

## List of References

1. Sturkenboom MCJM, Dieleman JP, Verhamme K, Straus S. Cardiovascular safety of selective COX-2 inhibitors and conventional NSAIDs, Report to CGB; Jan-2005.
2. Velentgas P, West W, Cannuscio CC, Watson DJ, Walker AM. Cardiovascular risk of selective cyclooxygenase-2 inhibitors and other non-aspirin non-steroidal anti-inflammatory medications [Abstract]. *Pharmacoepidemiology and Drug Safety* 2006;15:641-52.
3. Cooper C. Osteoarthritis and related disorders - epidemiology. In: Klippel JH, Dieppe PA, Arnett FC, et al., eds. *Rheumatology*. Volume 2. 2 ed. London: Mosby, 1998.
4. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum* 1998;41(5):778-99.
5. Yelin E, Callahan LF. The economic cost and social and psychological impact of musculoskeletal conditions. *Arthritis Rheum* 1995;38(10):1351-62.
6. Felson DT, Lawrence RC, Hochberg MC, McAlindon T, Dieppe PA, Minor MA, et al. Osteoarthritis: new insights, part 2: treatment approaches. *Ann Intern Med* 2000;133(9):726-37.
7. Managing Osteoarthritis: New ACR guidelines. *Women's Health in Primary Care* 2001;4(1):97-9.
8. Manek NJ. Medical management of osteoarthritis. *Mayo Clin Proc* 2001;76:533-9.
9. Sarzi-Puttini P, Cimmino MA, Scarpa R, Caporali R, Parazzini F, Zaninelli A, et al. Osteoarthritis: an overview of the disease and its treatment strategies. *Semin Arthritis Rheum* 2005;35(Suppl.1):1-10.
10. Reginster J-Y. Prevalence and burden of arthritis. *Rheumatology* 2002;41(Suppl 1):3-6.
11. Elders MJ. The increasing impact of arthritis on public health. *J Rheumatol* 2000;27(Suppl 60):6-8.
12. Nagle TL, Ting G. Chronic pain: key populations, market size, and the driving force of drug reformulations. *Pain Study #1* ed. Waltham, Massachusetts: Decision Resources, Inc., 2005:1-127.
13. Dieppe P, Buckwalter JA. Osteoarthritis and related disorders - management of limb joint osteoarthritis. In: Klippel JH, Dieppe PA, Arnett FC, et al., eds. *Rheumatology*. 2 ed. London: Mosby, 1998:
14. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, et al. Guidelines for the medical management of osteoarthritis: Part I. osteoarthritis of the hip. *Arthritis Rheum* 1995;38(11):1535-40.

15. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, et al. Guidelines for the medical management of osteoarthritis: Part II. osteoarthritis of the knee. *Arthritis Rheum* 1995;38(11):1541-6.
16. Jawad ASM. Analgesics and osteoarthritis: are treatment guidelines reflected in clinical practice? *Am J Ther* 2005;12:98-103.
17. American college of rheumatology subcommittee on osteoarthritis guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum* 2000;43(9):1905-15.
18. Case JP, Galiunas AJ, Block JA. Lack of efficacy of acetaminophen in treating symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled comparison trial with diclofenac sodium. *Arch Intern Med* 2003;163:169-78.
19. Wolfe F, Zhao S, Lane N. Preference for nonsteroidal antiinflammatory drugs over acetaminophen by rheumatic disease patients: a survey of 1,799 patients with osteoarthritis, rheumatoid arthritis, and fibromyalgia. *Arthritis Rheum* 2000;43(2):378-85.
20. Pincus T, Swearingen C, Cummins P, Callahan LF. Preference for nonsteroidal antiinflammatory drugs versus acetaminophen and concomitant use of both types of drugs in patients with osteoarthritis. *J Rheumatol* 2000;27(4):1020-7.
21. Towheed TE, Maxwell L, Judd MG, Catton M, Hochberg MC, Wells G. Acetaminophen for osteoarthritis (review) the cochrane collaboration®. John Wiley & Sons, Ltd, 2006:1-56.
22. Lee WM. Acetaminophen and the US acute liver failure study group: lowering the risks of hepatic failure. *Hepatology* 2004;40:6-9.
23. Garcia Rodriguez L, Hernández-Díaz S. Relative risk of upper gastrointestinal complications among users of acetaminophen and nonsteroidal anti-inflammatory drugs. *Epidemiology* 2001;12(5):570-6.
