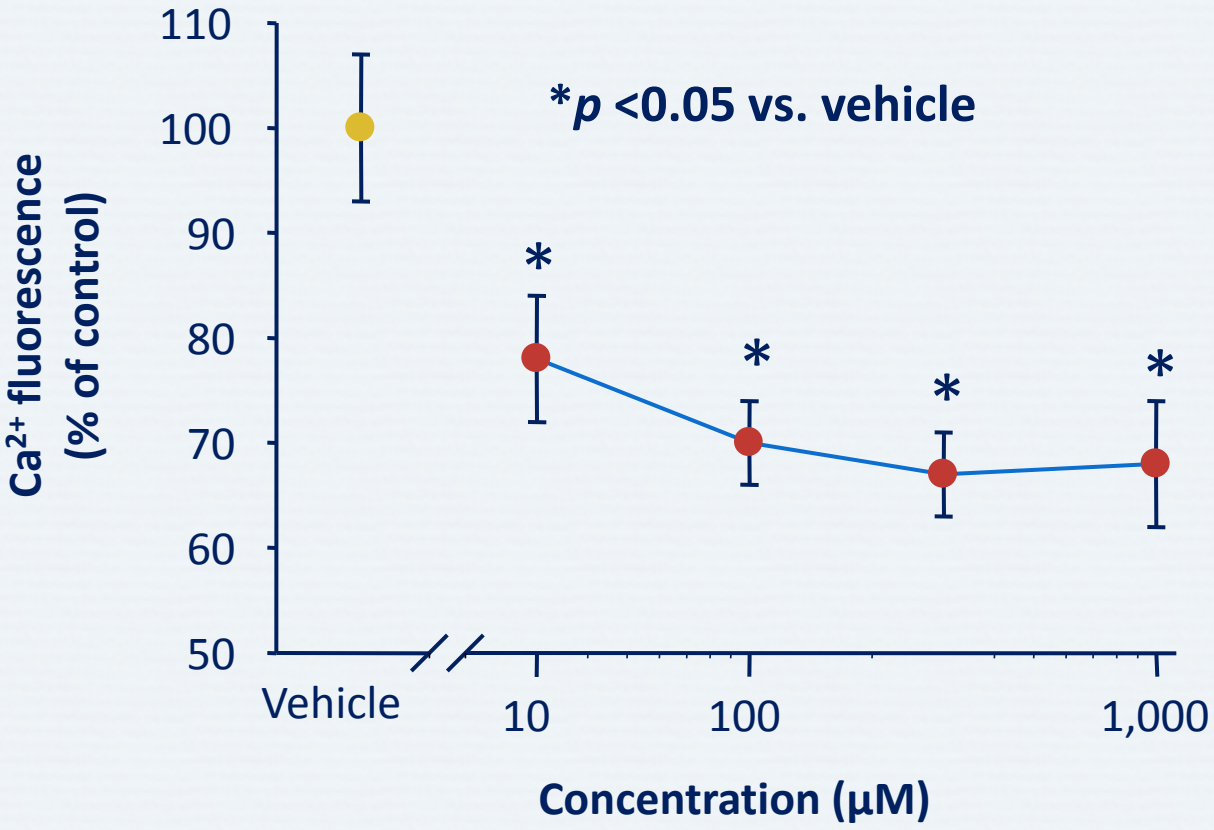
$\alpha_2\delta$ Ligands Bind to $\alpha_2\delta$ Subunit of Voltage-Gated Calcium Channels



Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands

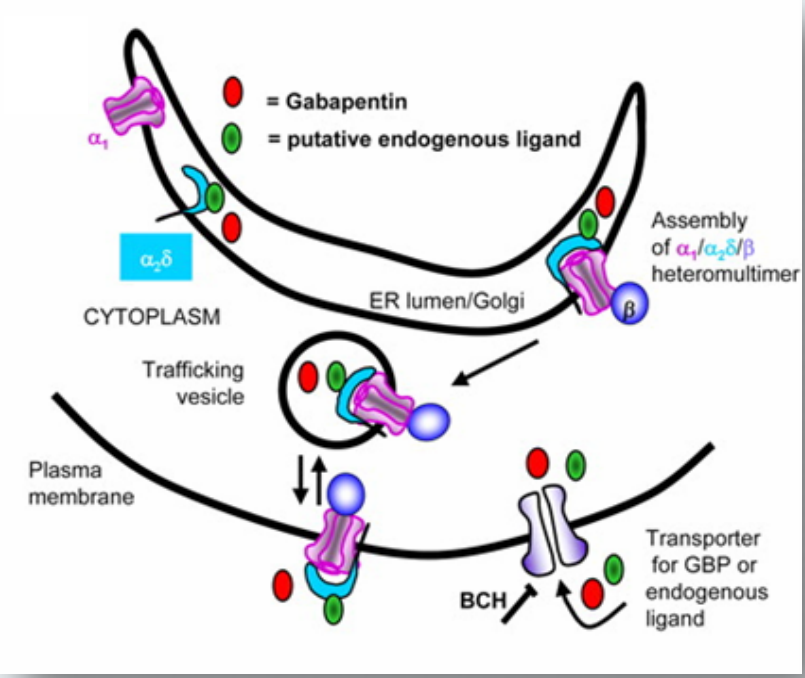
Arikkath J, Campbell KP. *Curr Opin Neurobio* 2003; 13(3):298-307;
Catterall WA. *J Bioenerg Biomembr* 1996; 28(3):219-30; Gee NS *et al. Biol Chem* 1996; 271(10):5768-76..

