NSAIDs: The Essentials

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ROTHMAN ORTHOPAEDICS

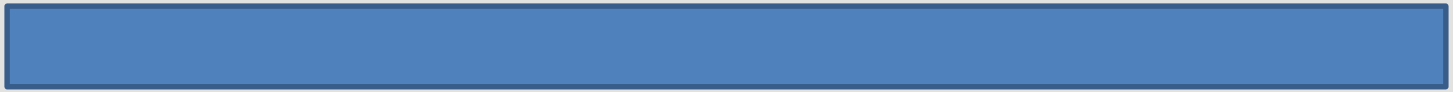
Case 1

- 27 yr old LHD pitcher is traded to your club and states during Spring Training PPE: “I need a prescription for Voltaren™ 75 mg BID for the season. I’ve done it for the past 5 seasons with my previous team.”
- No complaints of pain.

I have had this request and have to be obliged.

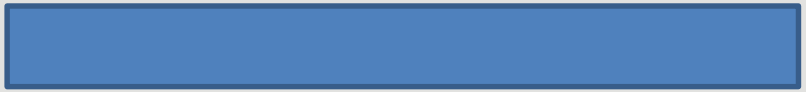
POLL OPEN

1. True



64.52%

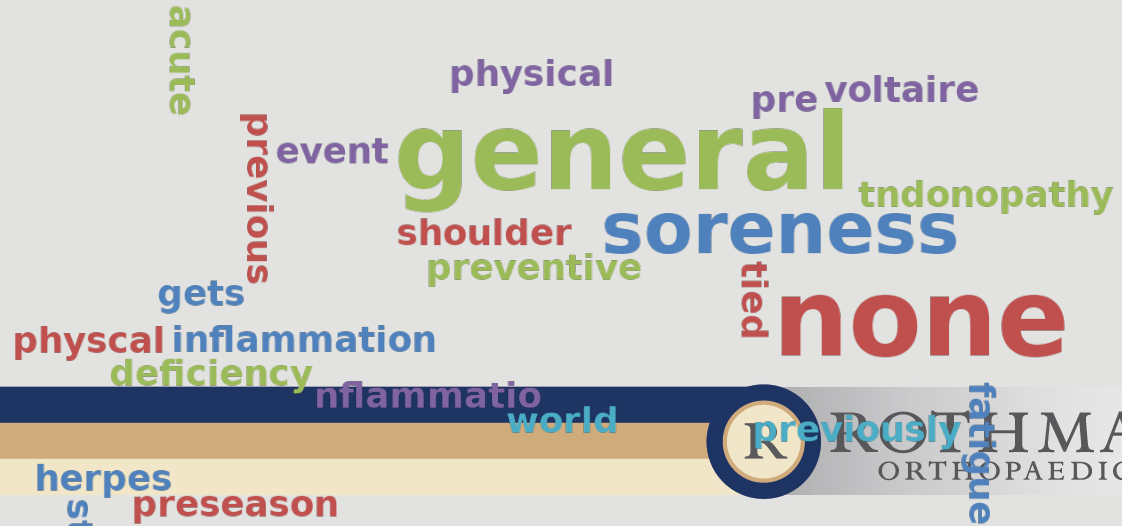
2. False



35.48%

What diagnosis goes into the EHR to rationalize in-season NSAID use?