24. Bannwarth B. Gastrointestinal Safety of Paracetamol: is there any cause for concern? *Expert Opin Drug Saf* 2004;3(4):269-72.
25. Rahme E, Pettitt D, LeLorier J. Determinants and sequelae associated with utilization of acetaminophen versus traditional nonsteroidal antiinflammatory drugs in an elderly population. *Arthritis & Rheum* 2002;46(11):3046-54.
26. Forman JP, Stampfer MJ, Curhan GC. Non-Narcotic Analgesic Dose and Risk of Incident Hypertension in US Women. *Hypertension* 2005;46:500-7.
27. Forman JP, Rimm EB, Curhan CC. Frequency of analgesic use and risk of hypertension among men. *Arch Intern Med* 2007;167:394-9.
28. Olsen Y, Daumit GL, Ford DE. Opioid prescriptions by U.S. primary care physicians from 1992 to 2001. *Journal of Pain* 2006;7(4):225-35.

29. King T, Ossipov MH, Vanderah TW, Porreca F, Lai J. Is paradoxical pain induced by sustained opioid exposure an underlying mechanism of opioid antinociceptive tolerance? *Neurosignals* 2005;14:194-205.
30. Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. *J Rheumatol* 1999;26(Suppl 26):18-24.
31. Coda BA, Bonica JJ. General considerations of acute pain. In: Loeser JD, Butler SH, Chapman CR, Turk DC, eds. *Bonica's management of pain*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2001:222-40.
32. Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs. *N Engl J Med* 1999;340(24):1888-99.
33. Scheiman JM. Unmet needs in non-steroidal anti-inflammatory drug-induced upper gastrointestinal diseases. *Drugs* 2006;66(Suppl 1):15-21.
34. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature New Biology* 1971;231:232-5.
35. Robert A, Nezamis JE, Lancaster C, Hanchar AJ. Cytoprotection by prostaglandins in rats: prevention of gastric necrosis produced by alcohol, HCl, NaOH, hypertonic NaCl, and thermal injury. *Gastroenterology* 1979;77:433-43.
36. Robert A, Nezamis JE, Lancaster C, Hanchar AJ. Gastric cytoprotective property of prostaglandins [Abstract]. *Gastroenterology* 1977;72(5):1121.
37. Redfern JS, Feldman M. Role of endogenous prostaglandins in preventing gastrointestinal ulceration: induction of ulcers by antibodies to prostaglandins. *Gastroenterology* 1989;96(2, Pt. 2):596-605.
38. Griffin MR, Scheiman JM. Prospects for changing the burden of nonsteroidal anti-inflammatory drug toxicity. *Am J Med* 2001;110(1A):33S-7S.
39. Bombardier C, Laine L, Reicin A, Shapiro D, Burgos-Vargas R, Davis B, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *N Engl J Med* 2000;343(21):1520-8.
40. Schnitzer TJ, Burmester GR, Mysler E, Hochberg MC, Doherty M, Ehsam E, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the therapeutic arthritis research and gastrointestinal event trial (TARGET), reduction in ulcer complications: randomised controlled trial. *Lancet* 2004;364:665-74.
41. Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. *JAMA* 2000;284(10):1247-55.
42. Singh G, Fort JG, Goldstein JL, Levy RA, Hanrahan PS, Bello AE, et al. Celecoxib versus naproxen and diclofenac in osteoarthritis patients: SUCCESS-I study. *Am J Med* 2006;119(3):255-66.

43. Goldstein JL, Eisen GM, Burke TA, Pena BM, Lefkowitz J, Geis GS. Dyspepsia tolerability from the patients' perspective: a comparison of celecoxib with diclofenac. *Aliment Pharmacol Ther* 2002;16:819-27.
44. Goldstein JL, Aisenberg J, Berger M, Dodge WE. Effects of concomitant aspirin (81 mg qd) on incidence of gastric and/or duodenal ulcers in healthy subjects taking celecoxib or naproxen: a randomized, placebo-controlled trial [Abstract]. *Gastroenterology* 2006;130:562.
45. Rahme E, Bardou M, Dasgupta K, Toubouti Y, Barkun A. Gastrointestinal effects of rofecoxib and celecoxib versus NSAIDs among patients on low dose aspirin [Abstract]. *Gastroenterology* 2004;126((Suppl 2)):17.
