

To the Editor:

Although we commend the AHA Scientific Statement by Antman and colleagues¹ on the use of NSAIDs, we are concerned that it overgeneralizes meta-analytic findings from chronic studies of arthritis to two other patient populations in which ample, high-quality clinical evidence has proven the benefits of NSAID use. The first population comprises patients with acute pain, particularly postoperative pain. Beginning with the 1992 AHCPR clinical practice guideline on treatment of acute pain after surgery or trauma-- the first US federal evidence-based clinical practice guideline on any topic --routine postoperative use of NSAIDs for acute pain control has been consistently recommended as a means to reduce opioid dose requirements and opioid-related side effects. Evidence supporting this “multimodal,” opioid-sparing approach includes meta-analyses of RCTs in which adverse events such as myocardial infarction have been monitored prospectively in many thousands of patients given brief (<1 week) courses of NSAIDs.² Such studies have not observed a cardiac safety signal. In fact, RCTs as recently as last year³ document improved outcomes such as quicker extubation and less inotrope use after coronary artery bypass graft operations in patients whose opioid requirements are reduced by coadministration of NSAIDs such as diclofenac.

Patients with cancer pain comprise the second large population placed at risk by stigmatizing NSAID use. The World Health Organization method for cancer pain relief is based upon a three-step “ladder” in which the first step is an NSAID. Steps two and three involve addition of weak or strong opioids, respectively, when pain is poorly controlled. The efficacy and population-based effectiveness of this strategy have been confirmed in numerous clinical studies, and it is the foundation for palliative care pharmacotherapy worldwide. At least part of the benefit of this method results from reduction of opioid requirements: the side effects of opioid therapy are often dose-limiting and commonly impair health-related quality of life in patients with cancer.⁴

Examples of overgeneralization of pharmacoepidemiologic observations from one group to another, with consequent detriment to the public welfare, have been seen before.⁵ Recent scientific statements based upon meta-analyses of chronic dosage in patients with

arthritis should not deter the selective, appropriate, evidence-based use of NSAIDs in acute and cancer-related pain.

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2. Forrest JB, Camu F, Greer H, Kehlet H, Abdalla M, Bonnet F, Ebrahim S, Escobar G, Jage J, Pocock S, Velo G, Langman MJS, Poro GB, Samama MM, Heitlinger E, for the Point Investigators. Ketorolac, diclofenac, and ketoprofen are equally safe for pain relief after major surgery. *Br J Anaesthesia*. 2002;88 (2): 227-233.
3. Maddali MM, Kurian E, Fahr J. Extubation time, hemodynamic stability, and postoperative pain control in patients undergoing coronary artery bypass surgery: an evaluation of fentanyl, remifentanyl, and nonsteroidal antiinflammatory drugs with propofol for perioperative and postoperative management. *J Clin Anesth*. 2006;18:605-610.
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5. Kao LW, Kirk MA, Evers SJ, Rosenfeld SH. Droperidol, QT prolongation, and sudden death: what is the evidence? *Ann Emerg Med*. 2003; 41: 546-558.

Response to Colucci/Carr/Wright, Javelin Pharmaceuticals

Drs. Colucci, Carr, and Wright express concern about the AHA Scientific Statement on the Use of NSAIDs because they fear it might lead to underuse of NSAIDs in patients who require acute pain control in surgical settings or who require relief of pain in the setting of malignancy.

We wish to reiterate that the AHA Scientific Statement on the Use of NSAIDs focused its recommendations for patients with known cardiovascular disease or risk factors for ischemic heart disease. We agree that in selected clinical scenarios such as the management of acute postoperative pain or chronic pain from malignancy, experienced clinicians may weigh the benefits and risks and conclude that treatment with a nonsteroidal anti-inflammatory drug is clinically justified. In the letter by Drs. Colucci, Carr, and Wright, they cite the benefits of quicker extubation and less inotropic use after CABG operations in patients whose opioid requirements are reduced by co-administration of an NSAID such as diclofenac. However, they fail to point out that reports also exist of increased risk when patients following surgery CABG surgery were treated with the COX-2 inhibitor valdecoxib.¹ Thus, the benefits of nonsteroidal anti-inflammatory drugs for the management of acute postoperative pain is not a simple picture. Once again, we reiterate our recommendations for a stepped care approach to the selection of NSAIDs in patients with known cardiovascular disease or risk factors for ischemic heart disease as described in Figure 7 of our Scientific Statement. A guiding principle is to administer NSAIDs to the lowest risk patients using drugs with the lowest risk profile at the lowest dose and for the shortest period of time.

1. Furberg et al. Parecoxib, valdecoxib and cardiovascular risk. *Circulation* 2005;111:249