PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

Nonopioid Analgesics

Alexandra McPherson, PharmD, MPH

Titles and Affiliations

Alexandra McPherson, PharmD, MPH

Palliative Care Clinical Pharmacy Specialist

MedStar Washington Hospital Center

Disclosures

Learning Objectives

1

Describe the pharmacodynamic and pharmacokinetic properties of acetaminophen and the nonsteroidal anti-inflammatory drugs (NSAIDs)

2

List the most common adverse effects associated with acetaminophen and NSAIDs

3

Recognize clinically important drug-drug interactions associated with acetaminophen and NSAIDs

4

Describe the role of nonopioid analgesics in the management of acute and chronic pain

Key Abbreviations

ASA	Aspirin
CNS	Central nervous system
COX	Cyclooxygenase
CV	Cardiovascular
GI	Gastrointestinal
INR	International normalized ratio
LBP	Lower back pain
NAPQI	N-acetyl-p-benzoquinone imine
NSAID	Nonsteroidal anti-inflammatory drug
OA	Osteoarthritis
PG	Prostaglandin
RUQ	Right upper quadrant
URI	Upper respiratory infection

Acetaminophen

Acetaminophen

Also known as…

- APAP (N-**a**cetyl-**p**ara-**a**mino**p**henol)
- Paracetamol
- Various brand names (Tylenol)

Indication(s)

- To lower a fever
- Treatment of mild to moderate noninflammatory nociceptive pain

Role in therapy

- Self-limiting painful conditions such as tension headache, mild to moderate musculoskeletal pain, dental pain
- Low back pain
- Osteoarthritis

medlineplus.gov/druginfo/meds/a681004.html.

Acetaminophen – Mechanism of Action

- Mechanism is poorly understood
- Weak COX-2 inhibitor
- Reduces PG in the CNS, inhibiting endogenous pyrogens
- Interacts with the endocannabinoid system
- Reduces nitric oxide pathway
- Activates descending serotonergic pain pathways
- Lacks anti-inflammatory activity (probably)

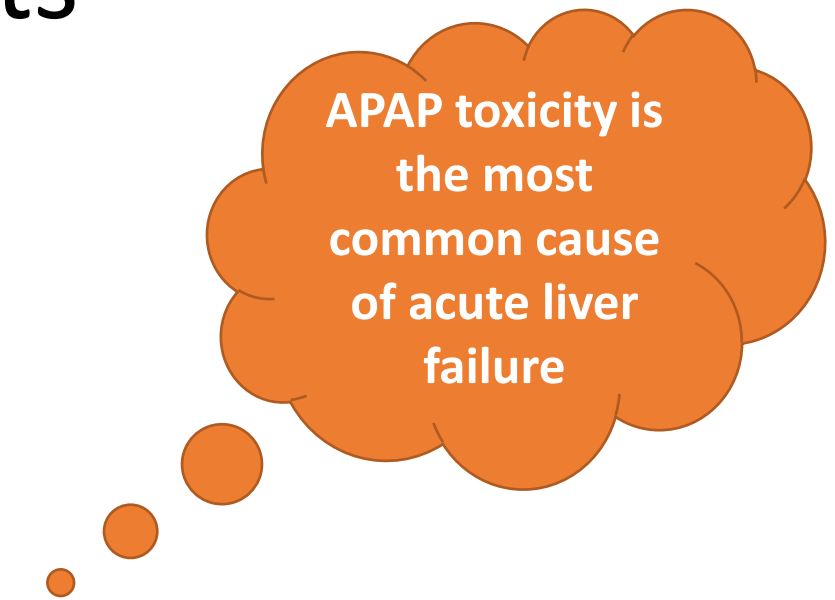
Analgesic
Antipyretic

Anti
Pain
Anti
Pyretic

Mallick-Searle. *Nurse Prac*. 2016;12(3)174-180
Smith. *Pain Physician*. 2009;12:269-280.

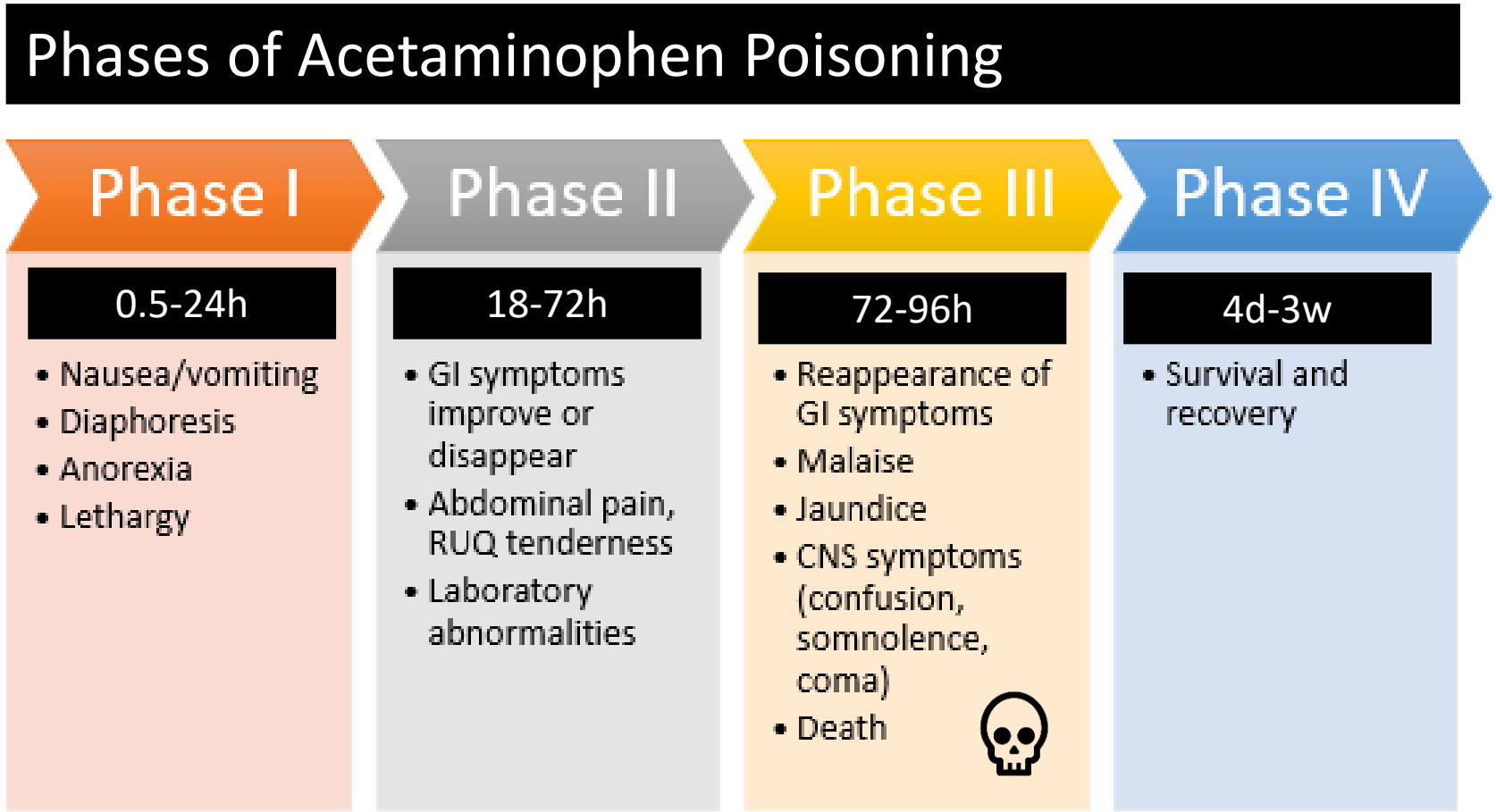
Acetaminophen – Adverse Effects

- Typically well tolerated
- Acetaminophen is metabolized by 3 pathways:
  - Glucuronidation (40%-65%)
  - Sulfation (20%-40%)
  - N-hydroxylation (via CYP 2E1)
    - Forms NAPQI (N-acetyl-p-benzo-quinone imine)
    - Highly reactive intermediate
    - Usually combines with glutathione, then excreted
    - With large acetaminophen ingestion, pathways become saturated and glutathione stores depleted
    - NAPQI concentrations increase, causing hepatoxicity



Farrell. *Medscape*. Jan 17, 2020.