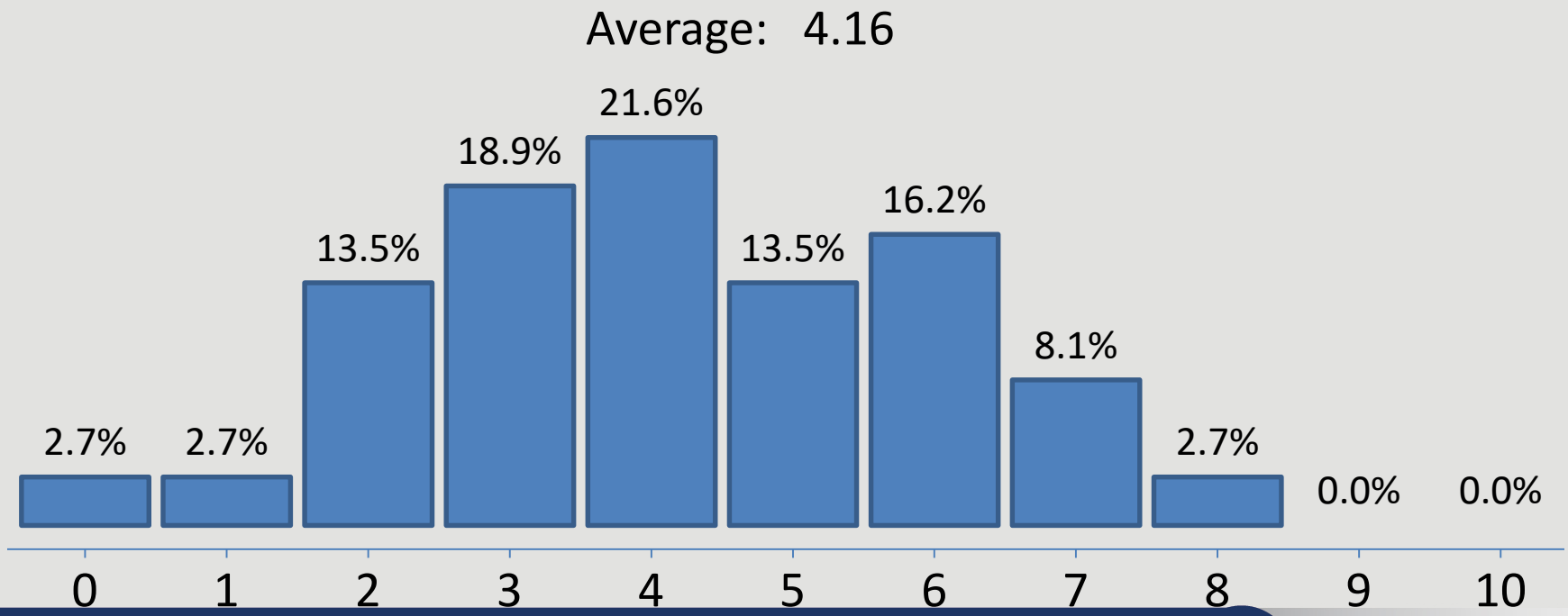
Enter Text and Press Send



ROTHMAN ORTHOPAEDICS

POLL OPEN

Within the class of NSAIDs, there are how many distinct subclasses-- each with their own side effect profile



Correct Answer : 9

ROTHMAN ORTHOPAEDICS

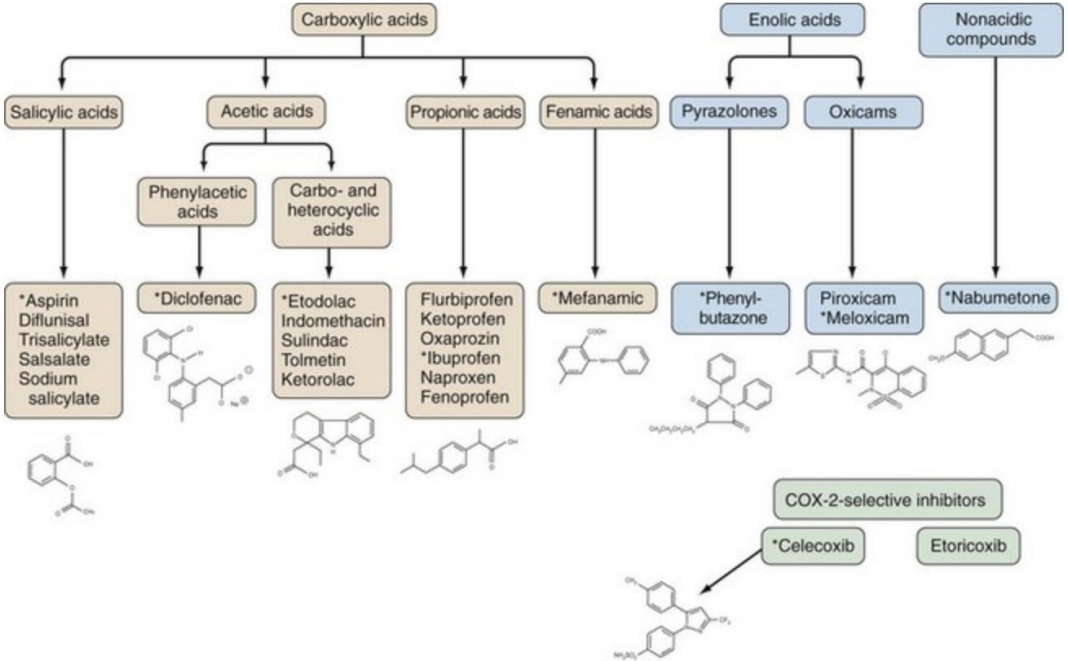


Figure 59-4 Classification and representative structures of the traditional nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2)-selective NSAIDs. NSAIDs. *Selected NSAID structure from each subclass.