46. Gastrointestinal review highlights of the class study (2001) . <http://www/fda.gov/ohrms/dockets> (accessed 12 Jan 2006)
47. Farkouh ME, Kirshner H, Harrington RA, Ruland S, Verheugt FWA, Schnitzer TJ, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the therapeutic arthritis research and gastrointestinal event trial (TARGET), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004;364:675-84.
48. Pilotto A, Franceschi M, Vitale DF, Zaninelli A, Masotti G, Rengo F. Upper gastrointestinal symptoms and therapies in elderly out-patients, users of non-selective NSAIDs or coxibs. *Aliment Pharmacol Ther* 2005;22:147-55.
49. Larkai EN, Smith JL, Lidsky MD, Graham DY. Gastrointestinal mucosa and dyspeptic symptoms in arthritic patients during chronic nonsteroidal anti-inflammatory drug use. *Am J Gastroenterol* 1987;82(11):1153-8.
50. Brun J. Nonsteroidal anti-inflammatory drug-associated dyspepsia: The scale of the problem. *American Journal of Medicine* 2001;110(1A):12s-3s.
51. Larkai EN, Smith JL, Lidsky MD, Sessoms SL, Graham DY. Dyspepsia in NSAID users: the size of the problem. *J Clin Gastroenterol* 1989;11(2):158-62.
52. Bombardier C, Lane L, Reicin A, Watson D, Ramey DR, Regan P. Fewer gastrointestinal protective agents, procedures, and hospitalizations with rofecoxib vs. naproxen in the VIGOR (VIOXX GI outcomes research) study [Abstract]. *Arthritis Rheum* 2000;4(Suppl 9):S225.
53. Bresalier RS, Sandler RS, Quan H, Bolognese JA, Oxenius B, Horgan K, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Eng J Med* 2005;352:1-11.
54. Nussmeier NA, Whelton AA, Brown MT, Langford RM, Hoeft A, Parlow JL, et al. Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery. *N Engl J Med* 2005;352(11):1081-91.
55. Solomon SD, McMurray JJ, Pfeffer MA, Wittes J, Fowler R, Finn P, et al. Cardiovascular risk associated with Celecoxib in a clinical trial for colorectal adenoma prevention. *N Engl J Med* 2005;352(11):1071-80.

56. Kearney P, Baigent C, Godwin H, Emberson J, Patrono C. Do selective cyclooxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomized trials. *BMJ* 2006;1-7.
57. Hernandez-Diaz S, Varas-Lorenzo C, Rodriguez LAG. Non-steroidal antiinflammatory drugs and the risk of acute myocardial infarction. *Basic Clinical Pharmacology & Toxicology* 2006;98:266-74.
58. McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *JAMA* 2006;296(13):E1-E12.
59. García Rodríguez LA, González-Pérez A. Long-term use of non-steroidal anti-inflammatory drugs and the risk of myocardial infarction in the general population. *BMC Med* 2005;3(17):1-6.
60. Memo to Galson S from Jenkins JK, Seligman PJ: Analysis and recommendations for Agency action regarding nonsteroidal anti-inflammatory drugs and cardiovascular risk, 2005.
61. Food and Drug Administration. COX-2 selective (includes Bextra, Celebrex, and Vioxx) and non-selective non-steroidal anti-inflammatory drugs (NSAIDS) (April 7, 2005). <http://www.fda.gov/cder/drug/infopage/cox2/> (accessed Feb 13, 2007)
62. Grosser T, Fries S, FitzGerald GA. Biological basis for the cardiovascular consequences of COX-2 inhibition: therapeutic challenges and opportunities. *J Clin Invest* 2006;116(1):4-15.
63. Mitchell JA, Lucas R, Vojnovic I, Hasan K, Pepper JR, Warner TD. Stronger inhibition by nonsteroidal anti-inflammatory drugs of cyclooxygenase-1 in endothelial cells than platelets offers an explanation for increased risk of thrombotic events. *FASEB J* 2006;20:2468-75.
64. Anning PB, Coles B, Morton J, Wang H, Uddin J, Morrow JD, et al. Nitric oxide deficiency promotes vascular side effects of cyclooxygenase inhibitors. *Blood* 2006;108(13):4059-62.
65. Aw T-J, Haas SJ, Liew D, Krum H. Meta-analysis of cyclooxygenase-2 inhibitors and their effects on blood pressure. *Arch Intern Med* 2005;165:490-6.