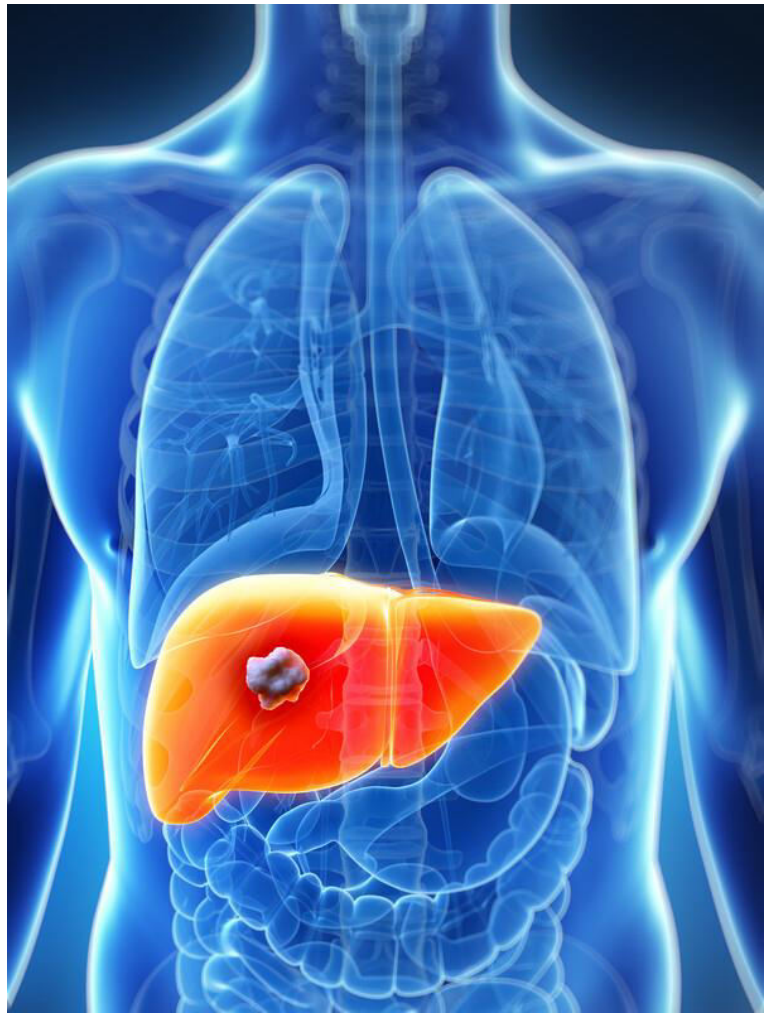
Acetaminophen – Adverse Effects



www.brainkart.com/article/Paracetamol---Toxicology-Poisons_16334/.

Acetaminophen – Adverse Effects

- Hepatotoxicity occurs after ingesting a single dose of 7.5-10 grams (20-25 grams = fatal)
  - Chronic acetaminophen toxicity also a risk
- Risks for increased metabolism to toxic metabolite include:
  - Supratherapeutic doses of acetaminophen
  - Heavy, chronic alcohol consumption (acute consumption may be protective!)
  - Malnutrition
- Patient-related variables
  - Alcoholic cirrhosis
  - Alcohol use (≥3 alcoholic drinks per day)
  - Taking >4 grams acetaminophen per day



medlineplus.gov/druginfo/meds/a681004.html.

Acetaminophen – Adverse Effects

- Acetaminophen is the most frequently prescribed analgesic in pregnancy
  - Has been associated with hyperkinetic disorder and attention-deficit / hyperactivity disorder
  - Acetaminophen or ibuprofen use during pregnancy or first year of life associated with increased asthma risk (though adjusting for URIs diminished association)
- Acetaminophen-associated skin reactions (rare but potentially fatal)
  - Stevens-Johnson syndrome (SJS)
  - Toxic epidermal necrolysis (TEN)

Liew. *JAMA Pediatr*. 2014;168(4):313-320.
Sordillo. *J Allergy Clin Immunol*. 2015;135:441-448.
U.S. Food and Drug Administration. 2013 Aug 1. www.fda.gov/drugs/drugsafety/ucm363041.htm.

Acetaminophen Drug Interactions

Alcohol

- Increased risk of hepatotoxicity
- Avoid concurrent use; minimize alcohol intake when using acetaminophen

Warfarin

- Increased risk of bleeding
- Limit acetaminophen to occasional use; monitor INR for several weeks when acetaminophen 2-4 grams daily is added or discontinued in patients on warfarin

Parra. *Pharmacotherapy.* 2007;27(5):675-683.

Acetaminophen – Dosing Limits

- Nonprescription use
  - Maximum daily dose 3,000 mg
- FDA total daily dose – not to exceed 4,000 mg
- With liver disease – not to exceed 2,000-3,000 mg/day (if NOT drinking alcohol; if drinking alcohol, no acetaminophen allowed)
- Combination analgesics
  - Acetaminophen not to exceed 325 mg (effective January 2014)

FDA. pain.sh/6e56k0k. www.accessdata.fda.gov/drugsatfda_docs/label/2015/204767s000lbl.pdf.

IV Acetaminophen (Ofirmev®)

Indicated for the management of mild to moderate pain, moderate to severe pain with opioids, & reduction of fever

May be used for postoperative pain

- 1000 mg q6h superior to placebo after hip/knee replacement surgery
- 1000 mg q6h or 650 mg q4h superior to placebo for postabdominal laparoscope surgical pain
- 1000 mg q6h superior to placebo for fever reduction

Administered as a 15 minute infusion

Available in 100 ml vial or bag, 10 mg/ml

Acetaminophen – Place in the Guidelines

- Acute or subacute low back pain
  - No difference compared to placebo at 4 weeks[1]
  - Insufficient evidence to recommend for or against the use of time-limited (<7 days) of acetaminophen therapy[2]
- Chronic low back pain
  - No sufficient evidence regarding the use of acetaminophen[1]
  - Recommend against chronic use of acetaminophen[2]
- Osteoarthritis of the hand, knee, and hip
  - Acetaminophen is “conditionally recommended”[3]

1. Qaseem. *Ann Intern Med*. 2017;166:514-530.
2. Pangarkar. *J Gen Intern Med*. 2019;34(11):2620-2629.
3. *Arthritis Rheum*. 2020;72(2):220-233.