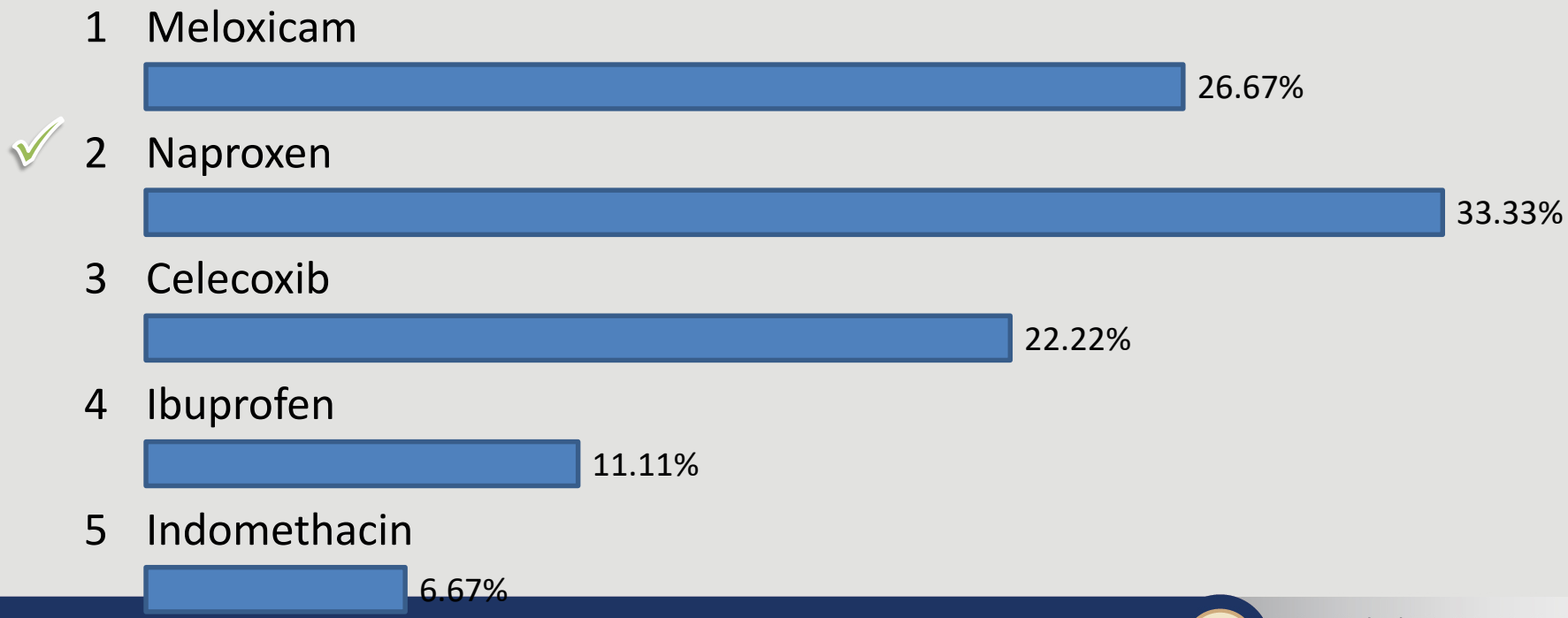
Case 2

- 56 yr old pitching coach with HTN, elevated cholesterol, type II DM, s/p CABG 2 years ago has a history of knee osteoarthritis. You watch him take a handful of Ibuprofen– it's like watching your kids eat Skittles™ on Halloween.

- You bring him back to the training room and note extensive crepitus and 2+ effusion. He has been putting off TKR until the “offseason” for the past 3 years. His last corticosteroid injection was 2 months ago and he is deriving diminishing returns from this modality.

POLL OPEN

From a harm reduction model, which of the following NSAIDs has the safest CV side effect profile?



CARDIOVASCULAR EFFECTS

GENERAL PUBLIC HE

Consume ter
NSAIDs: t ow

Judy Mullan,[1] Kathry

Table 3: Responses to the following yes/no questions.

