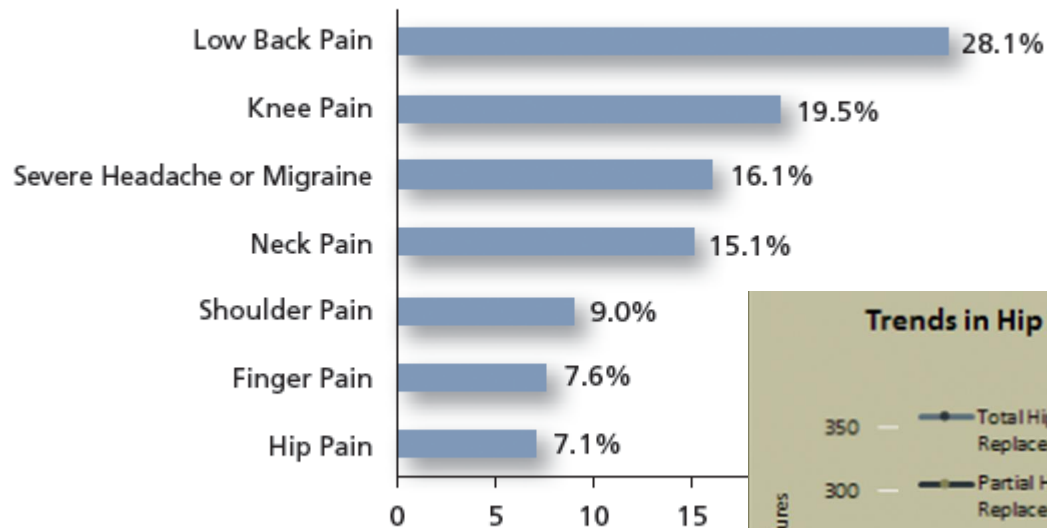


PAIN MANAGEMENT IN HIP SURGERY

Khoa D. Nguyen, MD, PhD
Dept. of Rheumatology, Cho Ray Hosital

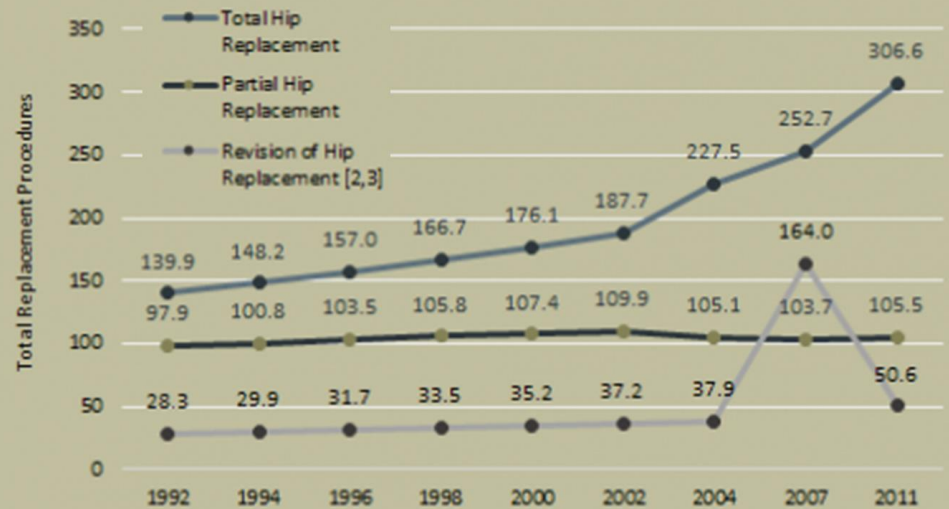
MUSCULOSKELETAL PAIN IS COMMON

Figure. Age-Adjusted Prevalence Rates of Select Causes of Chronic Pain in US Adults



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

Trends in Hip Replacement Procedures, All Ages, in the United States 1992-2011



Source: HCUP Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), 1991-2011. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp

Hip replacement increasing

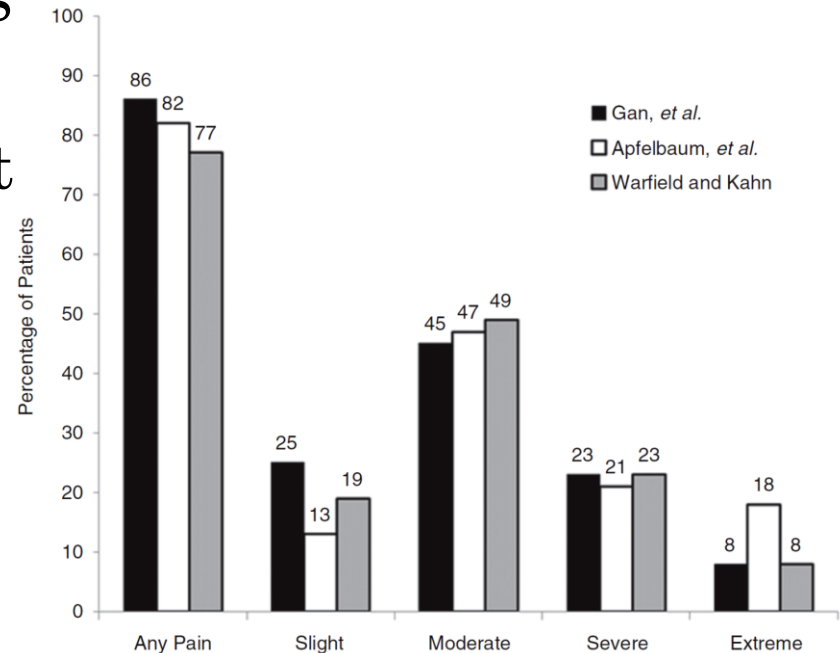
POSTOPERATIVE PAIN: INTRODUCTION

- Very common
- Causes acute effects and long-term consequences
- Should be alleviated as soon and as effective as possible
- Clinical pain management after surgery is far from being successful
- Perioperative and long-term pain control should be coordinated by
 - Anesthesiologists/orthopedics
 - Internists/rheumatologists



OPERATIVE PAIN – SCOPE OF THE PROBLEM

- Almost all patients experience pain after surgery, procedure, or injury
- Survey of 300 US adults undergoing surgery:
 - 86% experienced pain post surgery
 - 75% had moderate to extreme pain in the immediate postsurgical period
 - **74% still had pain post discharge**