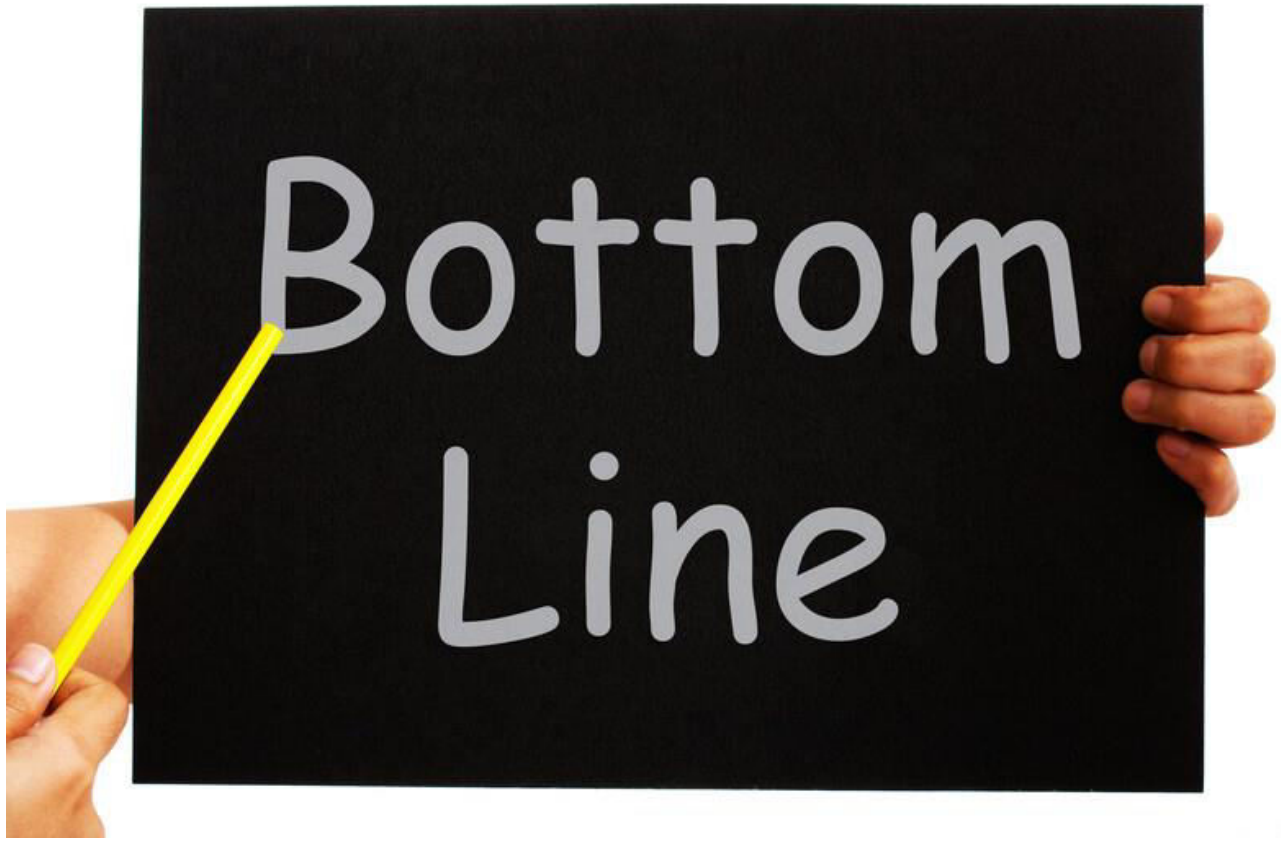
Acetaminophen – OA / LBP

- Paracetamol (acetaminophen) vs placebo for spinal pain (neck or low back pain) or osteoarthritis of the hip or knee
- Extracted data on pain, disability, and quality of life
  - Secondary outcomes were adverse effects, patient adherence, and use of rescue medications
- 12 reports (13 randomized trials) were included
  - High quality evidence acetaminophen is ineffective for reducing pain intensity and disability in the short term in low back pain
  - High quality evidence acetaminophen provides a significant but not clinically important effect on pain and disability in hip and knee OA in the short term
  - No difference in adverse effects between acetaminophen vs placebo

Machado. *BMJ*. 2015;350:h1225.

Acetaminophen – Summary

- **Mechanism of action**
  - Acts centrally
  - Analgesic and anti-pyretic
  - Lacks anti-inflammatory activity
- **Adverse effects**
  - Very well tolerated
  - Hepatotoxicity seen with acute and chronic use
- **Preferred analgesic in the following patient populations:**
  - Elderly
  - History of peptic ulcer disease, GI bleed
  - Patients taking anticoagulants



PM is a 72 year old man who has moderately severe osteoarthritis pain, notably in his hips and knees. His PCP advised him to avoid NSAIDs due to a history of GI bleeding from ibuprofen. He finds that acetaminophen 1000 mg every 4 hours adequately controls his pain, but you are concerned because he has a history of alcoholic liver disease and currently drinks about 6 beers a day.

Under what circumstances would you be comfortable allowing PM to take acetaminophen?

A. If PM agrees to reduce acetaminophen dose to no more than 4 grams a day
B. If PM pinky swears to stop drinking alcohol (eg, 6 beers per day)
C. A and B
D. Under no circumstances because he has a history of alcoholic liver disease

PM is a 72 year old man who has moderately severe osteoarthritis pain, notably in his hips and knees. His PCP advised him to avoid NSAIDs due to a history of GI bleeding from ibuprofen. He finds that acetaminophen 1000 mg every 4 hours adequately controls his pain, but you are concerned because he has a history of alcoholic liver disease and currently drinks about 6 beers a day.