66. Mitchell JA, Warner TD. COX isoforms in the cardiovascular system: understanding the activities of non-steroidal anti-inflammatory drugs. *Nature Reviews* 2006;5:75-86.
67. Flavahan NA. Balancing prostanoid activity in the human vascular system. *Trends in Pharmacological Sciences* 2006;28(3):106-10.
68. Pope JE, Anderson JJ, Felson DT. A meta-analysis of the effects of nonsteroidal anti-inflammatory drugs on blood pressure. *Arch Intern Med* 1993;153:477-84.

69. Gurwitz JH, Avorn J, Bohn RL, Glynn RJ, Monane M, Mogun H. Initiation of antihypertensive treatment during nonsteroidal anti-inflammatory drug therapy. *JAMA* 1994;272(10):781-6.
70. Whelton A, White W, Bello A, Puma J, Fort J. Effects of celecoxib and rofecoxib on blood pressure and edema in patients  $\geq 65$  years of age with systemic hypertension and osteoarthritis. *Am J Cardiol* 2002;90:959-63.
71. Sánchez-Borges M, Caballero-Fonseca F, Capriles-Hulett A. Safety of etoricoxib, a new cyclooxygenase 2 inhibitor, in patients with nonsteroidal anti-inflammatory drug-induced urticaria and angioedema. *Ann Allergy Asthma Immunol* 2005;95:154-8.
72. Sánchez-Borges M, Capriles-Hulett A, Caballero-Fonseca F. Adverse reactions to selective cyclooxygenase-2 inhibitors (Coxibs). *American Journal of Therapeutics* 2004;11(6):494-500.
73. Picado C. Non-steroidal anti-inflammatory drugs-induced urticaria and angioedema: more research on mechanisms needed. *Clin Exp Allergy* 2005;35:698-9.
74. Simon RA, Stevenson DD. Cross-reactivity of cyclooxygenase 2 inhibitors in patients with a history of cutaneous reactions to cyclooxygenase 1 inhibitors. *Ann Allergy Asthma Immunol* 2005;94(1):8-11.
75. Grattan CEH. Aspirin sensitivity and urticaria. *Clinical and Experimental Dermatology* 2003;28:123-7.
76. Sanchez-Borges M, Caballero-Fonseca F, Capriles-Hulett A. Tolerance of nonsteroidal anti-inflammatory drug-sensitive patients to the highly specific cyclooxygenase 2 inhibitors rofecoxib and valdecoxib. *Ann Allergy Asthma Immunol* 2005;94:34-8.
77. Nettis E, Colanardi MC, Ferrannini A, Vacca A, Tursi A. Short-term tolerability of etoricoxib in patients with cutaneous hypersensitivity reactions to nonsteroidal anti-inflammatory drugs. *Ann Allergy Asthma Immunol* 2005;95:438-42.
78. La Grenade L, Lee L, Weaver J, Bonnel R, Karwoski C, Governale L, et al. Comparison of reporting of Stevens-Johnson syndrome and toxic epidermal necrolysis in association with selective COX-2 inhibitors. *Drug Safety* 2005;28(10):917-24.
79. Szczeklik A, Nizankowska E, Bochenek G, Nagraba K, Mejza F, Swierczynska M. Safety of specific COX-2 inhibitor in aspirin-induced asthma. *Clinical and Experimental Allergy* 2001;31:219-25.
80. Gyllfors P, Bochenek G, Overholt J, Drupka D, Kumlin M, Sheller J, et al. Biochemical and clinical evidence that aspirin-intolerant asthmatic subjects tolerate the cyclooxygenase 2-selective analgetic drug celecoxib. *J Allergy Clin Immunol* 2003;111(5):1116-21.

81. Puerto Rico Package Circular: VOLTAREN (Novartis) (diclofenac sodium) enteric-coated tablets 25 mg, 50 mg, and 75 mg. (updated labeling in effect July 2005): 2005.
82. Rostom A, Goldkind L, Laine L. Nonsteroidal anti-inflammatory drugs and hepatic toxicity: a systematic review of randomized controlled trials in arthritis patients. *Clinical Gastroenterology and Hepatology* 2005;3(5):489-98.
83. Fries S, Grosser T, Price TS, Lawson JA, Kapoor S, DeMarco S, et al. Marked interindividual variability in the response to selective inhibitors for Cyclooxygenase-2. *Gastroenterology* 2006;130:55-64.