POSTOPERATIVE PAIN: ACUTE EFFECTS

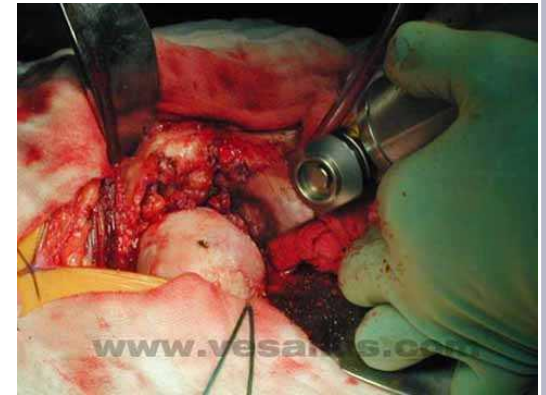
- Emotional and physical suffering for patients
- Sleep disturbance
- Respiratory side effects (decreased respiratory motion, inhibition of cough, sputum excretion)
- CV side effects (hypertension, arrhythmias)
- Increased oxygen consumption
- Impaired GI motility
- Delays mobilization and promotes thrombo-embolism
- Increased sympathetic activity

POSTOPERATIVE PAIN: CONSEQUENCES

- Poor wound healing
- Delay in long-term recovery
- Risk of behavioral changes
- **Severe acute pain is a risk factor for the development of chronic pain**
 - Up to 50% of pts with severe operative pain develop chronic pain

POSTOPERATIVE PAIN: ASSESSMENT

- Types (nociceptive, neuropathic, mixed)
- Severity: Using pain scales
- Comorbidities (pulmonary, CV, GI, renal conditions,...)
- Causes
 - Surgery related: Inflammation, tissue damage (inc. nerve injuries)
 - Underlying diseases: OA (hip/knee) osteoporosis, RA, AS, ...

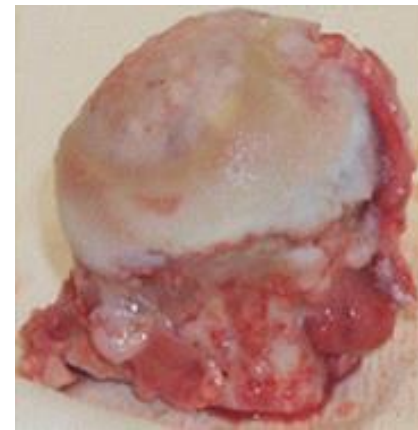


REASONS FOR HIP REPLACEMENT

- **Osteoarthritis: Most common, increasing prevalence**
- Trauma – Injury (inc. osteoporotic fractures)
- Rheumatoid arthritis, ankylosing spondylitis
- Osteonecrosis
- Other conditions that break down the hip joint.

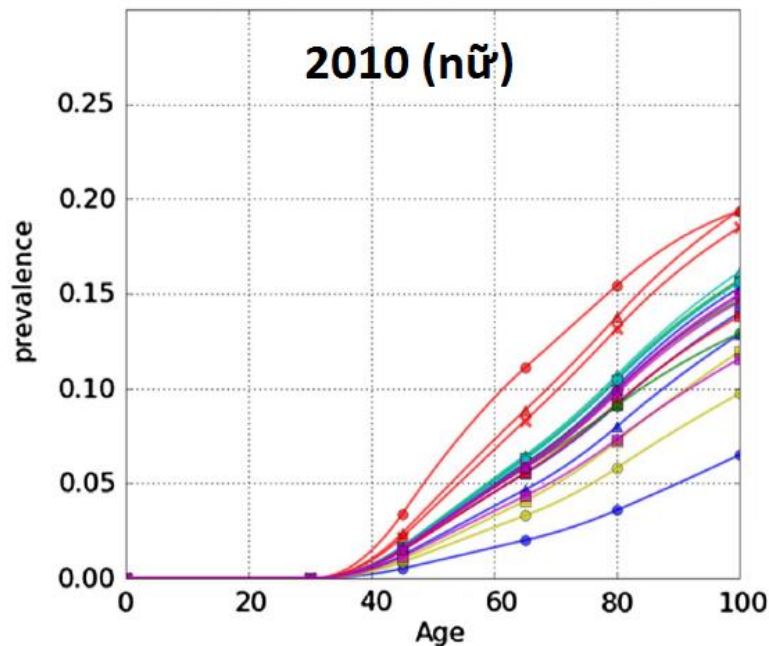
UNDERLYING CAUSES OF HIP SURGERY: HIP OSTEOARTHRITIS (OA)

- OA is one of the most common chronic conditions
 - Common among elderly
- 20-30% of people over age 70 suffer from OA of the hip
- Most common reason for total hip replacement