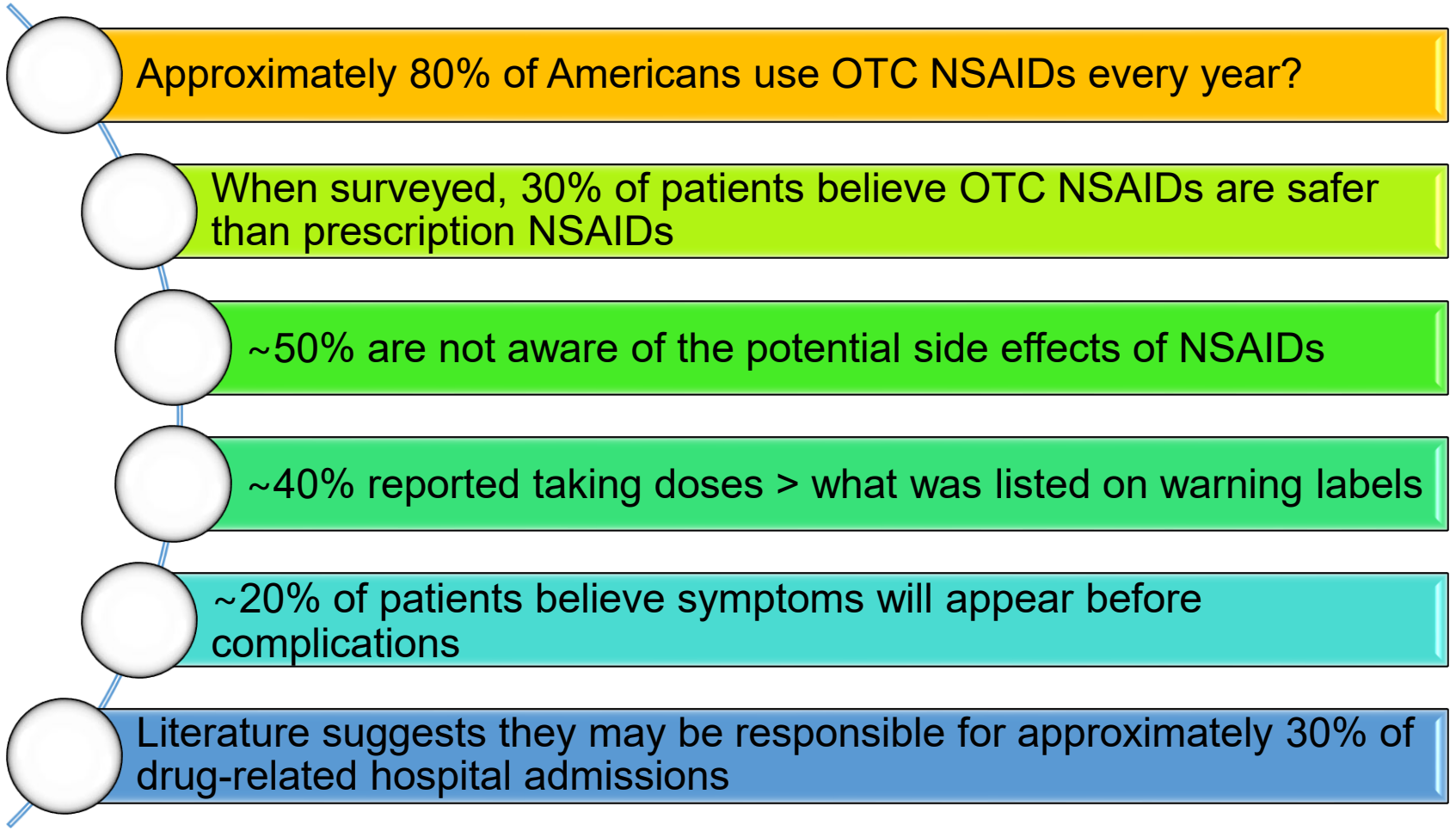
Under what circumstances would you be comfortable allowing PM to take acetaminophen?

A. If PM agrees to reduce acetaminophen dose to no more than 4 grams a day
B. If PM pinky swears to stop drinking alcohol (eg, 6 beers per day)
C. A and B
D. Under no circumstances because he has a history of alcoholic liver disease

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

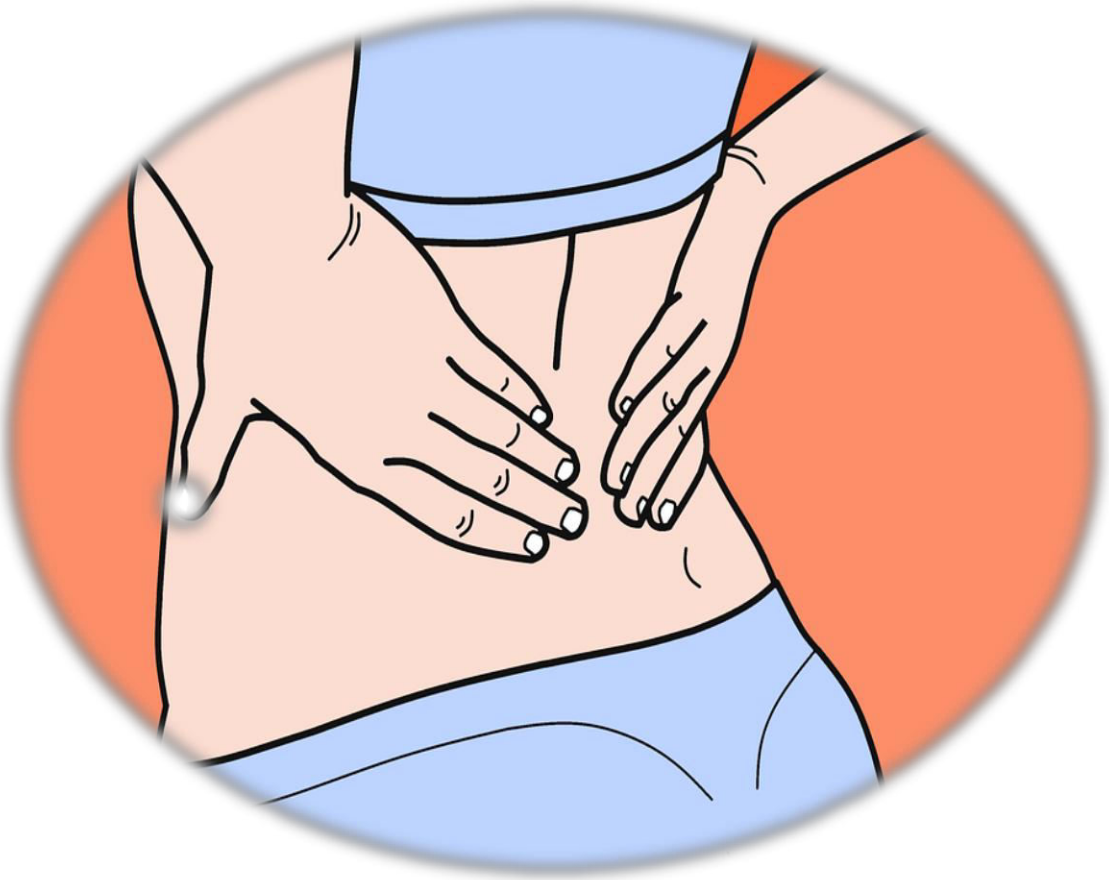
Did you know?

In 2018, more than 80 million NSAID prescriptions were filled



Wilcox. *J Rheumatol*. 2005;32:2218-2224.
Pirmohamed. *BMJ*. 2004;329:15-19.
Medical Expenditure Panel Survey (MEPS) 2008-2018. Agency for Healthcare Research and Quality (AHRQ), Rockville, MD.

NSAIDs



- **Indication**
  - To lower a fever
  - Treatment of mild to moderate pain that may be inflammatory in nature
- **Role in therapy**
  - Acute and chronic pain
  - Especially helpful in certain types of somatic pain such as muscle and joint pain, bone/dental pain, inflammatory pain, postoperative pain
  - As an adjuvant analgesic in patients taking opioids (opioid-sparing effect)

Ghlichloo. *StatPearls*. May 12, 2021.

NSAIDs – Mechanism of Action

- NSAIDs competitively inhibit the enzyme cyclooxygenase (COX), which prevents the formation of prostaglandins
- There are two COX isoforms

Ghlichloo. *StatPearls*. May 12, 2021.

NSAIDs – Mechanism of Action

COX-1

- Expressed in most tissues, variably
- "Housekeeping" enzyme
  - Regulates normal cellular processes
  - Gastric cytoprotection
  - Vascular homeostasis
  - Platelet aggregation
  - Kidney function
- Stimulated by hormones or growth factors

COX-2

- Expressed constitutively in the brain, kidney, bone, and female reproductive system
- Expressed at other sites during states of inflammation

Cheng. *Acta Pharmacologica Sinica*. 2005;26(8):926-933.

