Community Care
OF NORTH CAROLINA

Non-Opioid Pharmacologic Management of Pain

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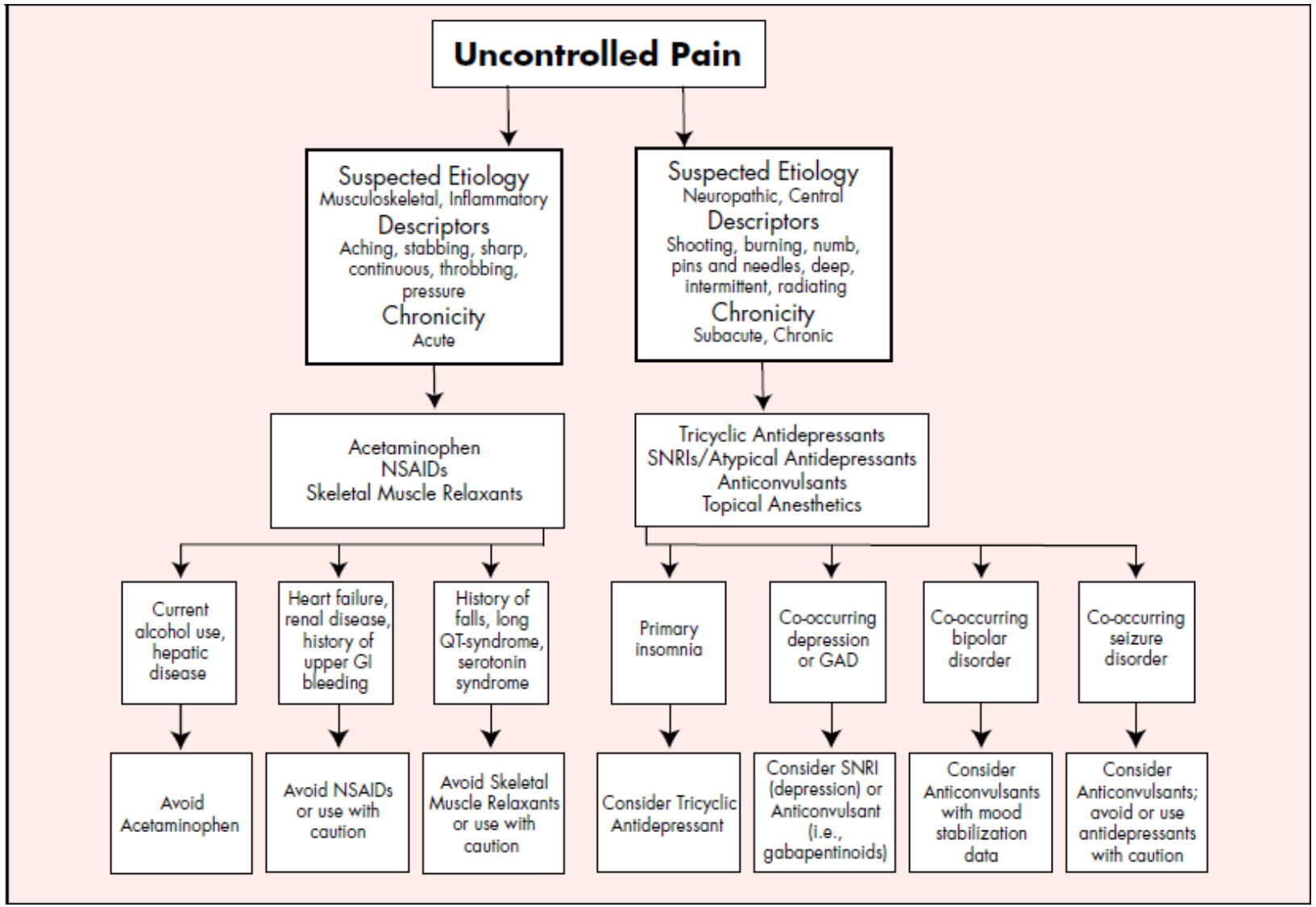
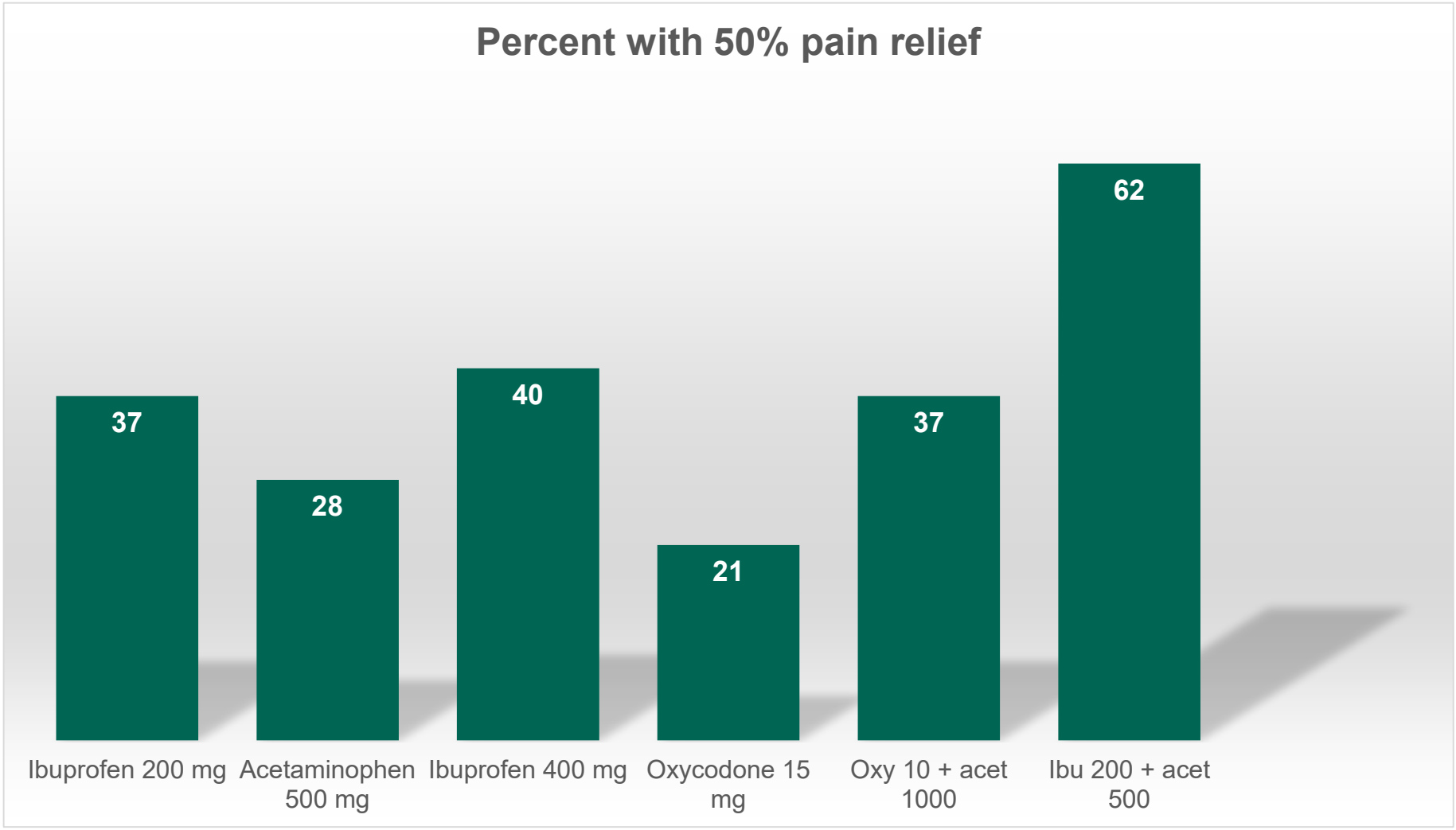
Learning Objectives:

- Identify the role of nonopioid medications for managing pain
- Describe common adverse effects associated with available nonopioid medications
- Discuss counseling strategies that support the efficacy of nonopioid analgesics

Algorithm for Selecting Nonopioid Analgesics



Acetaminophen and Ibuprofen for Acute Pain



NSAIDs

- Significant side effects include acute renal failure in hypovolemia or CKD, increased bleeding times, risk of upper and lower GI bleed, and CV toxicity
- Topical NSAIDs may provide symptomatic relief without significant systemic exposure

Table 3. Comparative Cyclooxygenase Activity[a] of Commercially Available Nonsteroidal Anti-inflammatory Drugs

5- to 50-fold COX-2 Preferential	Etodolac Meloxicam Celecoxib
<5-fold COX-2 Preferential	Diclofenac Sulindac Meclofenamate Piroxicam Diflunisal
COX-1 Preferential	Fenoprofen Ibuprofen Tolmetin Naproxen Aspirin Indomethacin Ketoprofen Flurbiprofen Ketorolac

[a]Based on log IC_{80} ratios of COX-1/COX-2.

COX = cyclooxygenase; IC = inhibitory concentration.

Table 4. Balancing the Risk of Cardiovascular and Gastrointestinal Toxicity of Nonsteroidal Anti-inflammatory Drugs

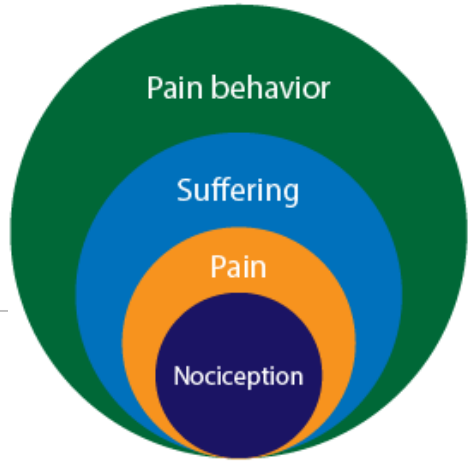
RISK CATEGORY	LOW GI RISK	MODERATE GI RISK	HIGH GI RISK
	0 risk factors	1–2 risk factors	Multiple risk factors, history of previous ulcer events, or continued use of corticosteroids or anticoagulants
Low CV risk	NSAID alone	NSAID + PPI/misoprostol	Alternative therapy or COX-2 + PPI/misoprostol
High CV risk (low-dose aspirin required)	Naproxen + PPI/ misoprostol	Naproxen + PPI/misoprostol	Alternative therapy recommended

COX = cyclooxygenase; CV = cardiovascular; GI = gastrointestinal; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton pump inhibitor

Skeletal Muscle Relaxants

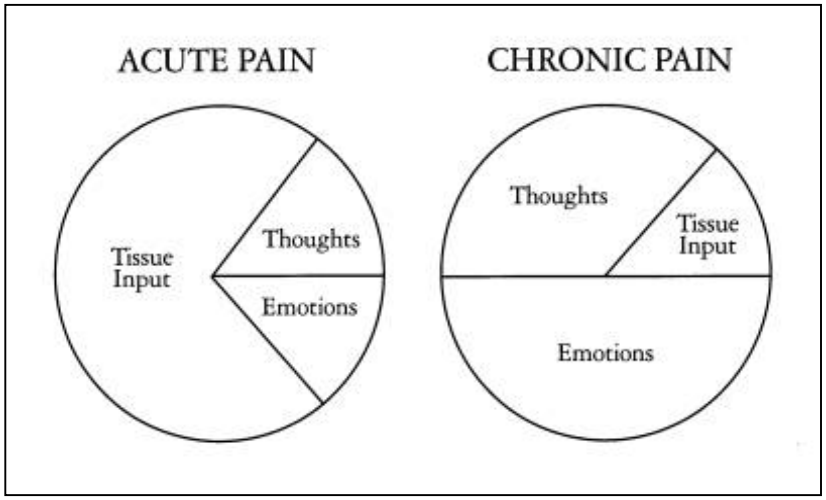
- All equally effective for short-term relief of low back pain
- Not more effective than NSAIDs for acute low back pain
- Not recommended for chronic pain
- All are sedating, while metaxalone is considered least sedating
- Tizanidine is structurally similar to clonidine (alpha agonist), which can result in reduced blood pressure and the risk of rebound hypertension upon abrupt discontinuation
- Carisoprodol is metabolized to meprobamate, a barbiturate, increasing its abuse potential
- Most possess serotonergic activity, consider prior to using concurrently with other serotonin active drugs