84. Rooney PJ, Capell HA, Paterson S, Buchanan WW, Dick WC. Continued use of non-steroidal anti-inflammatory drugs: an index of clinical efficacy. *Br J Clin Pharmacol* 1978;5:453-5.
85. Walker AM, Chan K-W, Yood RA. Patterns of interchange in the dispensing of non-steroidal anti-inflammatory drugs. *J Clin Epidemiol* 1992;45(2):187-95.
86. Crichton B, Green M. GP and patient perspectives on treatment with non-steroidal anti-inflammatory drugs for the treatment of pain in osteoarthritis. *Curr Med Res Opin* 2002;18(2):92-6.
87. Knott L. Treating osteoarthritis in practice - the TOP study. *Curr Med Res Opin* 2000;16(2):147-52.
88. Moride Y, Ducruet T, Rochon S, Lavoie F. Persistency of use of COX-2-specific inhibitors and non-specific non-steroidal anti-inflammatory drugs (NSAIDs) in Quebec. *Rheumatology* 2003;42(Suppl 3):iii17-iii22.
89. Rahme E, Toubouti Y, Hunsche E. Therapy switching and associated costs in elderly patients receiving COX-2 selective inhibitors or non-selective non-steroidal anti-inflammatory drugs in Quebec, Canada. *Rheumatology* 2006;45:903-10.
90. Zhao SZ, Wentworth C, Burke TA, Makuch RW. Drug switching patterns among patients with rheumatoid arthritis and osteoarthritis using COX-2 specific inhibitors and non-specific NSAIDs. *Pharmacoepidemiology and Drug Safety* 2004;13:277-87.
91. Harley C, Wagner S. Persistence with Cox-2 inhibitors in managed care: an analysis of claims data. *Managed Care Interface* 2003:38-44.
92. Schnitzer TJ, Kong SX, Mavros P, Mitchell JH, Straus WL, Watson DJ, et al. Persistence of use of selective COX-2 inhibitors versus nonselective NSAIDs: Analyses of a large pharmacy database in the united states [Abstract]. *EULAR* 2002;1.
93. Wolfe F, Michaud K, Burke TA, Zhao SZ. Longer use of COX-2-specific inhibitors compared to nonspecific nonsteroidal antiinflammatory drugs: A longitudinal study of 3639 patients in community practice. *J Rheumatol* 2004;31(2):355-8.

94. Langman M, Kahler KH, Kong SX, Zhang Q, Finch E, Bentkover JD, et al. Drug switching patterns among patients taking non-steroidal anti-inflammatory drugs: a retrospective cohort study of a general practitioners database in the United Kingdom. *Pharmacoepidemiol Drug Saf* 2001;10:517-24.
95. Hunt RH, Harper S, Watson DJ, Yu C, Quan H, Lee M, et al. The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events. *Am J Gastroenterol* 2003;98(8):1725-33.
96. Sift R, Van Staa T-P, Abenham L, Ebner D. A study of the longitudinal utilization and switching-patterns of non-steroidal anti-inflammatory drugs using a pharmacy based approach. *Pharmacoepidemiol Drug Saf* 1997;6:263-8.
97. Cannon CP, Curtis SP, FitzGerald GA, Krum H, Kaur A, Bolognese JA, et al. Cardiovascular outcomes with etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison. *Lancet* 2006;368:1771-81.
98. Watson DJ, Bolognese JA, Yu C, Krupa D, Curtis S. Use of gastroprotective agents and discontinuations due to dyspepsia with the selective cyclooxygenase-2 inhibitor etoricoxib compared with non-selective NSAIDs. *Curr Med Res Opin* 2004;20(12):1899-908.
99. Moore RA, Derry S, Makinson GT, McQuay HJ. Tolerability and adverse events in clinical trials of celecoxib in osteoarthritis and rheumatoid arthritis: systematic review and meta-analysis of information from company clinical trial reports. *Arthritis Res Ther* 2005;7(3):R644-R665.
100. Pally RM, Seger W, Adler JL, Ettlinger RE, Quaidoo EA, Lipetz R, et al. Etoricoxib reduced pain and disability and improved quality of life in patients with chronic low back pain: a 3 month, randomized, controlled trial. *Scand J Rheumatol* 2004;33:257-66.
101. Tugwell P, Wells G, Strand V, Maetzel A, Bombardier C, Crawford B, et al. Clinical improvement as reflected in measures of function and health-related quality of life following treatment with leflunomide compared with methotrexate in patients with rheumatoid arthritis: sensitivity and relative efficiency to detect a treatment effect in a twelve-month, placebo-controlled trial. *Arthritis Rheum* 2000;43(3):506-14.