$\alpha_2\delta$ Ligands Reduce Calcium Influx in Depolarized Human Neocortex Synaptosomes

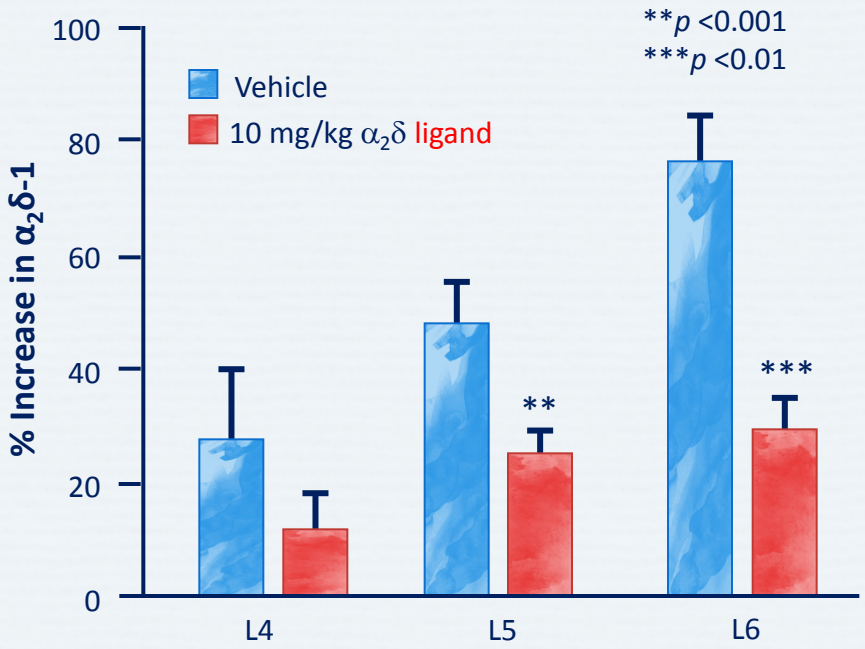


Fink K *et al. Neuropharmacology* 2002; 42(2):229-36.

$\alpha_2\delta$ Ligands Modulate Calcium Channel Trafficking



Hendrich et al. 2008



Bauer et al. 2009

- $\alpha_2\delta$ ligands reduce trafficking of voltage-gated calcium channel complexes to cell surface *in vitro*
- $\alpha_2\delta$ ligands prevent nerve-injury induced up-regulation of $\alpha_2\delta$ in the dorsal horn

BCH = 2-(−)-endoamino-bicycloheptene-2-carboxylic acid; ER = endoplasmic reticulum; GBP = gabapentin

Bauer CS *et al. Neurosci* 2009; 29(13):4076-88; Hendrich J *et al. Proc Natl Acad Sci U S A* 2008; 105(9):3628-33.