NSAIDs and COX Inhibition

- Aspirin irreversibly inhibits COX-1
  - Discontinue 1 week before surgery
- Rest of NSAIDS reversibly inhibit the COX enzymes
  - Pharmacologic effect depends on how long there is a significant serum level of the NSAID
- Most NSAIDS inhibit both COX-1 and COX-2 isoenzymes
  - Aspirin is entirely selective for inhibition of COX-1 isoenzyme
  - Celecoxib preferentially inhibits COX-2 isoenzyme
    - Provides some gastric protection
    - Associated with an increased risk of major coronary events

Younan. *Pract Pain Manag*. 2013;13(10).

NSAIDs – Adverse Effects

Gastrointestinal

- Epigastric pain, dyspepsia, nausea/vomiting (most common)
- Gastric ulceration with/without bleeding, peptic ulcer disease, or GI perforation

Cardiovascular

- Myocardial infarction, stroke
- Increase systolic blood pressure by ~ 4 mmHg

Renal

- Decreased synthesis of PGs involved in maintaining renal blood flow can result in sodium and water retention

Respiratory

- Bronchospasm, deterioration of symptoms in asthmatics

Ghlichloo. *StatPearls*. May 12, 2021.

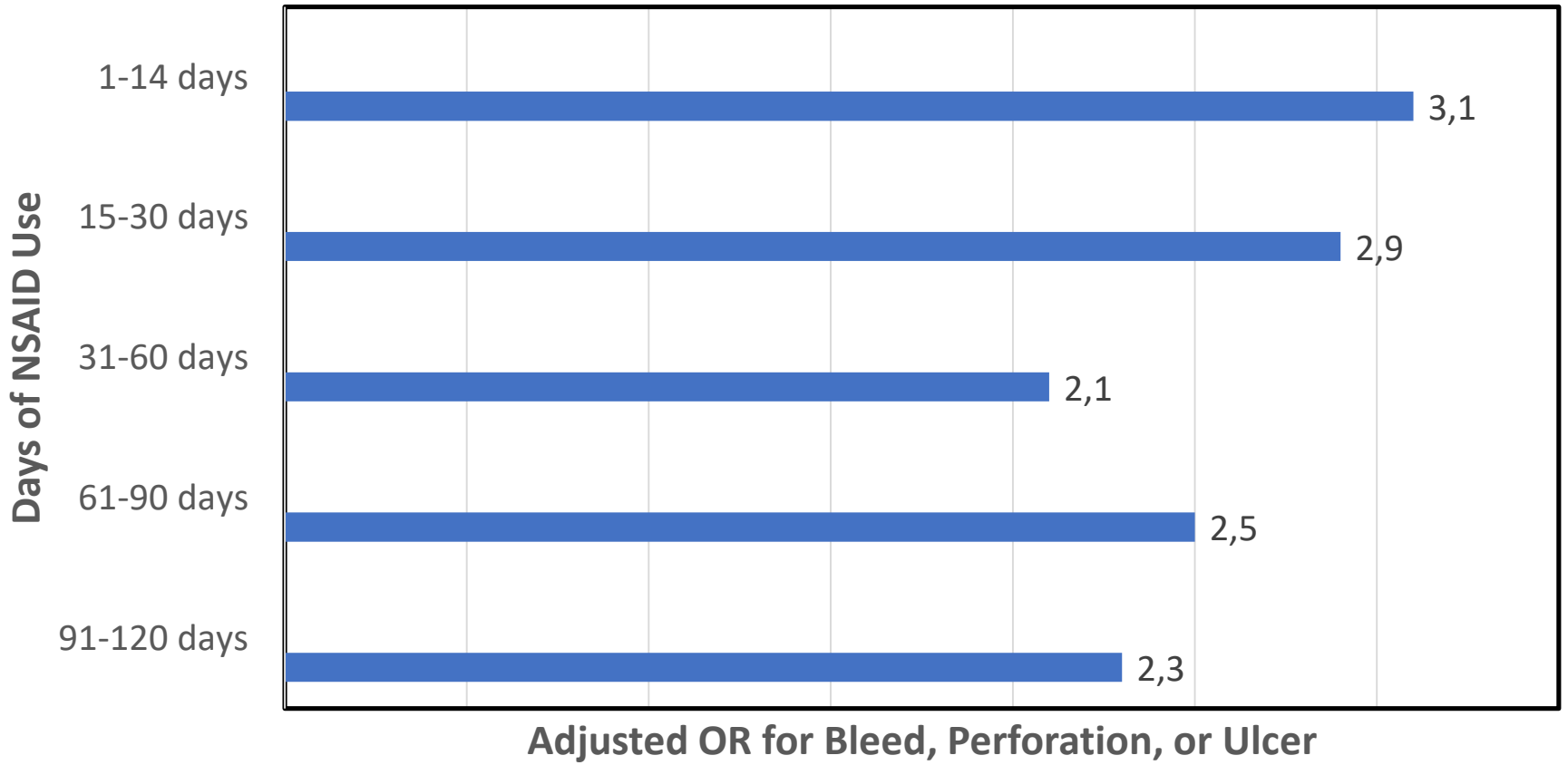
NSAIDs and Gastrointestinal Toxicity

- The nonsecretory cytoprotective effects of PG include:
  - Stimulation of mucin, bicarbonate, and phospholipid secretion by epithelial cells
  - Enhancement of mucosal blood flow and oxygen delivery to epithelial cells via local vasodilation
  - Increased epithelial cell migration towards the luminal surface
  - Enhanced epithelial cell proliferation

Primarily due to inhibition of COX-1

UpToDate. 2017. "Pathogenesis of gastroduodenal toxicity."
Fromm. *Clin Invest Med*. 1987;10(3):251-258.

NSAIDs and Gastrointestinal Toxicity



Helin-Salmivaara. *Scand J Gastroenterol*. 2007;42:923-932

NSAIDs and Gastrointestinal Toxicity

- Risk factors for NSAID-related GI toxicity:
  - History of peptic ulcer disease or upper GI bleed
  - ≥65 years old
  - Presence of comorbidities such as rheumatoid arthritis
  - Concomitant use of anticoagulants, aspirin or corticosteroids
  - H. pylori infection
- Strategies to prevent GI damage in chronic NSAID users:
  - **Proton pump inhibitor (PPI)**
  - Histamine-2 receptor antagonist (H2RA)
  - Use of COX-2 selective NSAIDs

Lanza. *Am J Gastroenterol*. 2009;104(3):728-738.
JMCP. 2013;19(9):S3-S19.
Antman. *Circulation*. 2007;115:1634-1642.

Aspirin and Gastrointestinal Toxicity

- **Aspirin doses as low as 10 mg/day inhibit gastric PG generation considerably**
- After stopping low-dose aspirin, human stomach requires 5-8 days to recover its COX-1 activity and synthesize protective PGs

Cryer. *Gastroenterology*. 1999;117(1):17-25.
Campbell. *JAMA*. 2007;297(18):2018-2024.