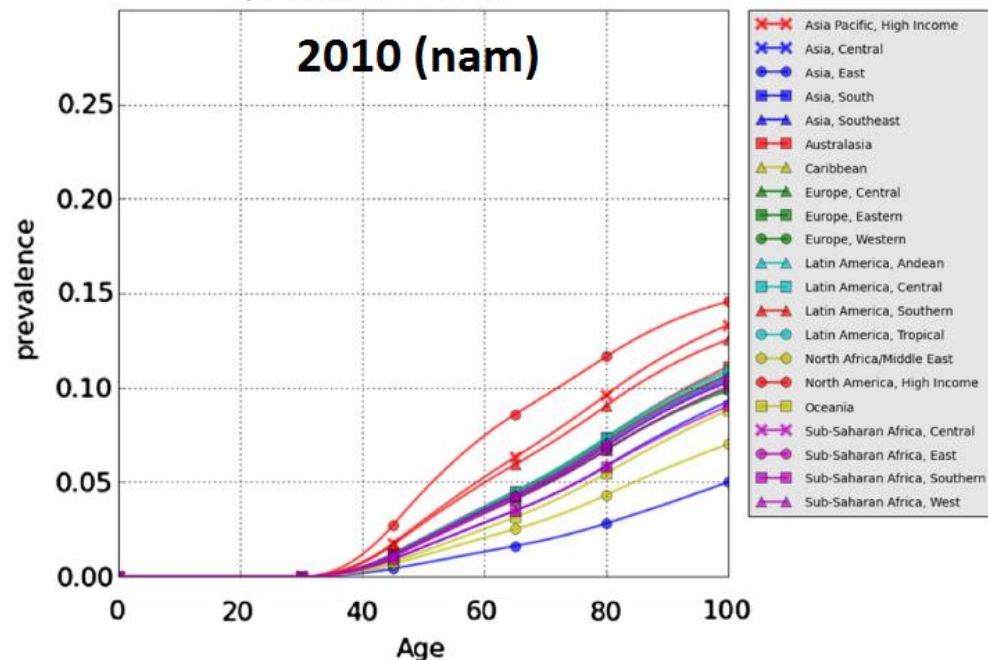


GLOBAL BURDEN OF HIP OA

Posterior osteoarthritis hip prevalence female

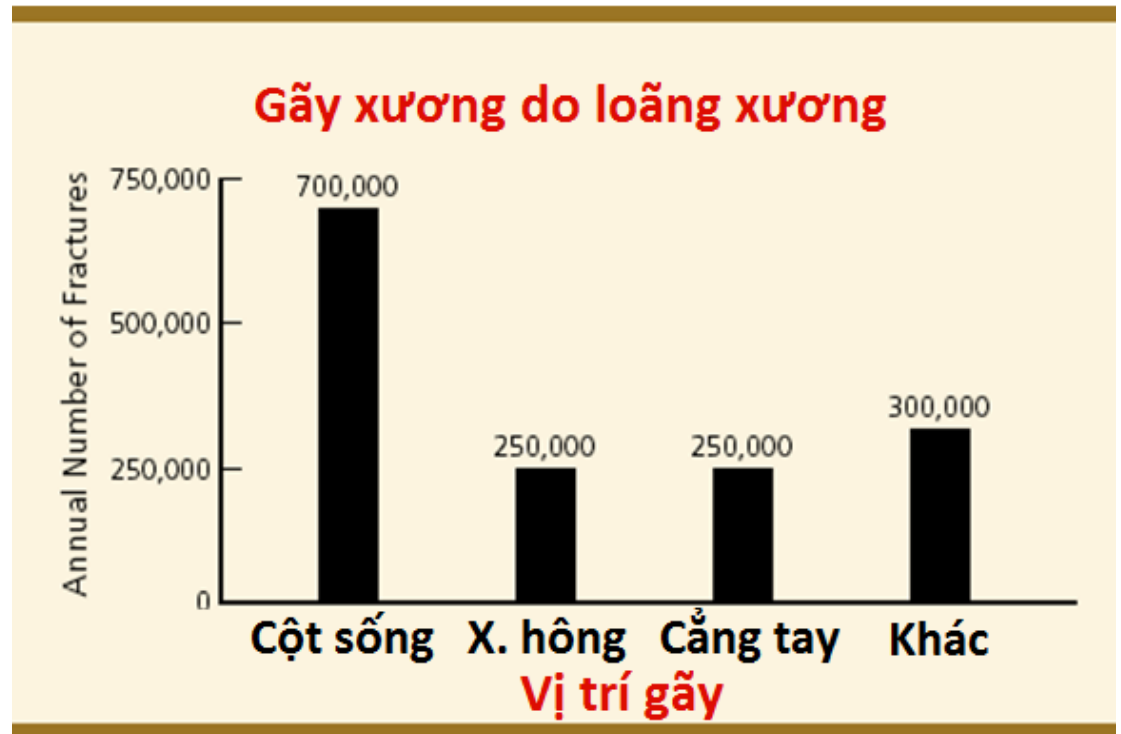
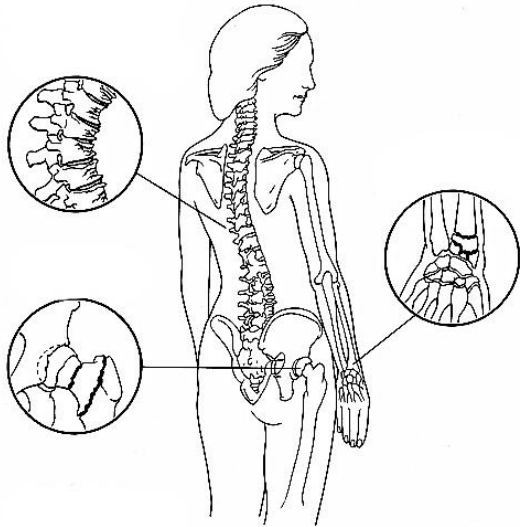


Posterior osteoarthritis hip prevalence male



The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study

HIP – A COMMON SITE OF OSTEOPOROTIC FRACTURES

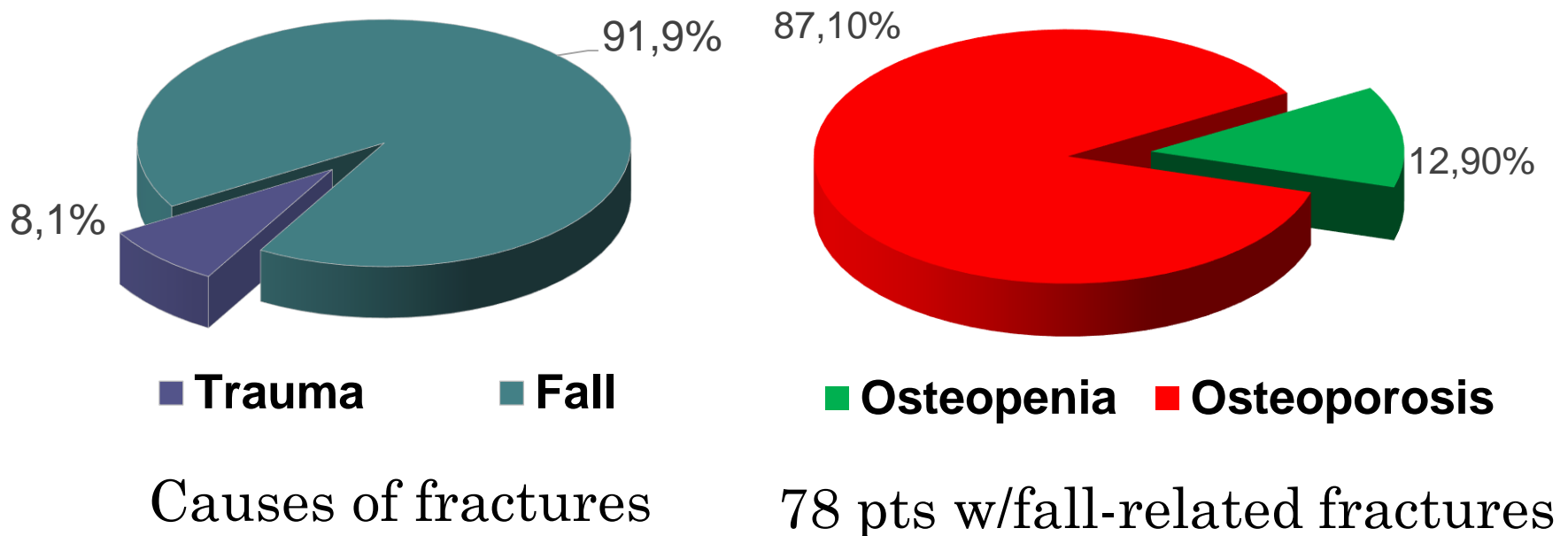


Estimated annual incidence of osteoporotic fractures (USA)

Riggs BL. Bone 1995;17(s5)

MOST PATIENTS WITH HIP FRACTURES HAVE OSTEOPOROSIS

(A survey of 148 patients with hip fractures, Cho Ray hospital, 2014)*



*H.T.K. Hoa & N.Đ. Khoa, Nội khoa Việt Nam, 2014

Vietnam

HỘI LOÃNG XƯƠNG THỂ GIỚI (IOF) DỰ BÁO: VIỆT NAM

CURRENT

- Population **92.4 million**
- Aged over 50 years **18%**
- Life expectancy **73 years**
- Hip fracture incidence per year **no data**
- Cost per hip fracture **1,000–4,000 USD**
- Number of DXA per million population **< 0.1**
- Fracture liaison services **not implemented**