102. Ehrich EW, Bolognese JA, Watson DJ, Kong SX. Effect of rofecoxib therapy on measures of health-related quality of life in patients with osteoarthritis. *Am J Man Care* 2001;7(6):609-16.
103. Sprangers MAG, de Begt EB, Andries F, van Agt HME, Bijl RV, de Boer JB, et al. Which chronic conditions are associated with better or poorer quality of life. *Journal of Clinical Epidemiology* 2000;53:895-907.



104. Ricci JA, Stewart WF, Chee E, Leotta C, Foley K, Hochberg MC. Pain exacerbation as a major source of lost productive time in US workers with arthritis. *Arthritis and Rheumatism* 2005;53(5):673-81.
105. Capone MK, Sciulli MG, Tacconelle S, Grana M, Ricciotti E, Renda G, et al. Pharmacodynamic interaction of naproxen with low-dose aspirin in healthy subjects. *J Am Coll Cardiol* 2005;45(8):1295-301.
106. Cannon CP, Curtis SP, Bolognese JA, Laine L. Clinical trial design and patient demographics of the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) Study Program: Cardiovascular outcomes with etoricoxib versus diclofenac in patients with osteoarthritis and rheumatoid arthritis. *Am Heart J* 2006;152(2):237-45.
107. Wolfe F, Mitchell DM, Sibley JT, Fries JF, Bloch DA, Williams CA, et al. The mortality of rheumatoid arthritis. *Arthritis Rheum* 1994;37(4):481-94.
108. New information for healthcare professionals concomitant use of ibuprofen and aspirin (Sept 8, 2006). [http://www.fda.gov/cder/drug/InfoSheets/HCP/ibuprofen\\_aspirinHCP.htm](http://www.fda.gov/cder/drug/InfoSheets/HCP/ibuprofen_aspirinHCP.htm) (accessed Feb 13, 2007)
109. Warner TD, Giuliano F, Vojnovic I, Bukasa A, Mitchell JA, Vane JR. Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: a full in vitro analysis. *Proc Natl Acad Sci USA* 1999;96:7563-8.
110. Riendeau D, Percival MD, Brideau C, Charleson S, Dube D, Ethier D, et al. Etoricoxib (MK-0663): preclinical profile and comparison with other agents that selectively inhibit cyclooxygenase-2. *J Pharmacol Exp Ther* 2001;296(2):558-66.
111. McAdam BF, Catella-Lawson F, Mardini IA, Kapoor S, Lawson JA, FitzGerald GA. Systemic biosynthesis of prostacyclin by cyclooxygenase (COX)-2: the human pharmacology of a selective inhibitor of COX-2. *Proc Natl Acad Sci USA* 1999;96:272-7.
112. Van Hecken A, Schwartz JI, Depré M, De Lepeleire I, Dallob A, Tanaka W, et al. Comparative inhibitory activity of rofecoxib, meloxicam, diclofenac, ibuprofen and naproxen on COX-2 versus COX-1 in healthy volunteers. *J Clin Pharmacol* 2000;40:1-12.
113. Dallob A, Hawkey CJ, Greenberg H, Wight N, De Schepper P, Waldman S, et al. Characterization of etoricoxib, a novel, selective COX-2 inhibitor. *J Clin Pharmacol* 2003;43:573-85.
114. Emery P, Zeidler H, Kvien KT, Guslandi M, Naudin R, Stead H, et al. Celecoxib versus diclofenac in long-term management of rheumatoid arthritis: randomized double-blind comparison. *Lancet* 1999;354:2106-11.

115. Sikes DH, Agrawal NM, Zhao WW, Kent JD, Recker DP, Verburg KM. Incidence of gastroduodenal ulcers associated with valdecoxib compared with that of ibuprofen and diclofenac in patients with osteoarthritis. *Eur J Gastroenterol Hepatol* 2002;14(10):1101-11.
116. Pavelka K, Recker DP, Verburg KM. Valdecoxib is as effective as diclofenac in the management of rheumatoid arthritis with a lower incidence of gastrointestinal ulcers: results of a 26-week trial. *Rheumatol* 2003;42(10):1207-15.