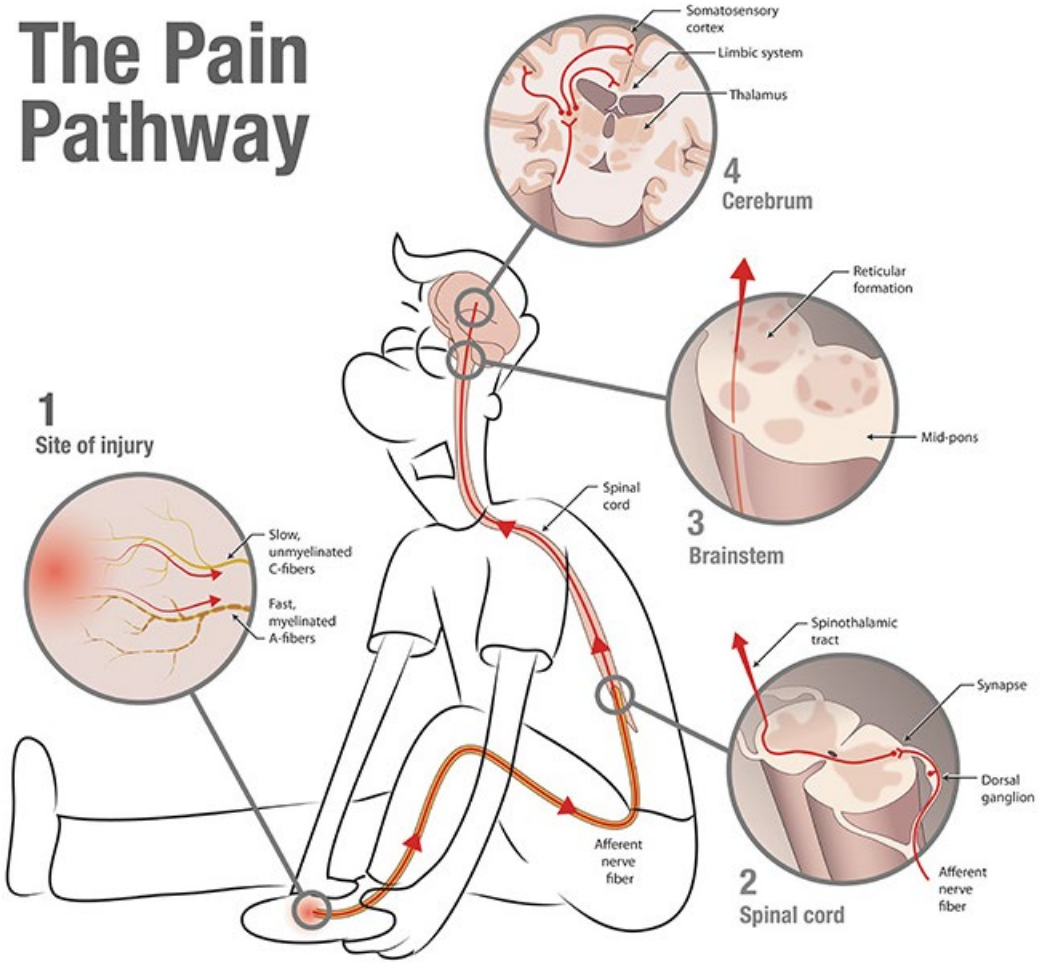
Pain is Complicated



Four Types of Pain

1. Nociceptive
2. Neuropathic
3. Central Sensitization
4. Opioid Withdrawal





Antidepressants

TCAs

- Secondary amines have less anticholinergic side effects, ie – sedation
- Use lowest dose possible for pain management and sleep
- Postural hypotension and QT prolongation are possible. Screen for known heart disease, syncope, palpitations, dyspnea or chest pain. Avoid in those with CV disease or established conduction abnormalities