NSAIDs and Gastrointestinal Toxicity – Preventive Measures

Dyspepsia, abdominal pain, or gastric discomfort

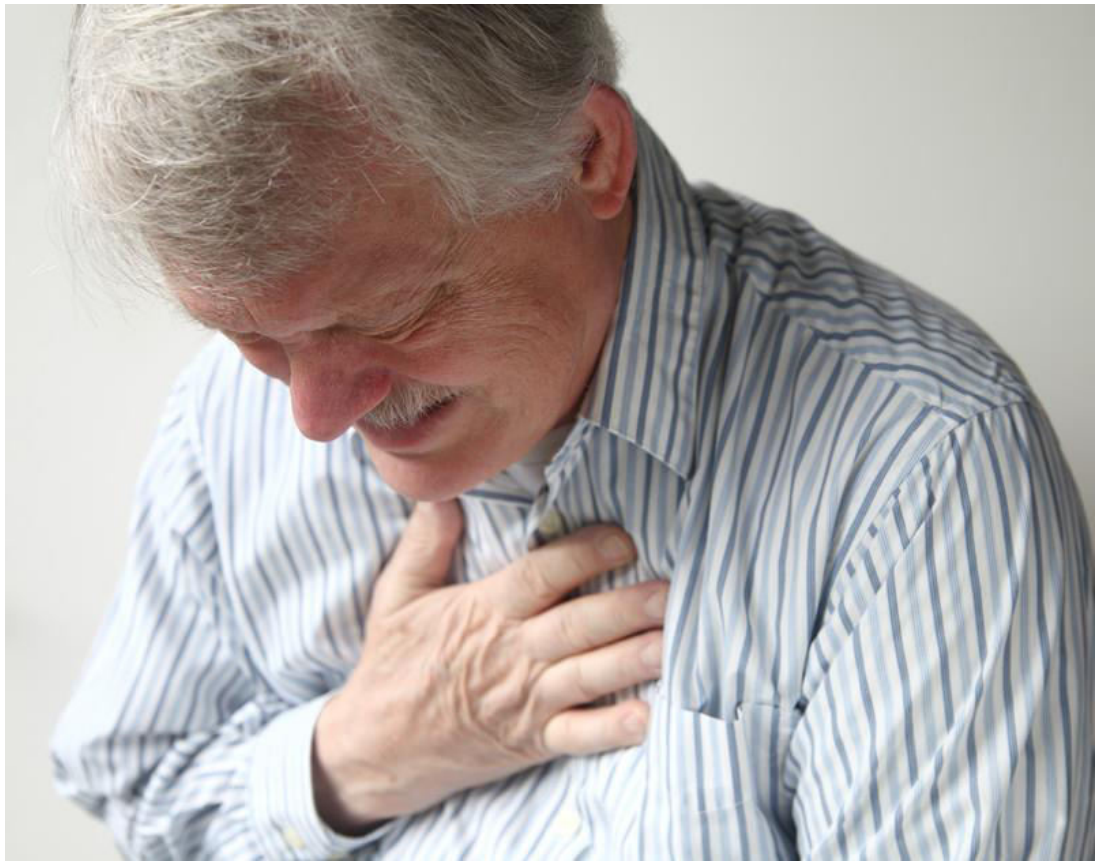
- Combine NSAID with PPI or H_2 antagonist

History of GI Bleed

- Avoid NSAIDs in patients with a history of NSAID-related upper GI bleeding
- Add PPI/misoprostol
- Celecoxib ± PPI/misoprostol

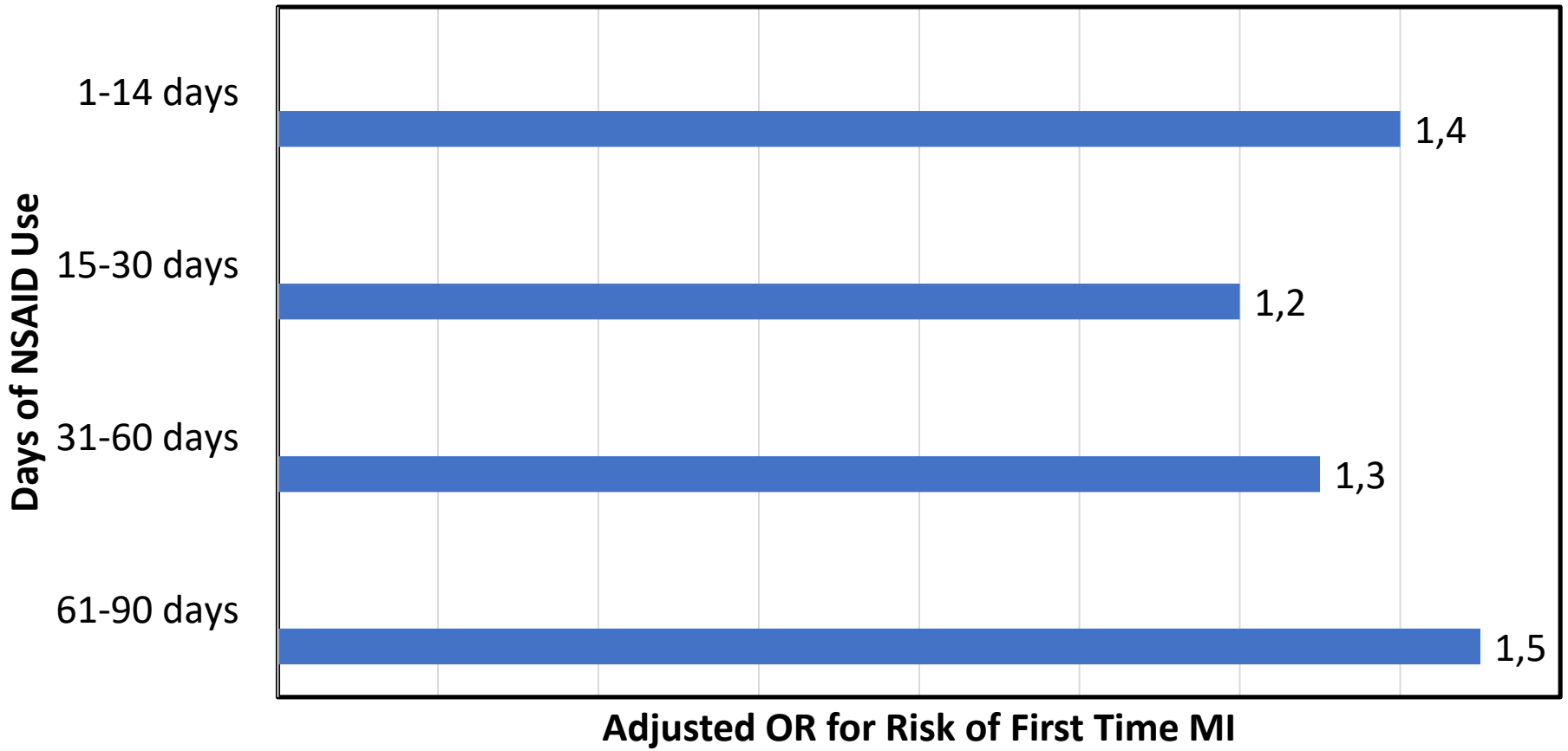
Risser. *Am Fam Physician*. 2009;80(12):1371-1378.

NSAIDs and Cardiovascular Risk



- NSAIDs have been associated with increased risk of:
  - Myocardial infarction
  - Stroke
  - Heart failure
  - Atrial fibrillation
  - Cardiovascular death

NSAIDs and Cardiovascular Risk



Helin-Salmivaara. *Eur Heart J*. 2006;27:1657-1663

So, you have heart disease and your knees hurt…

- **PRECISION Trial** – compared cardiovascular safety of celecoxib, ibuprofen, and naproxen
- 24,081 patients with osteoarthritis (90%) or rheumatoid arthritis (10%) and established CV disease or increased risk of developing CV disease were randomized to receive:
  - Celecoxib 100 mg po BID
  - Ibuprofen 600 mg po TID
  - Naproxen 375 mg po BID
- Mean treatment duration was 20.3 months, and the mean follow-up period was 34.1 months
- About half were taking low-dose ASA at baseline

Nissen. *N Engl J Med*. 2016 Nov 13 (epub).