	Correct Responses n (%)	Incorrect Responses n (%)	No Responses n (%)
When should you seek medical advice before taking this medicine?			
If you suffer from asthma	187 (71.4%)	39 (14.9%)	36 (13.7%)
If you have a history of kidney disease	175 (66.8%)	40 (15.3%)	47 (17.9%)
If you are taking medicine that thins the blood e.g. warfarin	177 (67.6%)	45 (17.2%)	40 (15.3%)
If you are on medicine for high blood pressure or heart problems	193 (73.7%)	33 (12.6%)	36 (13.7%)
If you have a sleeping disorder	91 (34.7%)	103 (39.3%)	68 (26.0%)
Is it safe to take this medicine?			
If you have kidney problems	194 (74.0%)	28 (10.7%)	40 (15.3%)
If you have blood pressure or heart problems	165 (63%)	56 (21.4%)	41 (15.6%)
If you have asthma	146 (55.7%)	71 (27.1%)	45 (17.2%)
If you have a sleeping disorder	106 (40.5%)	96 (36.6%)	60 (22.9%)
Can you take this medicine?			
If you are allergic to aspirin	162 (61.8%)	79 (30.2%)	21 (8.0%)
If you are allergic to ibuprofen	230 (87.8%)	14 (5.3%)	18 (6.9%)
If you are allergic to milk products	149 (56.9%)	69 (26.3%)	44 (16.8%)

Clinical Focus: Pain Management, Orthopedics, and Sports Injuries

Nonprescription Pain Medication Use in Collegiate Athletes: A Comparison of Samples

Stephen Stache , MD, Jeremy D. Close , MD, Christopher Mehallo , DO & Kristopher Fayock , MD

Pages 19-23 | Published online: 13 Mar 2015

Misleading graphic we've all seen

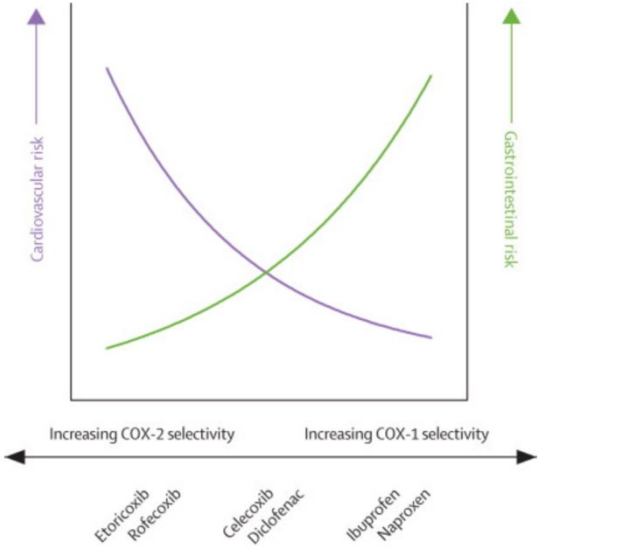


Figure 1 Currently suggested, but misleading, graphic of relation between COX-1 and COX-2 selectivity and cardiovascular and gastrointestinal side-effects [1, 2, 3]