SNRIs

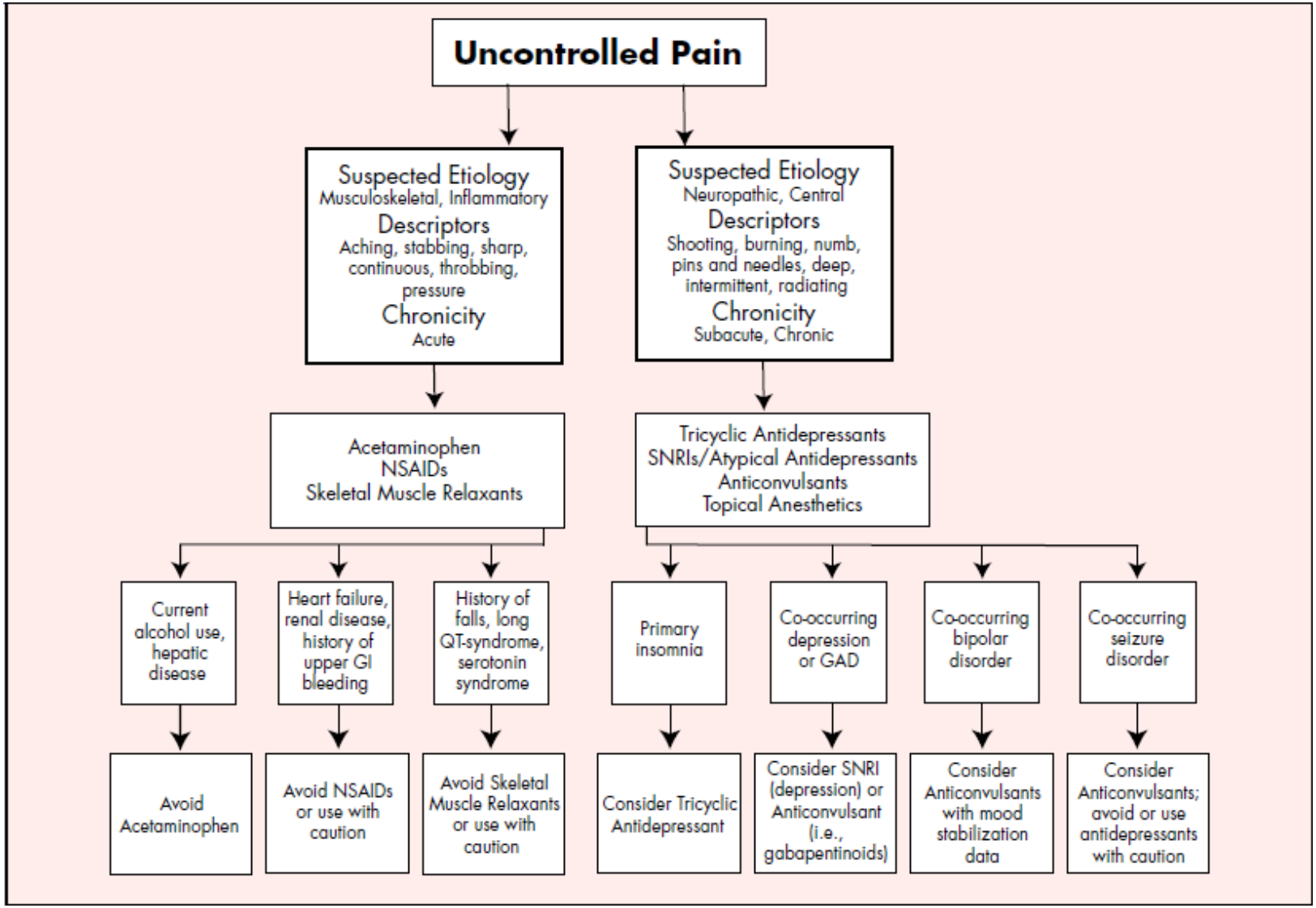
- Exhibit efficacy in neuropathic pain, fibromyalgia, and chronic musculoskeletal pain
- Dose-dependent increases in blood pressure should be expected
- GI side effects (nausea, diarrhea) are common when initiated and may subside with time

Tricyclic Antidepressants	SNRIs	Atypical Antidepressants	SSRIs
3° amines Doxepin Imipramine Amitriptyline Clomipramine Trimipramine 2° amines Protriptyline Nortriptyline Desipramine H1-Ki	Venlafaxine Desvenlafaxine Duloxetine Milnacipran	Bupropion Trazodone	Paroxetine Escitalopram

Anticonvulsants

- Gabapentin, Pregabalin: Start at lower doses and titrate slow for improved tolerability. Sedation, ataxia, weight gain, and edema are common side effects. May have efficacy for co-occurring anxiety disorder.
  - Gabapentin: 100mg QHS then 100mg TID, continue up to 1800mg per day depending on renal function
- Consider Valproic Acid or Topiramate for co-occurring migraine headaches
- Some anticonvulsants require therapeutic drug monitoring (carbamazepine, valproic acid). All anticonvulsants have risk for drug-induced rashes, increased suicidal ideation, and significant drug-drug interactions.

Summary


Uncontrolled Pain
Suspected Etiology
Musculoskeletal, Inflammatory
Descriptors
Aching, stabbing, sharp, continuous, throbbing, pressure
Chronicity
Acute
Suspected Etiology
Neuropathic, Central
Descriptors
Shooting, burning, numb, pins and needles, deep, intermittent, radiating
Chronicity
Subacute, Chronic
Acetaminophen
NSAIDs
Skeletal Muscle Relaxants
Tricyclic Antidepressants
SNRIs/Atypical Antidepressants
Anticonvulsants
Topical Anesthetics
Current alcohol use, hepatic disease
Heart failure, renal disease, history of upper GI bleeding
History of falls, long QT-syndrome, serotonin syndrome
Primary insomnia
Co-occurring depression or GAD
Co-occurring bipolar disorder
Co-occurring seizure disorder
Avoid Acetaminophen
Avoid NSAIDs or use with caution
Avoid Skeletal Muscle Relaxants or use with caution
Consider Tricyclic Antidepressant
Consider SNRI (depression) or Anticonvulsant (i.e., gabapentinoids)
Consider Anticonvulsants with mood stabilization data
Consider Anticonvulsants; avoid or use antidepressants with caution

References

- Nonopioid Pain Medications: Dosage, Adverse Effects, and More. American Pharmacists Association Pain Institute. March 2018.
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- Herndon C. Chronic Pain Management: Best Practices and Clinical Pearls. American Pharmacists Association Pain Institute. March 2018.