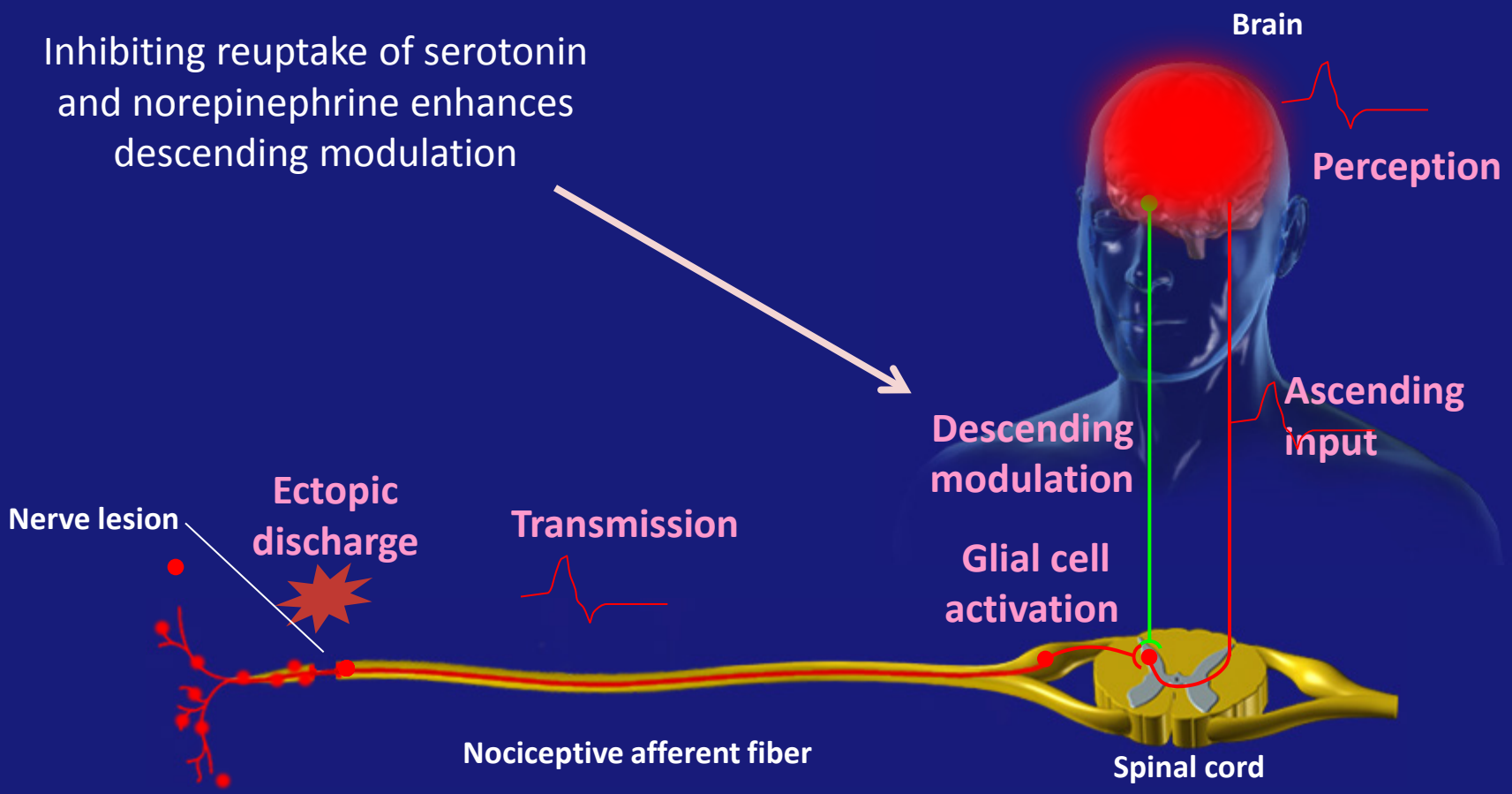
Adverse Effects of $\alpha_2\delta$ Ligands

System	Adverse effects
Digestive system	Dry mouth
CNS	Dizziness, somnolence
Other	Asthenia, headache, peripheral edema, weight gain

$\alpha_2\delta$ ligands include gabapentin and pregabalin
CNS = central nervous system

Attal N, Finnerup NB. *Pain Clinical Updates* 2010; 18(9):1-8.

How Antidepressants Modulate Pain



Verdu B *et al. Drugs* 2008; 68(18):2611-2632.

Suggested Mechanisms of Analgesic Action of Antidepressants

Mechanism of Action	Site of Action	TCA	SNRI
Reuptake inhibition	Serotonin Noradrenaline	+ +	+ +
Receptor antagonism	α-adrenergic NMDA	+ +	- (+) milncipran
Blocking or activation of ion channels	Sodium channel blocker Calcium channel blocker Potassium channel activator	+ + +	(+) venlafaxine/ - duloxetine ? ?
Increasing receptor function	$GABA_B$ receptor	+ amitripline/ desipramine	?
Opioid receptor binding/ opioid-mediated effect	Mu- and delta-opioid receptor	(+)	(+) venlafaxine
Decreasing inflammation	Decrease of PGE2 production decrease of TNFα production		

GABA = γ-aminobutyric acid; NDMA = N-methyl-D-aspartate; PGE = prostaglandin E;
SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant; TNF = tumor necrosis factor

Verdu B *et al. Drugs* 2008; 68(18):2611-32.