PROJECTED 2050

- Population **111 million** ↑
- Aged over 50 years **41%** ↑
- Life expectancy **81 years** ↑

—■ number of hip fracture (000s)



Số phụ nữ trên 50 tuổi bị
Loãng xương
ước tính trên **7 triệu**
vào **2050**

GENERAL PAIN MANAGEMENT

- Pharmacological
 - Opioid
 - Non-opioid analgesics
 - Local anesthetics/procedures
- Non-pharmacological
 - Change/Adjust Position
 - Diversion Activities
 - Relaxation Techniques
 - Meditation
 - Acupuncture/Acupressure
 - Heat, cold, massage
 - Hypnosis
- Control of underlying causes



OPIOIDS

- Used to use high IV doses for operative pain → side effects and negative impact on operative recovery
- Still play an important role in the acute treatment of moderate to severe pain in the early postoperative period
- Common opioids:
 - Morphine
 - Hydromorphone
 - Fentanyl (IV, transdermal)
 - Tramadol
 - Oral opioids

OPIOID SIDE EFFECTS

- Nausea and vomiting
- Constipation
- Urinary retention
- Respiratory depression
- Apnea
- Sedation
- Confusion
- Tolerance
- Restricted Ambulation
- May increase risk of surgical infection



Longer Hospital
Stays

&

Increased
Costs

What are solutions for minimizing opioid use?

Practice Guidelines for Acute Pain Management in the Perioperative Setting

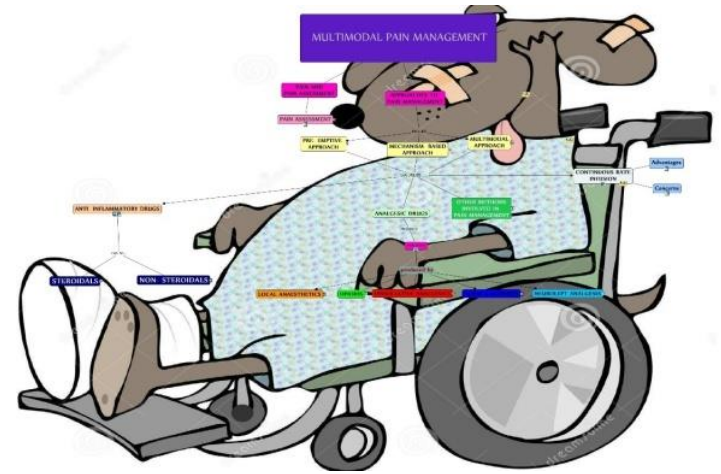
An Updated Report by the American Society of Anesthesiologists Task Force on Acute Pain Management

V. Multimodal Techniques for Pain Management

14. Whenever possible, anesthesiologists should use multimodal pain management therapy
 15. The following drugs should be considered as part of a postoperative multimodal pain management regimen:
 - COX-2 selective NSAIDs (COXIBs)
 - Nonselective NSAIDs
 - Acetaminophen
 - Calcium channel α -2- δ antagonists (e.g., gabapentin, pregabalin)
 16. Unless contraindicated, all patients should receive an around-the-clock regimen of NSAIDs, COXIBs, or acetaminophen
 17. Regional blockade with local anesthetics should be considered as part of a multimodal approach for pain management
 18. Dosing regimens should be administered to optimize efficacy while minimizing the risk of adverse events
 19. The choice of medication, dose, route, and duration of therapy should be individualized
-

MULTIMODAL THERAPY: WHAT IS IT?

- Synchronous administration of ≥ 2 pharmacological agents or approaches with distinct mechanisms of action



American Society of Anesthesiologists Task Force on Acute Pain Management. Practice Guidelines for Acute Pain Management in the Perioperative Setting.

Anesthesiology. 2012;116:248-273.

MULTIMODAL ANALGESIA

- The state-of-the-art is multimodal therapy with:
 - Opioids
 - IV
 - Intraspinal (IS)
 - Oral route
 - NSAIDs
 - APAP (Paracetamol)
 - Local anesthetics
 - Wound site infiltration or perfusion
 - Peripheral nerve infusions via catheters
 - Epidural
 - IV

MULTIMODAL THERAPY

○ Key Practice Guidelines Recommendations

Anesthesiologists who manage perioperative pain should, after thoughtfully considering the risks and benefits for the individual patient, use therapeutic options such as:

- Epidural or intrathecal opioids
- Systemic opioid patient-controlled analgesia (PCA)
- Regional anesthesia techniques

MULTIMODAL THERAPY

○ Key Practice Guidelines Recommendations

- Unless contraindicated, patients should receive an around-the-clock regimen of **nonsteroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors, or acetaminophen.**
- Dosing regimens should be administered to optimize efficacy while minimizing the risk for adverse events.
- The choice of medication, dose, route, and duration of therapy should be individualized.

PERIOPERATIVE PAIN MANAGEMENT

Technique	Examples	Advantages	Disadvantages
Non-opioid systemic analgesics	Acetaminophen (oral, rectal, injectable)	<ul style="list-style-type: none"> • Similar benefit to intravenous (IV) PCA opioid • Fewer ADRs 	<ul style="list-style-type: none"> • None noted
	Injectable NSAIDs	<ul style="list-style-type: none"> • Improved pain scores • Reduced analgesic use 	<ul style="list-style-type: none"> • NSAID risks / ADRs
	Oral NSAIDs (both non- and selective)	<ul style="list-style-type: none"> • Reduce opioid use and adverse effects 	<ul style="list-style-type: none"> • NSAID risks / ADRs
	Gabapentinoids (gabapentin or pregabalin)	Combined w/opioids → <ul style="list-style-type: none"> • Improved pain scores • Reduced analgesic use 	<ul style="list-style-type: none"> • None noted

Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council

Recommendation 15

- The panel recommends that clinicians provide adults and children with acetaminophen and/or nonsteroidal anti-inflammatory drugs (NSAIDs) as part of multimodal analgesia for management of postoperative pain in patients without contraindications (strong recommendation, high-quality evidence).