Viewpoint

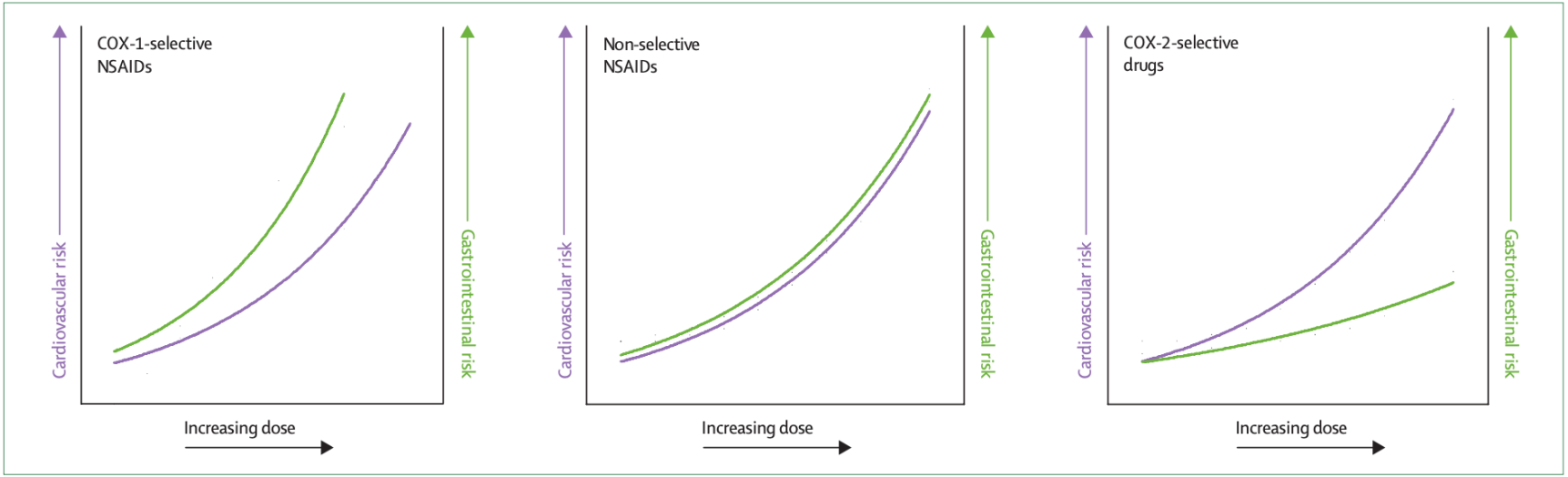


Figure 3: Proposed figure to show association between dose, cardiovascular risk, and gastrointestinal risk for COX-1-selective NSAIDs, non-selective NSAIDs, and COX-2-selective drugs

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Management of Patients on Nonsteroidal Anti-inflammatory Drugs: A Clinical Practice Recommendation From the First International Working Party on Gastrointestinal and Cardiovascular Effects of Nonsteroidal Anti-inflammatory Drugs and Anti-platelet Agents

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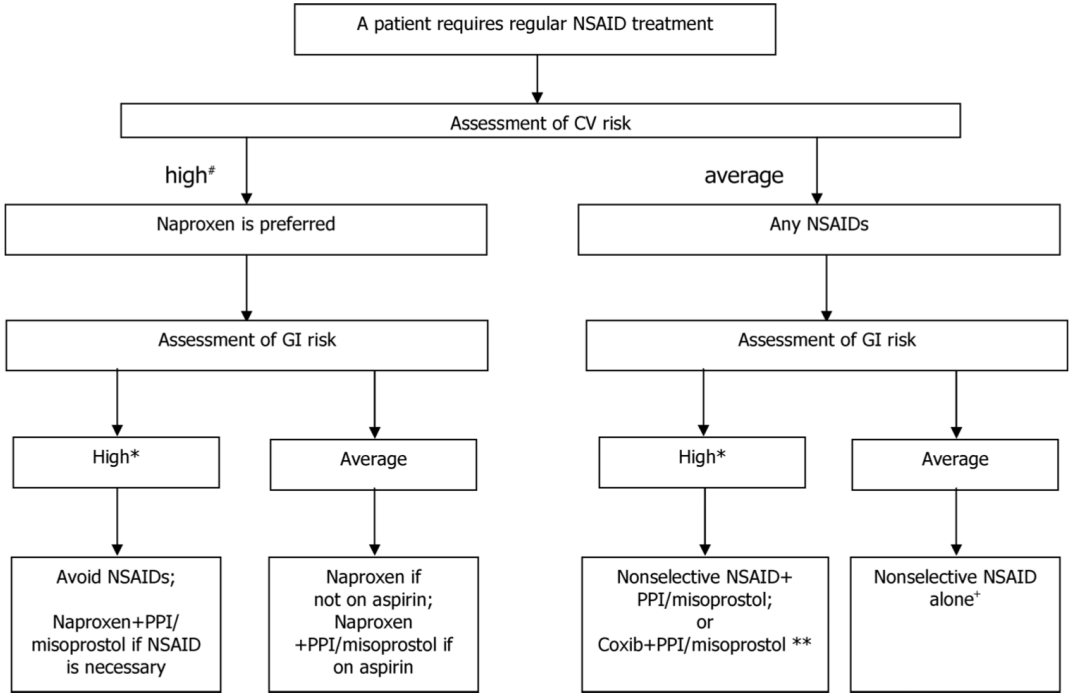

Figure 1. Management algorithm of patients on NSAIDs and aspirin. GI = gastrointestinal; CV = cardiovascular; NSAID = nonsteroidal antiinflammatory drug; PPI = proton pump inhibitor; coxib = cyclooxygenase-2 selective inhibitor. *High GI risk was defined as age ≥70 yr, prior upper GI event, and concomitant use of concomitant aspirin, corticosteroids, or anticoagulants. **Coxib + PPI/misoprostol was recommended for patients with prior complicated upper GI event or multiple GI risk factors. #High CV risk was defined as established coronary artery disease, any CV disease that required prophylactic low-dose aspirin, or an estimated 10-yr CV risk of greater than 20%. +A nonselective NSAID includes both naproxen and a nonselective NSAID.