Adverse Effects of Antidepressants

System	TCAs	SNRIs
Digestive system	Constipation, dry mouth, urinary retention	Constipation, diarrhea, dry mouth, nausea, reduced appetite
CNS	Cognitive disorders, dizziness, drowsiness, sedation	Dizziness, somnolence
Cardiovascular	Orthostatic hypotension, palpitations	Hypertension
Other	Blurred vision, falls, gait disturbance, sweating	Elevated liver enzymes, elevated plasma glucose, sweating

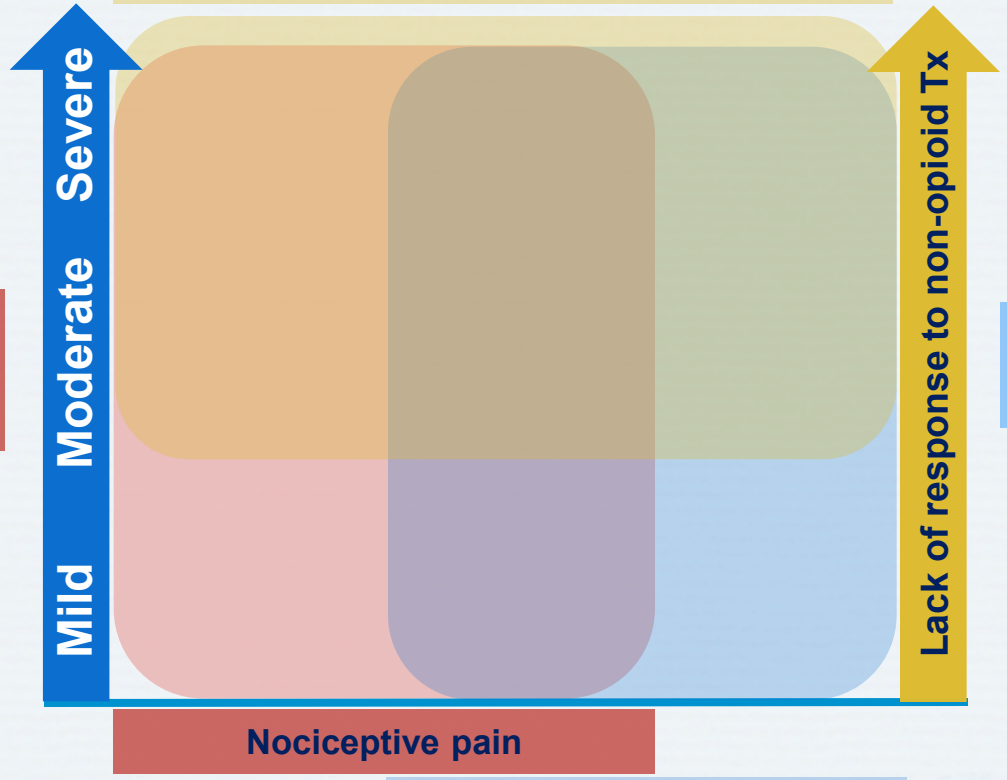
CNS = central nervous system; TCA = tricyclic antidepressant; SNRI = serotonin-norepinephrine reuptake inhibitor

Attal N, Finnerup NB. Pain Clinical Updates 2010; 18(9):1-8.

Assessment of Pain Pathophysiology Can Help Guide Appropriate Medication Therapy

Opioids
For management of **moderate** to **severe** pain in appropriate patients

Most opioid treatment guidelines for chronic pain recommend use for patients after inadequate response to non-opioid therapy*



Acetaminophen
nsNSAIDs/coxibs

$\alpha_2\delta$ ligands
Antidepressants

***Selected on the basis of the pathophysiology of patient's pain, provided there are no contraindications for its use**
Coxib = COX-2-specific inhibitor;
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Chou R *et al. J Pain* 2009; 10(2):113-30;
Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

But… Patients with Chronic Pain of Just One Type of Pain Pathophysiology May be Rare

- Patients may have different pathophysiologic mechanisms contributing to their pain
  - e.g., complex regional pain syndrome has multiple potential mechanisms, including nerve injury and inflammation – “mixed pain state”