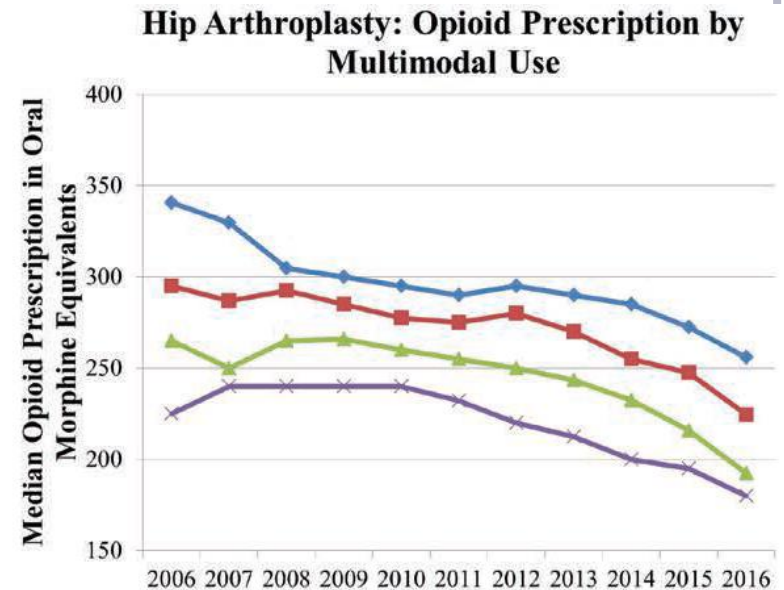
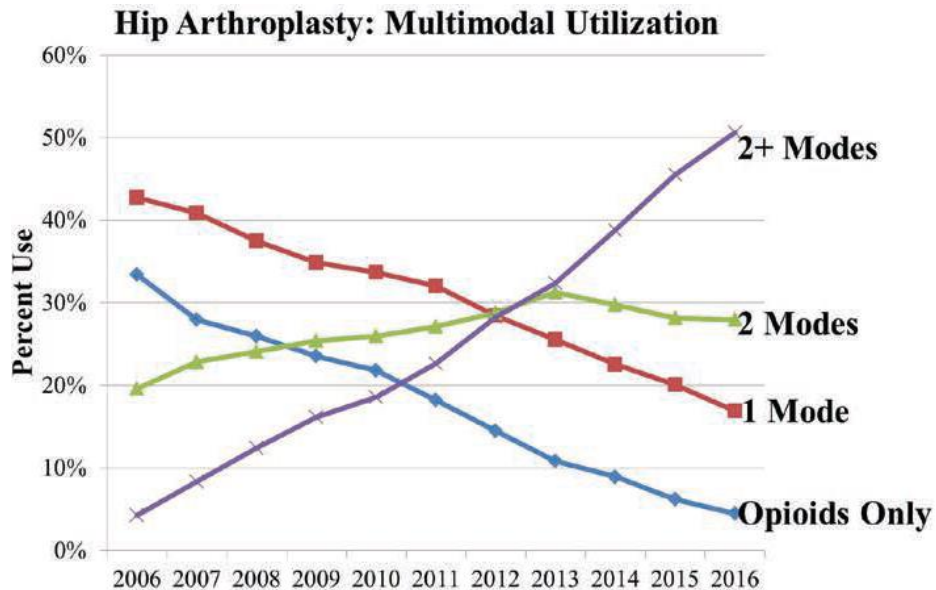
MULTIMODAL (“BALANCED”) ANALGESIA

○ Benefits:

- Improve analgesia
- Reduce opioid requirements (“opioid-sparing” effect)
- Thereby reduce the adverse effects of opioids.

Association of Multimodal Pain Management Strategies with Perioperative Outcomes and Resource Utilization

A Population-based Study



- Total hip/knee arthroplasties (N = 512,393 and N = 1,028,069)
- 85.6% (N = 1,318,165) of patients received multimodal analgesia
- Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors seemed to be the most effective modalities used.

MULTIMODAL APPROACHES: PARACETAMOL

- **Acetaminophen (APAP) – oral, single dose**
 - Cochrane review¹
 - 51 studies, 5762 patients, 3277 active, 2425 placebo
 - 50% ↓ in pain with 50% APAP group, 20% placebo group for 4 hours
 - A systematic review² identified 21 studies comparing APAP alone or in combination with NSAIDs and reported increased efficacy with the combination of 2 agents than w/ either alone
- **Acetaminophen – Parenteral**
 - Orthopedic surgery, laminectomy, abdominal, gynecological, cardiac, and thyroidectomy
 - Dosing: 1 gram IV, either single dose or every 6 hours
 - Summary APAP patients:
 - Improved patient satisfaction with pain control, lower morphine consumption (up to 61%) and decreased incidence of vomiting

¹Toms L et al. *Cochrane Database Syst Rev.* 2008;(4):CD004602.

²Ong CK et al. *Anesth Analg.* 2010;110(4):1170-1179.

Memis D et al. *J Crit Care.* 2010;25(3):458-462.

Macario A, Royal MA. *Pain Pract.* 2011;11(3):290-296.

MULTIMODAL APPROACHES: NSAIDS

- **Nonselective or Cox-2 selective NSAIDs**

- **Oral NSAIDs**

- Single dose oral ibuprofen¹ – Summary 72 randomized clinical trials (RCTs), 9168 patients: ≥ 50% pain relief in approximately half of patients with moderate to severe postoperative pain,
- COX-inhibitors

- **Injectable NSAIDs**

- Ketorolac and ibuprofen (studied in United States)
- Others: Diclofenac, meloxicam, ...
- Indicated for short-term moderate to severe acute pain that requires analgesia at the opioid level

- **Advantages**

- Significant reduction in pain
- Reduction in opioid consumption (~25-30%)

¹Derry C et al. *Cochrane Database Syst Rev.* 2009;(1):CD004234

1. Cassinelli EH et al. *Spine (Phila Pa 1976).* 2008;33(12):1313-1317.

2. Wong HY et al. *Anesthesiology.* 1993;78(1):6-14.

3. Southworth S et al. *Clin Ther.* 2009;31(9):1922-1935.

Combining Paracetamol (Acetaminophen) with Nonsteroidal Antiinflammatory Drugs: A Qualitative Systematic Review of Analgesic Efficacy for Acute Postoperative Pain

Cliff K. S. Ong, PhD,* Robin A. Seymour, PhD,† Phillip Lirk, MD,‡
and Alan F. Merry, MBChB, FANZCA, FPMANZCA, FRCA§

RESULTS: Twenty-one human studies enrolling 1909 patients were analyzed. The NSAIDs used were ibuprofen ($n = 6$), diclofenac ($n = 8$), ketoprofen ($n = 3$), ketorolac ($n = 1$), aspirin ($n = 1$), tenoxicam ($n = 1$), and rofecoxib ($n = 1$). The combination of paracetamol and NSAID was more effective than paracetamol or NSAID alone in 85% and 64% of relevant studies, respectively. The pain intensity and analgesic supplementation was $35.0\% \pm 10.9\%$ and $38.8\% \pm 13.1\%$ lesser, respectively, in the positive studies for the combination versus paracetamol group, and $37.7\% \pm 26.6\%$ and $31.3\% \pm 13.4\%$ lesser, respectively, in the positive studies for the combination versus the NSAID group. No statistical difference in median quality scores was found between experimental groups.