117. ICH topic E 9 Statistical Principles for clinical trials ICH harmonised tripartite guideline (September, 1998). <http://www.emea.eu.int/pdfs/human/ich/036396en.pdf> (accessed Feb 22, 2006)
118. Armitage P, Colten T. *Encyclopedia of Biostatistics*. New York: John Wiley Publishers, 1998:1739-40.
119. Piaggio G, Elourne DR, Altman DG, Pocock SJ, Evans SJW. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA* 2006;295(10):1152-60.
120. Clopper CJ, Pearson ES. The use of Confidence or fiducial limits illustrated in the case of the binomial. *Biometrika* 1934;26(4):404-13.
121. Therneau TM, Grambsch PM. Testing proportional hazards. In: Dietz K, Gail M, Krickeberg K, Tsiatis A, Samet J, eds. *Modeling survival data: extending the Cox model*. New York: Springer, 2000:127-52.
122. Bellamy N. WOMAC osteoarthritis index: a user's guide. In: London, Ontario: Western Ontario and McMaster Universities, 1995:1-32.
123. Smith SC, Jr., Blair SN, Bonow RO, Brass LM, Cerqueira MD, Dracup K, et al. AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular Disease: 2001 update. *J Am Coll Cardiol* 2001;38(5):1581-3.
124. American college of rheumatology subcommittee on osteoarthritis guidelines. Recommendation for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum* 2000;43(9):1905-15.
125. Neiman H. Wolters Kluwer health, custom study - NSAID/PPI compliance, note: the study was conducted using two cohorts of patients age 50 and above, over an 18 month time period (June 2002 - December 2003, May 2005 - November 2006).
126. Watson DJ, Yu Q, Bolognese JA, Reicin AS, Simon TJ. The upper gastrointestinal safety of rofecoxib vs. NSAIDs: an updated combined analysis. *Curr Med Res Opin* 2004;20(10):1539-48.
127. Henry D, Lim LLY, Rodriguez LAG, Gutthann SP, Carson JL, Griffin M, et al. Variability in risk of gastrointestinal complications with individual non-steroidal anti-inflammatory drugs: results of a collaborative meta-analysis. *BMJ* 1996;312:1563-6.

128. Lanas A, García-Rodríguez LA, Arroyo MT, Gomollón F, Feu F, González-Pérez A, et al. Risk of upper gastrointestinal ulcer bleeding associated with selective cyclo-oxygenase-2 inhibitors, traditional non-aspirin non-steroidal anti-inflammatory drugs, aspirin and combinations. *Gut* 2006;55:1731-8.
129. Patrono C, Patrignani P, García Rodríguez LA. Cyclooxygenase-selective inhibition of prostanoid formation: transducing biochemical selectivity into clinical read-outs. *J Clin Invest* 2001;108(1):7-13.
130. Catella-Lawson F, Reilly MP, Kapoor SC, Cucchiara AJ, DeMarco S, Tournier B, et al. Cyclooxygenase inhibitors and the antiplatelet effects of aspirin. *N Engl J Med* 2001;345(25):1809-17.
131. Dubois RW, Melmed GY, Henning JM, Laine L. Guidelines for the appropriate use of non-steroidal anti-inflammatory drugs, cyclo-oxygenase-2-specific inhibitors and proton pump inhibitors in patients requiring chronic anti-inflammatory therapy. *Aliment Pharmacol Ther* 2004;19:197-208.
132. Kaplowitz N. Rules and laws of drug hepatotoxicity. *Pharmacoepidemiology and Drug Safety* 2006;15:231-3.
133. Burleigh ME, Babaev VR, Oates JA, Harris RC, Gautam S, Riendeau D. Cyclooxygenase-2 promotes early atherosclerotic lesion formation in LDL receptor-deficient mice. *Circulation* 2002;105:1816-23.
134. Krul ES, Napawan N, Butteiger DT, Hayes K, Krause L, Frierdich GE, et al. Atherosclerosis is reduced in cholesterol-fed ApoE(-/-) mice administered an ASBT inhibitor or a selective COX-2 inhibitor [Abstract]. *Arterioscler Thromb Vasc Biol* 2002;(P409):1.
135. Antiplatelet Trialists' Collaboration. Secondary prevention of vascular disease by prolonged antiplatelet treatment. *BMJ* 1988;296:320-31.
136. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy-I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 1994;308:81-106.
137. Singh G, Mithal A, Triadafilopoulos G. Both selective COX-2 inhibitors and non-selective NSAIDs increase the risk of acute myocardial infarction in patients with arthritis: selectivity is with the patient, not the drug class [Abstract]. *Ann Rheum Dis* 2005;64(Suppl III):85.