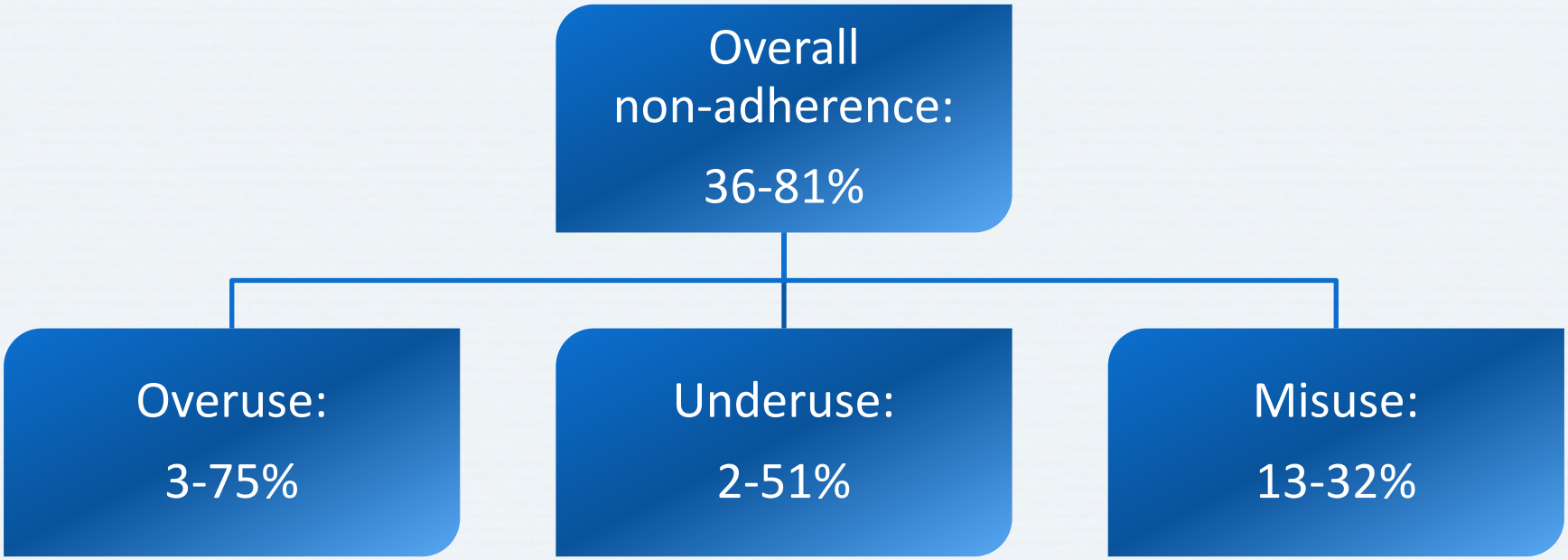
- Therapies that will work better for a particular patient are likely to depend on the mechanisms contributing to the patient’s pain

- Patients with mixed pain may benefit from combination therapy

Dowd GS *et al. J Bone Joint Surg Br* 2007; 89(3):285-90; Vellucci R. *Clin Drug Investig* 2012; 32(Suppl 1):3-10.

Adherence

Non-adherence to chronic pain medication is common…



But rates vary substantially from study to study

Broekmans S *et al. Eur J Pain* 2009; 13(2):115-23.

Demographic and Medication-Related Factors Can Help Predict Non-adherence

- Younger age
- Health insurance compensation
- Cigarette smoking
- Self-medication
- Greater number of prescribed analgesics
- Greater number of pills to be taken

Broekmans S *et al. Clin J Pain* 2010; 26(2):81-6

Non-adherence Is Also Related to Patient Concerns

Type of non-adherence	Patient concern				
	Level of pain	Perceived need	Mistrust in doctor	Side effects	Concern over withdrawal
Non-adherence	NS	NS	p <0.01	p <0.01	p <0.001
Overuse	NS	p <0.001	NS	p <0.05	NS
Underuse	p <0.05	NS	p <0.01	NS	p <0.01

NS = non-significant

Rosser BA *et al. Pain* 2011; 152(5):1201-5.

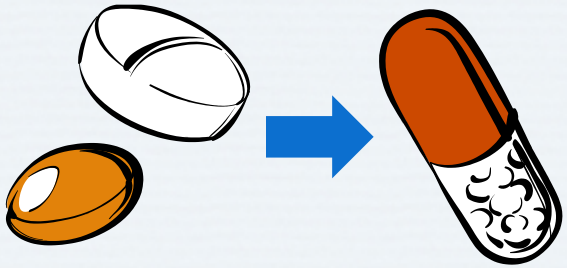
Strategies to Improve Adherence

- **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: Summary

- It can be challenging to choose the best treatment for chronic and acute pain
- An approach combining physical and psychosocial interventions is recommended
- Choice of pharmacotherapy may be guided in part by the type(s) of pain
- Adherence to therapy is necessary for optimal patient outcomes