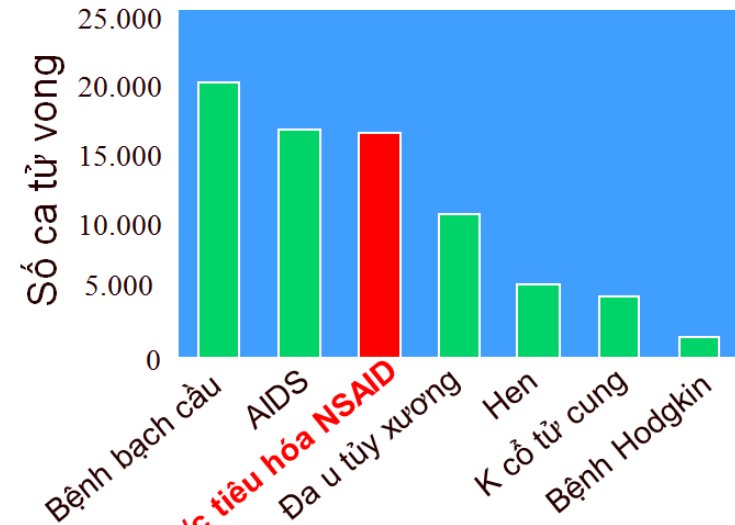
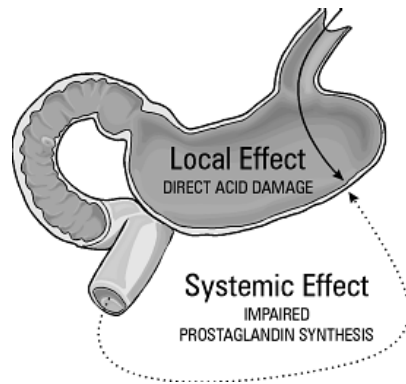
CONCLUSION: Current evidence suggests that a combination of paracetamol and an NSAID may offer superior analgesia compared with either drug alone. (Anesth Analg 2010;110:1170–9)

NSAIDS FOR OPERATIVE PAIN: RISKS

- **GI complications**
- **CV risk**
- Renal dysfunction
- Platelet dysfunction (maybe some risk w/ non-selective NSAIDs)
- Operative site bleeding (?)
- Others

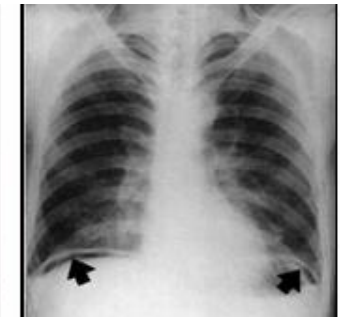
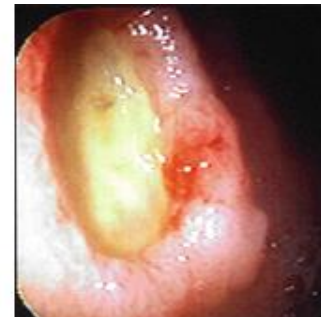
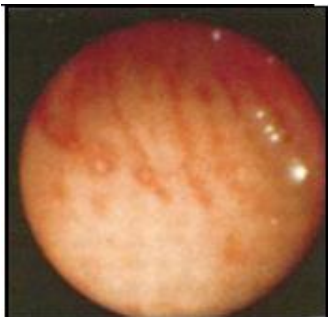
NSAID AND GI SIDE EFFECTS

- Nonspecific symptoms: dyspepsia, diarrhea
- Severe complications: Ulcer, bleeding, obstruction, maybe life threatening



Các nguyên nhân tử vong (Hoa Kỳ, 1997)

Wolfe et al., NEJM 340:1888-1899 (1999)



AMERICAN COLLEGE OF GASTROENTEROLOGY GUIDELINES FOR PREVENTION OF NSAID-RELATED ULCER COMPLICATIONS

Table 1. Patients at increased risk for NSAID GI toxicity

High risk

1. History of a previously complicated ulcer, especially recent
2. Multiple (>2) risk factors

Moderate risk (1–2 risk factors)

1. Age >65 years
2. High dose NSAID therapy
3. A previous history of uncomplicated ulcer
4. Concurrent use of aspirin (including low dose) corticosteroids or anticoagulants

Low risk

1. No risk factors

H. pylori is an independent and additive risk factor and needs to be addressed separately (see text and recommendations).

PREVENTION:

1. Prostaglandin (misoprostol)
2. H₂ receptor antagonists
3. PPI
4. COX-2 inhibitors
→ better GI safety than nsNSAIDs

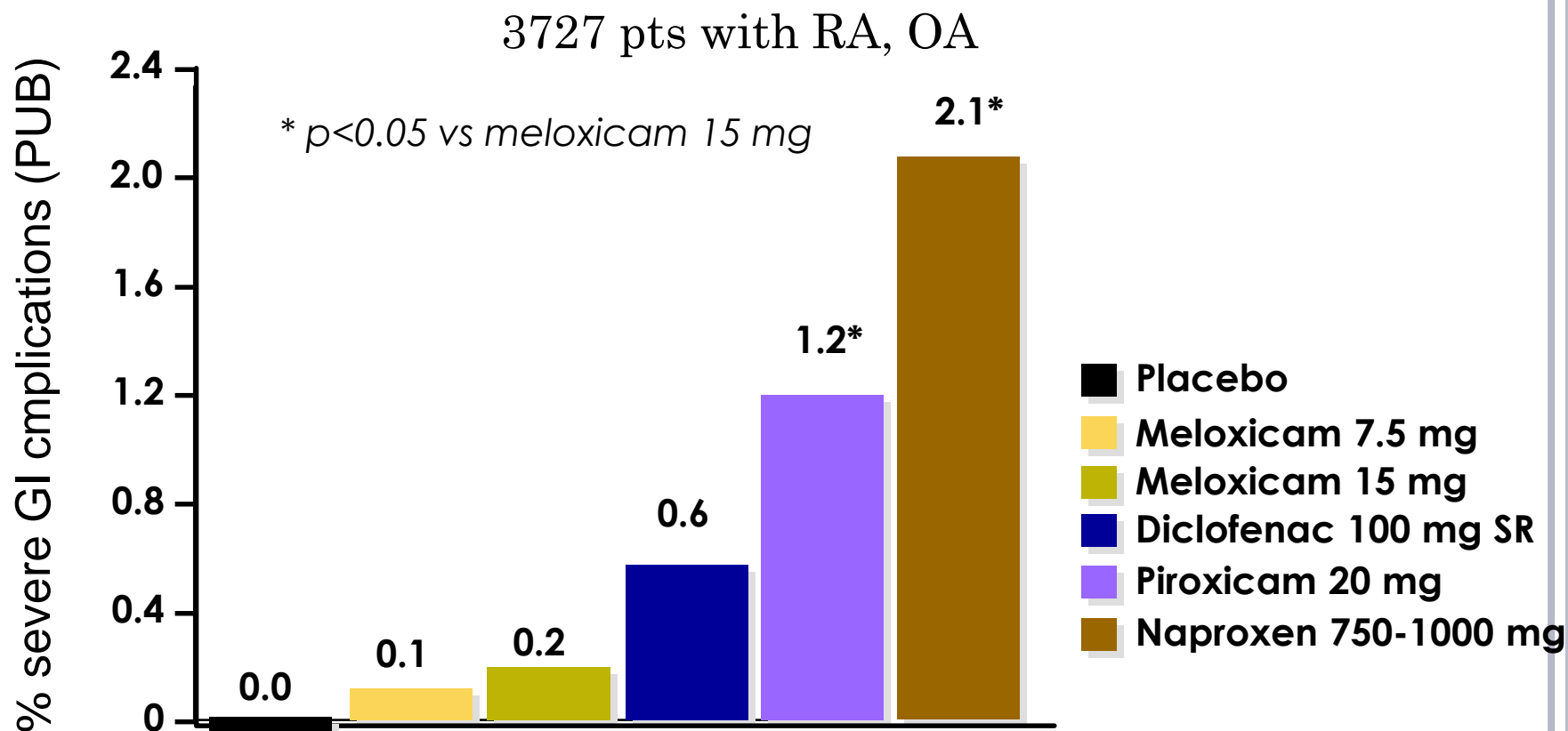
NON-SELECTIVE NSAIDs AND COX-2 SELECTIVE INHIBITORS