PLOS ONE

RESEARCH ARTICLE

Risk of acute myocardial infarction during use of individual NSAIDs: A nested case-control study from the SOS project

Gwen M. C. Masclee[1], Huub Straatman[2], Andrea Arfè[3], Jordi Castellsague[4], Edeltraut Garbe[5], Ron Herings[2], Bianca Kollhorst[5], Silvia Lucchi[6], Susana Perez-Gutthann[4], Silvana Romio[3,7], René Schade[7], Tania Schink[5], Martijn J. Schuemie[7], Lorenza Scotti[3], Cristina Varas-Lorenzo[4], Vera E. Valkhoff[8], Marco Villa[6], Miriam C. J. M. Sturkenboom[9]*

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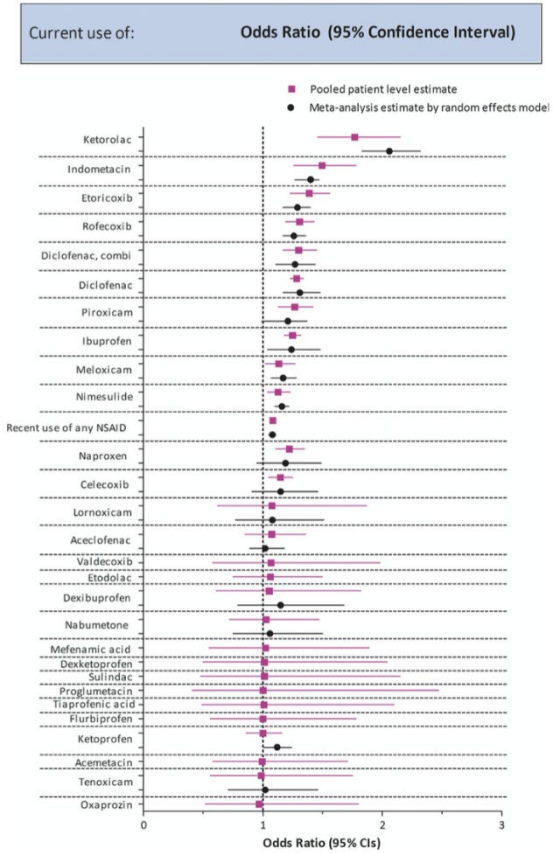
OPEN ACCESS

Citation: Masclee GMC, Straatman H, Arfè A, Castellsague J, Garbe E, Herings R, et al. (2018) Risk of acute myocardial infarction during use of individual NSAIDs: A nested case-control study

Abstract



GI TOXICITY

ANNALS of Hepatology

The Official Journal of the Mexican Association of Hepatology, the Latin-American Association for Study of the Liver and the Canadian Association for the Study of the Liver

March-A

Recent Advances i Non Steroidal Anti-i

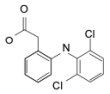
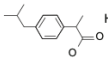
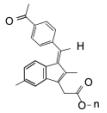
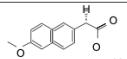
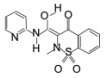
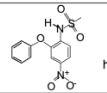
* Liver and Transplantation Unit, Montpellier School of Medici

ABSTRACT

Non-steroidal-anti-inflammatory drugs (NSAIDs) make a heterogenous pharmaco-therape drugs worldwide with various indications, modes of administration and increasing autome injury with variable severity. The recent identification of genetic markers might facilita hepatotoxicity risk.

Key words. Non-steroidal-anti-inflammatory drugs. NSAID. Hepatotoxicity. Drug-induced

Table 1. Characteristics of most common NSAIDs associated with hepatotoxicity.[1-11]

NSAID	NSAID Class	Molecular structure	Clinical Phenotype	Proposed mechanism	Frequency* LiverTox** (8) RUCAM Evaluation***	Increase transaminases Symptomatic hepatitis (Transaminases > 3N)
Diclofenac	Acetic acid derivatives		Acute hepatitis Hepatocellular	Metabolic-Idiosyncratic Increased toxic metabolic formation Mitochondrial dysfunction	34.1% > 50 cases	15% 2-4%
Ibuprofen	Propionic acid derivatives		Acute hepatitis Hepatocellular Cholestatic Vanishing bile duct syndrome	Metabolic-Idiosyncratic Mitochondrial dysfunction	14.6%	Same as placebo at low dosages but > 16% for higher dosages
Sulindac	Acetic acid derivatives		Acute hepatitis Cholestatic or mixed	Immunoallergic-Idiosyncratic	12.4% > 50 cases	Severe rare hepatitis 0.1% of users (5/100,000)
Acetylsalicylic acid	Salicylates		Acute hepatitis Hepatocellular Reye syndrome	Intrinsic toxicity-dose dependent Mitochondrial dysfunction	12%	
Naproxen	Propionic acid derivatives		Acute hepatitis Hepatocellular Cholestatic	Metabolic and Immunoallergic Idiosyncratic	11.1%	4% of users 9-12 cases/ 100,000
Piroxicam	Enolic acid derivatives		Acute hepatitis Cholestatic hepatocellular	Immunoallergic-Idiosyncratic Increased toxic metabolic formation	9.3%	3-18% of users 1-5/100,000
Nimesulide	Sulfonanilides		Acute hepatitis hepatocellular Cholestatic	Metabolic-Idiosyncratic Mitochondrial dysfunction	5.8% > 50 cases	15% <1%