So you have heart disease and your knees hurt…

- Primary outcome event: CV death (including hemorrhagic death, nonfatal MI or nonfatal CVA)
- 68.8% patients DC'd study drug; 27.4% DC'd during follow up

Celecoxib		Ibuprofen		Naproxen	
Intent to treat	On treatment	Intent to treat	On treatment	Intent to treat	On treatment
188 (2.3%)	134 (1.7%)	201 (2.5%)	155 (1.9%)	218 (2.7%)	44 (1.8%)

- Risk of GI events significantly lower with celecoxib than naproxen or ibuprofen
- Risk of renal events significantly lower with celecoxib than ibuprofen, but celecoxib not significantly less than naproxen

Nissen. *N Engl J Med*. 2016 Nov 13 (epub).

So you have heart disease and your knees hurt…

- Limitations
  - Dosage of celecoxib was limited to 200 mg per day, lower than doses previously associated with CV toxicity
  - Ibuprofen and naproxen doses were allowed to be increased
  - Ibuprofen and naproxen (but not celecoxib) inhibit aspirin binding to platelet COX-1, thus the cardioprotective effects of aspirin may have been blunted in patients who were taking ibuprofen or naproxen
- Conclusion
  - Researchers state celecoxib is noninferior to ibuprofen and naproxen from a cardiovascular perspective
  - Others state the celecoxib dose is too low to support this conclusion

Nissen. *N Engl J Med*. 2016 Nov 13 (epub).

Trials on gastrointestinal and cardiovascular toxicity with NSAIDs

- **CONCERN Trial –** Compared the risk of recurrent upper GI bleeding with celecoxib vs naproxen plus a proton pump inhibitor
  - Patients with cardiothrombotic disease and arthritis after upper GI bleed
    - All receiving aspirin therapy
  - After ulcer healing, 514 patients were randomized to either:
    - Celecoxib 100 mg po BID plus esomeprazole 20 mg po daily
    - Naproxen 500 mg po BID plus esomeprazole 20 mg po daily
  - Primary endpoint: recurrent upper GI bleeding within 18 months
    - Cumulative incidence of recurrent bleeding at 18 months
      - Celecoxib group: 5.6%
      - Naproxen group: 12.3%
  - **Conclusion: In patients at high risk of both cardiovascular and GI events who require concomitant aspirin and NSAID, celecoxib + PPI is preferred over naproxen + PPI**

Chan. *Lancet*. 2017;389(10087):2375-2382.

NSAIDs and Cardiovascular Risk – Preventive Measures

- Avoid COX-2 inhibitors/nonselective NSAIDs in patients at risk of CV events
- Avoid NSAIDs in patients with CHF
- Use NSAIDs with caution in patients with HTN
  - If NSAIDs required, regularly monitor blood pressure

Risser. *Am Fam Physician*. 2009;80(12):1371-1378.

NSAIDs and Renal Toxicity

- Acute kidney injury (hemodynamic and acute tubular injury)
- Hyperkalemia ± metabolic acidosis
- Hyponatremia
- Hypervolemia and sodium retention
- Exacerbation of hypertension
- Acute interstitial nephritis
- Nephrotic syndrome
- Acute or chronic papillary necrosis
- Progression of chronic kidney disease

Baker. *Am J Kidney Dis*. 2020;76(4):546-557.

NSAIDs and Renal Toxicity

- Preventive measures
  - Stage 1-3 CKD
    - Short-term use for ≤5 days is acceptable
    - Long-term use may also be acceptable on a case-by-case basis with close monitoring
  - Stage 4 CKD
    - Consider short-term, low-dose NSAID use on a case-by-case basis with close monitoring
    - In patients with underlying hyperkalemia, NSAID use is contraindicated
  - Stage 5 CKD, no kidney replacement therapy
    - NSAIDs are absolutely contraindicated, except under circumstances of palliative care
  - Use NSAIDs with caution when combined with medications that potentially decrease renal function (eg, ACE inhibitors, beta blockers)

Baker. *Am J Kidney Dis*. 2020;76(4):546-557.

NSAIDs and Pregnancy

- On October 15, 2020, the FDA released a new warning regarding NSAID use in pregnancy
  - Use of NSAIDs around 20 weeks or later in pregnancy may cause rare but serious kidney problems in an unborn baby
  - Can result in low levels of amniotic fluid and possible related complications

FDA. pain.sh/t2k.

Other NSAID-Related Adverse Effects

Adverse Effect	Preventive or Therapeutic Measures
Hepatic complications	Avoid NSAIDs in patients with cirrhosis due to potential hematologic and renal complications
Respiratory (aspirin-exacerbated respiratory disease)	Use NSAIDs and aspirin with caution in patients with asthma, especially in those with nasal polyps or recurrent sinusitis
Clotting problems contributing to significant bleeding	• Avoid NSAIDs in patients with platelet defects or thrombocytopenia • Avoid concurrent use of NSAIDs and anticoagulants • If NSAIDs are necessary in patients on anticoagulant therapy, expect an increase in INR • Avoid daily low-dose ASA if CV risk is low (<3% annual risk)

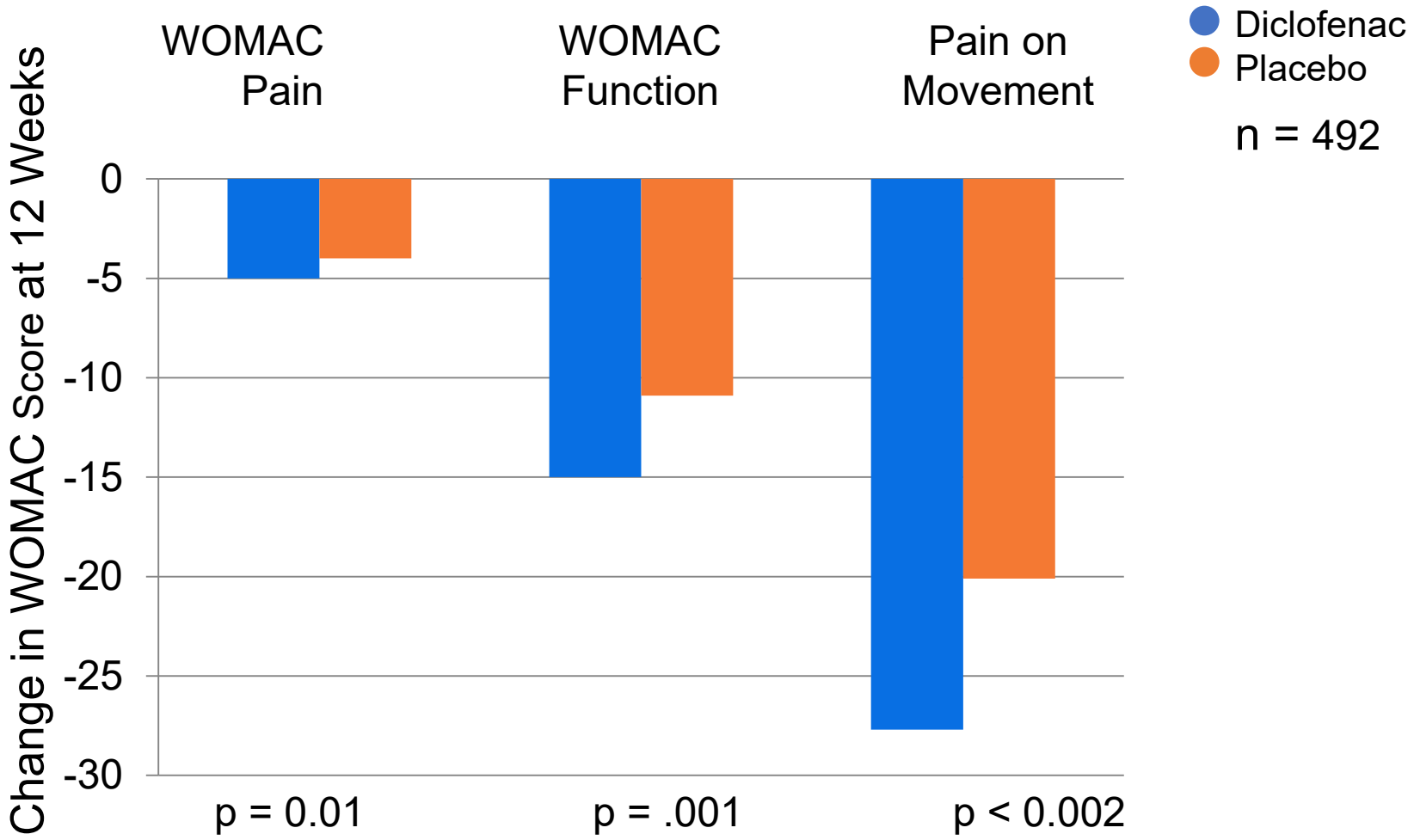
Risser. *Am Fam Physician*. 2009;80(12):1371-1378.