Classic NSAIDs (non-selective)	COX-2 somewhat selective	COX-2 selective
Aspirin (1853)* Phenylbutazone (1949) Indomethacin (1963) Ibuprofen (1969) Fenoprofen (1972) Ketoprofen (1972) Naproxen (1974) Tiaprofenic (1975) Sulindac (1977) Diclofenac (1977) Flurbiprofen (1977) Diflusal (1977) Piroxicam (1981) Tenoxicam (1981)	Nimesulide (1985) Acemetacin (1985) Nabumetone (1986) Etodolac (1987)	Meloxicam (1995) Nhóm COXIBs <ul style="list-style-type: none"> - Celecoxib (1999) - Rofecoxib (1999)* - Valdecoxib (2000)* - Parecoxib (2001) - Etoricoxib (2001) - Lumiracoxib (2002)
<p>Log [IC₅₀ ratio] (WHMA COX-2/COX-1)</p> <p>Các NSAIDs cổ điển</p> <p>Chọn lọc COX-2</p> <p>Chọn lọc COX-1</p> <p>Tỷ lệ ức chế COX-2 dưới 5 lần COX-1</p> <p>Tỷ lệ ức chế COX-2 hơn 5 lần COX-1</p> <p>Tỷ lệ ức chế COX-2 hơn 50 lần COX-1</p> <p>Tỷ lệ ức chế COX-2 hơn 50 lần COX-1</p> <p>NSAIDs in the 'Chọn lọc COX-1' group (from top to bottom): fenoprofen, ampyrone, ibuprofen, tolmetin, naproxen, aspirin, indomethacin, ketoprofen, suprofen, flurbiprofen, ketorolac.</p> <p>NSAIDs in the 'Chọn lọc COX-2' group (from top to bottom): celecoxib, nimesulide, etodolac, meloxicam, valdecoxib, etoricoxib, rofecoxib, lumiracoxib.</p>		

COMMONLY USED NSAIDs/COXIBS (IN VIETNAM)

DRUG	CLASS	ROUTES
Ketorolac	nsNSAID	Oral, injectable
Ibuprofen	nsNSAID	Oral
Piroxicam	nsNSAID	Oral, injectable
Diclofenac	nsNSAID	Oral, injectable
Meloxicam	COX-2 selective	Oral, injectable
Celecoxib	COX-2 selective/coxib	Oral
Etoricoxib	COX-2 selective/coxib	Oral