** Frequencies are based on the WHO Program for International Drug Monitoring, Vigibase and on drug-induced liver injury registries from Europe and the US, total cases for NSAIDs = 6023: ** LiverTox.[8] *** RUCAM evaluation: ibuprofen; acetylsalicylic acid; naproxen; nimesulide.*

NSAIDS increase GI and CV events, but COX-2's increase mortality

Adverse outcomes in NSAIDs vs placebo*

Outcomes	NSAID	Event rates/y	Rate ratio (95% CI)†
Major vascular event‡	Coxib	1.15% vs 0.82%	1.37 (1.14 to 1.66)
	Naproxen	NA	0.93 (0.69 to 1.27)
	Diclofenac	NA	1.41 (1.12 to 1.78)
	Ibuprofen	NA	1.44 (0.89 to 2.33)
Upper GI event§	Coxib	0.38% vs 0.19%	1.81 (1.17 to 2.81)
	Naproxen	NA	4.22 (2.71 to 6.56)
	Diclofenac	NA	1.89 (1.16 to 3.09)
	Ibuprofen	NA	3.97 (2.22 to 7.10)
Heart failure hospitalization	Coxib	0.66% vs 0.26%	2.28 (1.62 to 3.20)
	Naproxen	NA	1.87 (1.10 to 3.16)
	Diclofenac	NA	1.85 (1.17 to 2.94)
	Ibuprofen	NA	2.49 (1.19 to 5.20)
All-cause mortality	Coxib	1.66% vs 1.42%	1.22 (1.04 to 1.44)
	Naproxen	NA	1.03 (0.71 to 1.49)
	Diclofenac	NA	1.20 (0.94 to 1.54)
	Ibuprofen	NA	1.61 (0.90 to 2.88)

**Coxib = selective cyclooxygenase-2 inhibitor; GI = gastrointestinal; NA = not applicable; NSAID = nonsteroidal antiinflammatory drug; other abbreviations defined in Glossary. Some coxib trials used a non-NSAID control rather than placebo.*

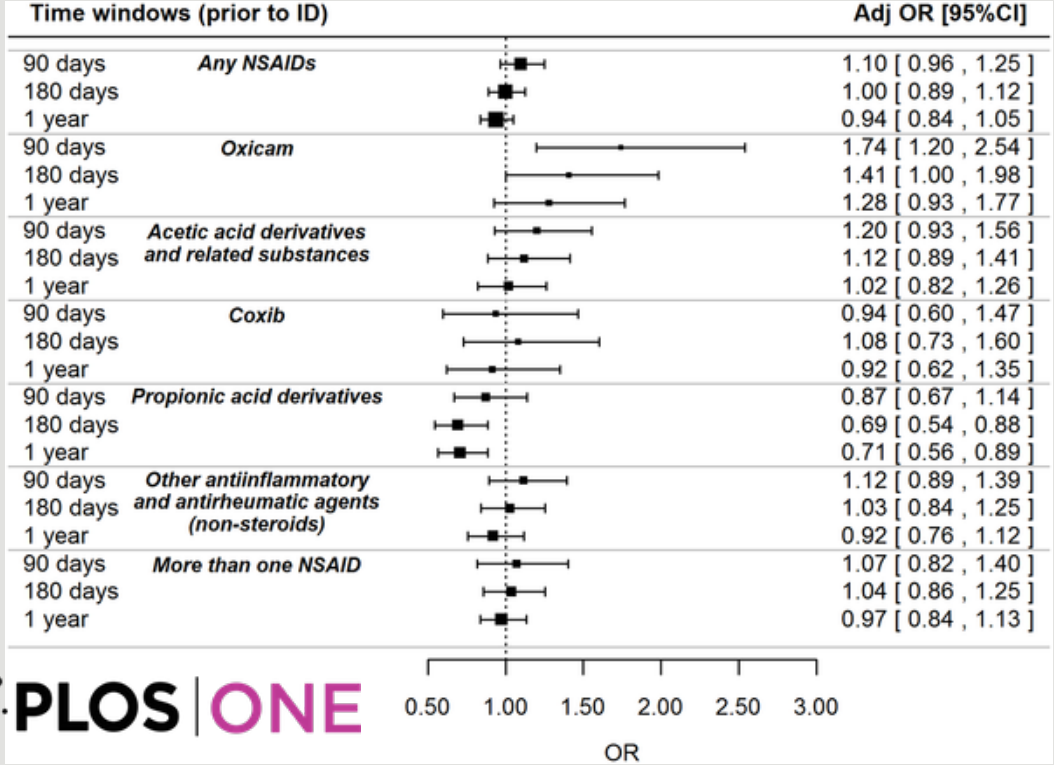
†Results for coxibs vs placebo are from direct treatment comparisons in 184 trials (n = 88 367). Results for traditional NSAIDs (naproxen, diclofenac, and ibuprofen) vs placebo are from direct treatment comparisons and indirect treatment comparisons based on trials of coxibs vs placebo and coxibs vs traditional NSAIDs.