138. Andersohn F, Suissa S, Garbe E. Use of first- and second-generation cyclooxygenase-2-selective nonsteroidal antiinflammatory drugs and risk of acute myocardial infarction. *Circulation* 2006;113:1950-7.
139. Andersohn F, Schade R, Suissa S, Garbe E. Cyclooxygenase-2 selective nonsteroidal anti-inflammatory drugs and the risk of ischemic stroke: a nested case-control study. *Stroke* 2006;37:1725-30.

140. Helin-Salmivaara A, Virtanen A, Vesalainen R, Grönroos JM, Klaukka T, Idänpään-Heikkilä JE, et al. NSAID use and the risk of hospitalization for first myocardial infarction in the general population: a nationwide case-control study from Finland. *Eur Heart J* 2006;27:1657-63.
141. Watson DJ, Rhodes T, Cai B, Guess HA. Lower risk of thromboembolic cardiovascular events with naproxen among patients with rheumatoid arthritis. *Arch Intern Med* 2002;162:1105-10.
142. Johnson AG, Nguyen TV, Day RO. Do nonsteroidal anti-inflammatory drugs affect blood pressure? A meta-analysis. *Ann Intern Med* 1994;121(4):289-300.
143. Catella-Lawson F, McAdam B, Morrison BW, Kapoor S, Kujubu D, Antes L, et al. Effects of specific inhibition of cyclooxygenase-2 on sodium balance, hemodynamics, and vasoactive eicosanoids. *J Pharmacol Exp Ther* 1999;289(2):735-41.
144. Gertz BJ, Krupa D, Bolognese JA, Sperling RS, Reicin A. A comparison of adverse renovascular experiences among osteoarthritis patients treated with rofecoxib and comparator non-selective non-steroidal anti-inflammatory agents. *Curr Med Res Opin* 2002;18(2):82-91.
145. Thun MJ, Henley SJ, Patrono C. Nonsteroidal anti-inflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues. *J Natl Cancer Inst* 2002;94(4):252-66.
146. Whelton A, Lefkowitz JL, West CR, Verburg KM. Cardiorenal effects of celecoxib as compared with the nonsteroidal anti-inflammatory drugs diclofenac and ibuprofen. *Kidney International* 2006:1-8.
147. Lee TA, Bartle B, Weiss KB. Impact of NSAIDs on mortality and the effect of preexisting coronary artery disease in US veterans. *Am J of Med* 2007;120:98.e9-98.e16.
148. Rahme E, Nedjar H. Risks and benefits of COX-2 inhibitors vs non-selective NSAIDs: does their cardiovascular risk exceed their gastrointestinal benefit? a retrospective cohort study. *Rheumatology* 2007:1-4.
149. Fischer LM, Schlienger RG, Matter CM, Jick H, Meier CR. Current use of nonsteroidal anti-inflammatory drugs and the risk of acute myocardial infarction. *Pharmacotherapy* 2005;25(4):503-10.
150. Gislason GH, Jacobsen S, Rasmussen JN, Rasmussen S, Buch P, Friberg J, et al. Risk of death or reinfarction associated with the use of selective cyclooxygenase-2 inhibitors and nonselective nonsteroidal Anti-inflammatory drugs after acute myocardial infarction. *Circulation* 2006;113:2906-13.

151. Temple R. Meta-analysis and epidemiologic studies in drug development and postmarketing surveillance. *JAMA* 1999;281(9):841-4.
152. Hernandez-Diaz S, Varas-Lorenzo C, Rodriguez LAG. Non-steroidal antiinflammatory drugs and the risk of acute myocardial infarction. *Pharmacol Toxicol* 2006;98:266-74.
153. Wolfe F, Flowers N, Burke TA, Arguelles LM, Pettitt D. Increase in lifetime adverse drug reactions, service utilization, and disease severity among patients who will start COX-2 specific inhibitors: quantitative assessment of channeling bias and confounding by indication in 6689 patients with rheumatoid arthritis and osteoarthritis. *J Rheumatol* 2002;29(5):1015-22.
154. MacDonald TM, Morant SV, Goldstein JL, Burke TA, Pettitt D. Channeling bias and the incidence of gastrointestinal haemorrhage in users of meloxicam, coxibs, and older, non-specific non-steroidal anti-inflammatory drugs. *Gut* 2003;52:1265-70.