NSAIDs: DIFFERENT RISKS OF GI COMPLICATIONS

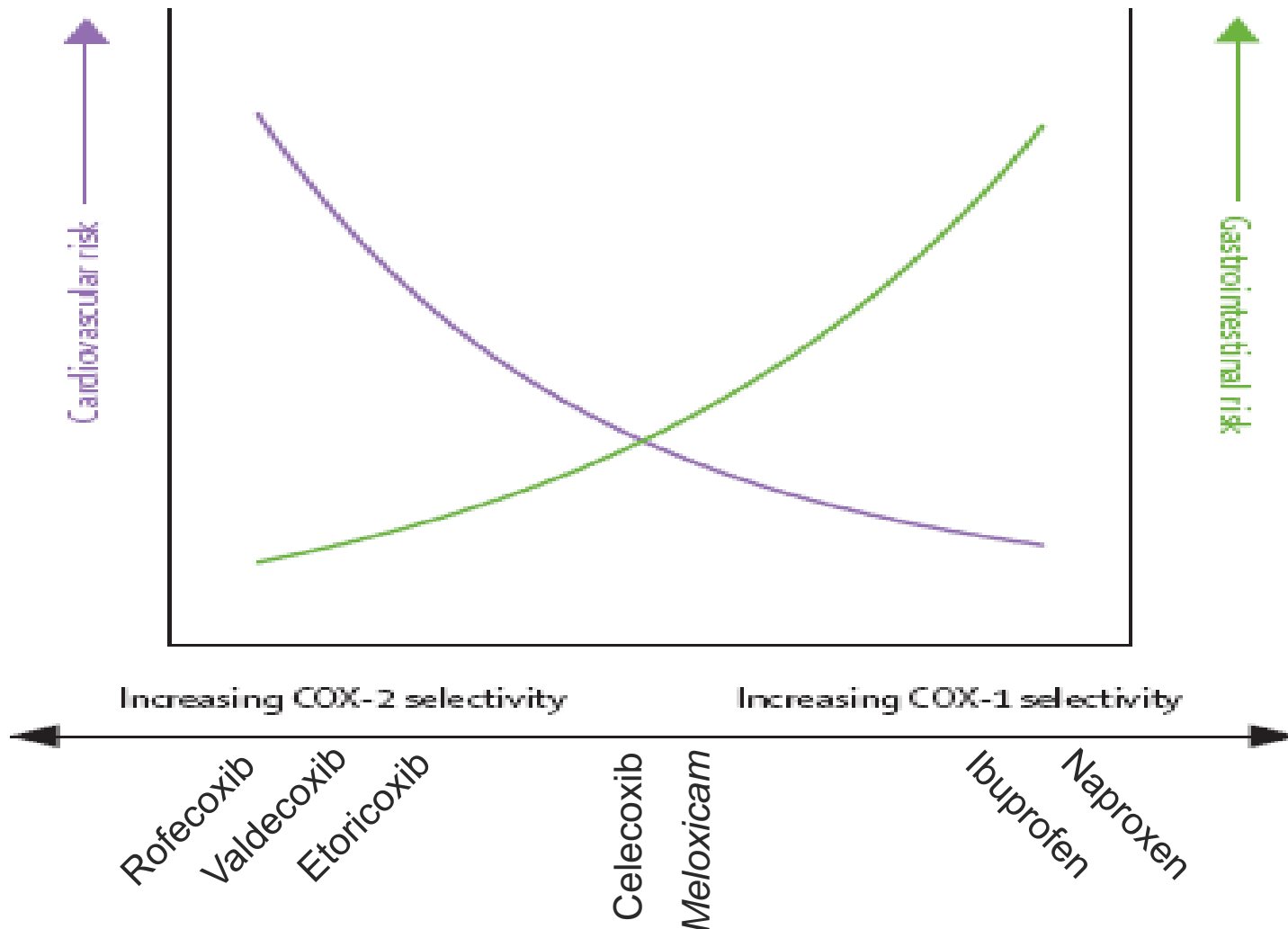


PUB: perforations, ulcerations and bleedings - Thủng, loét, và xuất huyết

RA: Rheumatoid arthritis - Viêm khớp dạng thấp

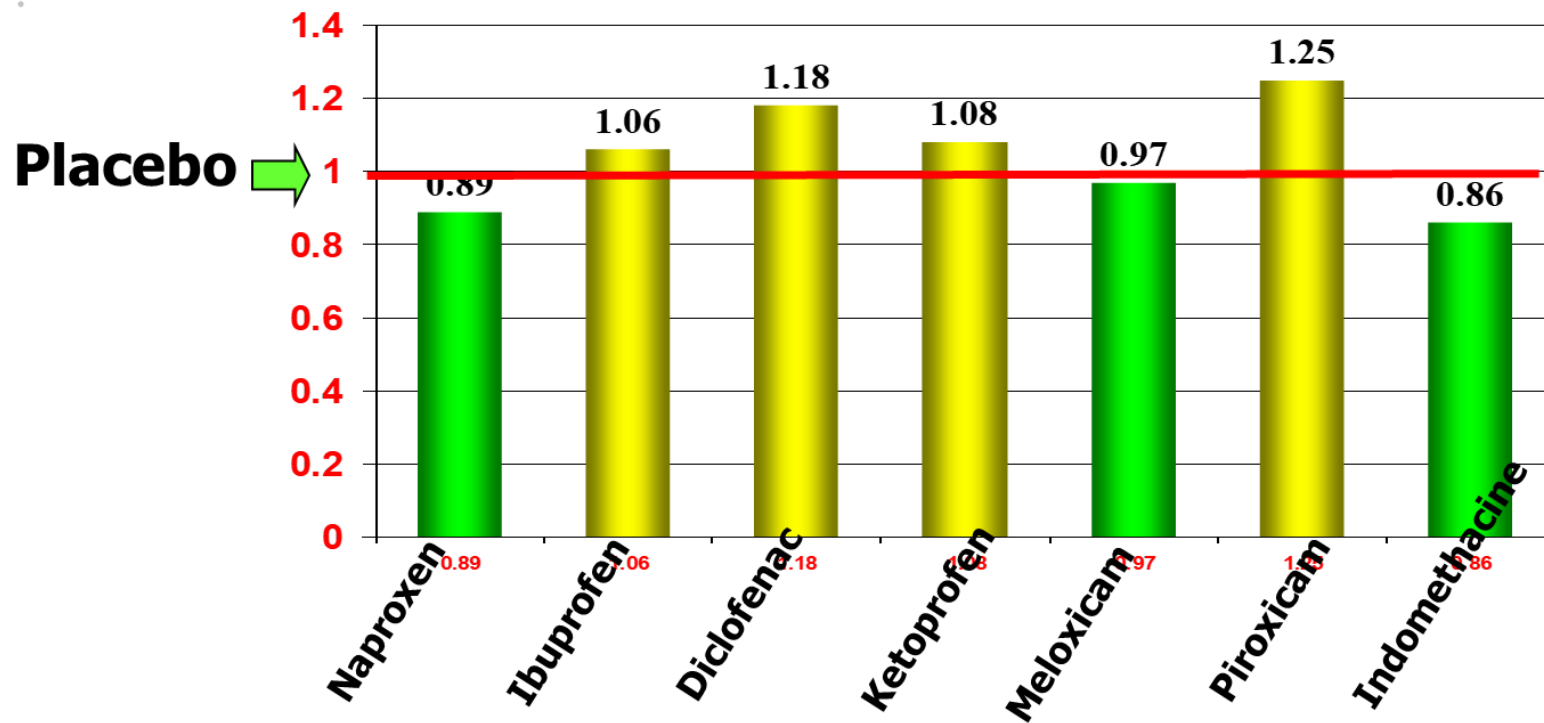
OA: Osteoarthritis - Thoái hóa khớp

NSAIDs: A NEED TO BALANCE BETWEEN GI AND CV RISKS



CV RISKS DIFFERENT AMONG NSAIDS

Multivar.adjusted odds ratio (MI risk)



NSAIDS AND CV RISKS: NO NSAID IS ABSOLUTELY SAFE

7/9/2015



Consumer Health Information
www.fda.gov/consumer

FDA Strengthens Warning of Heart Attack and Stroke Risk for Non-Steroidal Anti-Inflammatory Drugs

Next time you reach into the medicine cabinet seeking relief for a headache, backache or arthritis, be aware of important safety information for non-steroidal anti-inflammatory drugs.

FDA is strengthening an existing warning in prescription drug labels and over-the-counter (OTC) Drug Facts labels to indicate that non-steroidal anti-inflammatory drugs (NSAIDs) can increase the chance of a heart attack or stroke, either of which can lead to death. Those serious side effects can occur as early as the first few weeks of using an NSAID, and the risk might rise the longer people take NSAIDs. (Although aspirin is also an NSAID, this revised warning doesn't apply to aspirin.)



The Risks and What's New
Prescription NSAIDs are an important treatment for the symptoms of many debilitating conditions, including osteoarthritis, rheuma-

tion, some combination medicines that relieve various symptoms, such as multi-symptom cold products, contain NSAIDs.

"Be careful not to take more than

TAKE HOME MESSAGE

- Acute pain is common in hip surgery. But, many pts may also have chronic pain before and after surgery due to underlying conditions (OA, RA, AS, osteoporosis, osteonecrosis)
- To optimize perioperative pain control, multi-modal therapies are recommended, which should include paracetamol and/or a NSAID (unless contraindicated)
- nsNSAIDs and COX-2 selective inhibitors are highly effective as part of multi-modal pain therapies, but benefits and risks of adverse effects need to be weighed

THANK YOU