‡Nonfatal myocardial infarction, nonfatal stroke, or vascular death.

§Perforation, obstruction, or bleeding.

KIDNEY DYSFUNCTION

Fig 2. Association between NSAIDs and risk of CKD, stratified by classes and time windows.

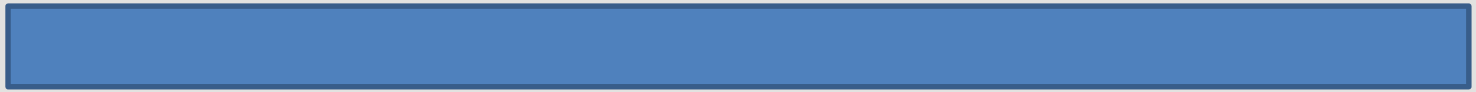


Ingrasciotta Y, Sultana J, Giorgianni F, Fontana A, Santangelo A, et al. (2015) Association of Individual Non-Steroidal Anti-Inflammatory Drugs and Chronic Kidney Disease: A Population-Based Case Control Study. PLOS ONE 10(4): e0122899. https://doi.org/10.1371/journal.pone.0122899
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0122899

My club checks LFTs and kidney function test periodically throughout the season in our athletes on NSAIDs.

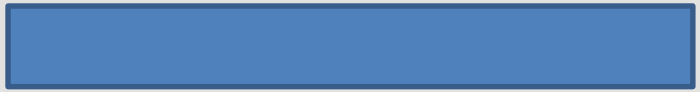
POLL OPEN

1 True



68.09%

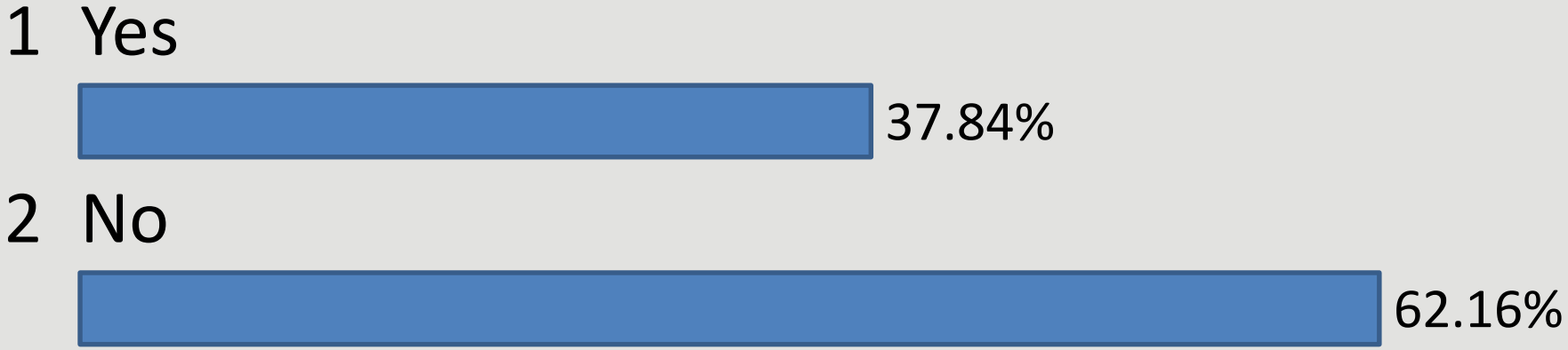
2 False



31.91%

POLL OPEN

For those that do…Ever find something that resulted in a decrease in dosage or d/c altogether?



Summary

- NSAID usage in athletes is common and low (but not zero) risk
- NSAID usage in our staff is common and higher risk
- Know your NSAIDs and tailor NSAID treatment to your particular patient.