What About Topical NSAIDs?

Comparative C_{max} of diclofenac	Formulation	C_{max} (ng/mL)
	Diclofenac 50 mg tablet	1298
	Diclofenac 75 mg tablet	2367
	Diclofenac epolamine patch (Flector®)	8.8
	Diclofenac gel 1% (Voltaren® Gel)	53.8
	Diclofenac gel 3% (Solaraze®)	4
	Diclofenac / DSMO soln. (Pennsaid®)	19.4

Arthrotec package insert. New York, NY: Pfizer; 2010; Flector package insert. Bristol, TN: King Pharmaceuticals; 2009; Voltaren Gel package insert. Chadds Ford, PA: Endo Pharmaceuticals; 2009; Solaraze package insert. Melville, NY: PharmaDerm; 2008; Pennsaid package insert. St. Louis, MO: Covidien; 2010.

Diclofenac Gel (Voltaren® Gel) in OA of the Knee



Barthel. *Semin Arthritis Rheum*. 2009; 39(3):203-212.

NSAID Drug Interactions

Bisphosphonates

- Increased risk of GI or esophageal ulceration
- Use caution with concomitant therapy; avoid if possible

Digoxin

- Renal clearance of digoxin inhibited
- Monitor digoxin levels; adjust dose as indicated

Aspirin

- Increased risk of gastroduodenal ulcers and bleeding
- Avoid concurrent use is possible
- Consider use of gastroprotective agents (eg, PPIs)

www.ncbi.nlm.nih.gov/pmc/articles/PMC4508078/.
pubmed.ncbi.nlm.nih.gov/19298582/.
www.ncbi.nlm.nih.gov/pmc/articles/PMC5772852/.

Salicylate/NSAID Drug Interactions

Anticoagulants/Antiplatelets, Alcohol

- Increased risk of bleeding
- Avoid if possible

Methotrexate

- Decreased clearance of methotrexate
- Avoid with high-dose methotrexate therapy
- Monitor methotrexate levels with concurrent therapy

Sulfonylureas

- Increased risk of hypoglycemia
- Monitor blood glucose levels with dose changes

Antihypertensives

- Inhibition of antihypertensive effect
- Monitor blood pressure, potassium levels closely

Krinskey. *Handbook of Nonprescription Drugs*, 18th ed. APhA, 2014.
Li. *Br J Pharmacol*. 2007;151(4):483-493.

Ibuprofen Drug Interactions

Aspirin

- Decreased antiplatelet effect of aspirin
- Aspirin should be taken at least 30 minutes before or 8 hours after ibuprofen
- Use acetaminophen (or other analgesic) instead of ibuprofen

Phenytoin

- Displacement from protein-binding sites
- Monitor free phenytoin levels; adjust dose as indicated

Krinskey. *Handbook of Nonprescription Drugs*, 18th ed. APhA, 2014.
www.fda.gov/media/76636/download.
Dasgupta. *Ther Drug Monit*. 1996;18(1):97-99.

Aspirin Drug Interactions

Valproic acid

- Displacement from protein-binding sites and inhibition of valproic acid metabolism
- Avoid concurrent use
- Use naproxen instead of aspirin (no interaction)

Krinskey. *Handbook of Nonprescription Drugs*, 18th ed. APhA, 2014.
Johnson. *Drug Saf.* 1993;8(2):99-127.

NSAIDs — Summary

- Use at the **lowest possible dose** for the **shortest possible duration**
- Labeled NSAID dosing varies by formulation
- Use caution/avoid in the following patient populations:
  - GI disorders/bleeding
  - Cardiovascular disease, heart failure, or a history of stroke
  - Renal impairment
  - Asthma

Matthews. *Am J Manag Care.* 2013;19(14 suppl):s273-277.

Self-Assessment #2

AF is a 74 year old female with recently diagnosed rheumatoid arthritis. Her rheumatologist would like to start an NSAID to treat her inflammatory pain, but AF has a cardiac history (takes aspirin 81 mg po daily) and has experienced an upper GI bleed in the past.

According to the CONCERN trial, which of the following is the best option for AF?

A. Celecoxib 100 mg po BID
B. Celecoxib 100 mg po BID plus esomeprazole 20 mg po daily
C. Naproxen 500 mg po q12h
D. Naproxen 500 mg po q12h plus esomeprazole 20 mg po daily

AF is a 74-year-old female with recently diagnosed rheumatoid arthritis. Her rheumatologist would like to start an NSAID to treat her inflammatory pain, but AF has a cardiac history (takes aspirin 81 mg po daily) and has experienced an upper GI bleed in the past.

According to the CONCERN trial, which of the following is the best option for AF?

A. Celecoxib 100 mg po BID
B. Celecoxib 100 mg po BID plus esomeprazole 20 mg po daily
C. Naproxen 500 mg po q12h
D. Naproxen 500 mg po q12h plus esomeprazole 20 mg po daily

AF is a 74-year-old female with recently diagnosed rheumatoid arthritis. Her rheumatologist would like to start an NSAID to treat her inflammatory pain, but AF has a cardiac history (takes aspirin 81 mg po daily) and has experienced an upper GI bleed in the past.

According to the CONCERN trial, which of the following is the best option for AF?

A. Celecoxib 100 mg po BID
B. Celecoxib 100 mg po BID plus esomeprazole 20 mg po daily
C. Naproxen 500 mg po q12h
D. Naproxen 500 mg po q12h plus esomeprazole 20 mg po daily

PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

Nonopioid Analgesics

Alexandra McPherson, PharmD, MPH