

## Cardiovascular Events Associated with NSAIDs

Author	Year	Type of Study	Primary Endpoint	Study Population	Increased Risk
Levesque et al <sup>1</sup>	2005	Retrospective, population- based, nested, matched, case-control	1 <sup>st</sup> hospitalization with a diagnosis of acute MI, nonfatal or fatal	113927 elderly persons without previous MI & newly treated w/ an NSAID	Relative Risk Rofecoxib 1.24 ( more pronounced at higher doses). No increase risk with celecoxib RR 0.99 compared to other NSAIDS
Fischer et al <sup>2</sup>	2005	Retrospective case-control analysis	First time acute MI	8688 patients 88 years or younger, with first time acute MI and 33923 subjects matched to age, sex, calendar time, general practice attendance	Odds Ratio Current NSAID use 1.07
Johnsen, et al. <sup>3</sup>	2005	Population-based case-control	First-time hospitalization for MI	10280 cases of first time hospitalization for MI and 102797 sex and age matched controls	Relative Risk Rofecoxib 1.8 Celecoxib 1.25 other Cox-2's 1.45 Naproxen 1.5 conventional NSAIDS 1.68
Hippisley-Cox, et al. <sup>4</sup>	2006	Nested Case Control	First ever adverse upper GI outcome and those with first ever recorded	4436 patients with an adverse upper GI event aged 25 years or more at diagnosis. 88867 controls matched according to age, calendar time, sex, and practice	Odds Ratios Naproxen (2.12, 1.73, 2.58) Diclofenac (1.96, 1.78, 2.15) other Cox-2 inhibitors (1.75, 1.41, 2.15) other non-selective NSAIDS (1.67, 1.43, 1.94). There was no significant increased risk for current use of celecoxib (1.11, 0.87, 1.41), but number of patients taking celecoxib was low.
Kimmel et al. <sup>5</sup>	2005	Case-control, non-matched	Non-fatal MI's	1718 Case-patients with a first, nonfatal MI admitted to 36 hospitals in a 5-county area. 6800 controls randomly selected from the same counties.	Odds Ratio NSAIDS 0.61 All Cox 2 0.73 Rofecoxib 1.16 Celecoxib 0.43
Mamdani et al. <sup>6</sup>	2003	Population-based retrospective cohort study	Hospitalization for AMI	593808 Canadian residents of Ontario, 66 years and older between and 1000 control subjects matched by age and sex	Adjusted rate ratios Celecoxib 0.9 Rofecoxib 1.0 Non-naproxen 1.2
Schlienger et al <sup>7</sup>	2002	Population based case-control analysis	First-time AMI Free patients, but all tables listed Adjusted odds ratio according to first-time AMI	3319 patients 75 years or less free of metabolic or cardiovascular diseases. 13139 controls matched by age, sex, practice attended, and calendar	Adjusted odds ratios Current NSAID users 1.21

Graham et al. <sup>8</sup>	2005	Nested case-control	Incident serious coronary heart disease, defined as acute MI requiring admission or sudden cardiac death	8143 individuals 18-84 years who filled at least one prescription for a COX2 selective or non-selective NSAID. 31496 matched by date of the case event year of birth, sex, and health plan region	Adjusted odds ratio Ibuprofen 1.06 Naproxen 1.14 Rofecoxib all doses 1.34 Rofecoxib (<25mg/day) 1.23 Rofecoxib (>25mg/day) 3.00 Other NSAIDS 0.03-1.13
Mamdani et al. <sup>9</sup>	2004	Population-based retrospective cohort	Primary diagnosis of CHF	38882 individuals 66 years and older who were prescribed study and 100000 randomly selected non-NSAID users matched by sex and age	% study cohort w/ admission procedures for CHF in past 5 years Non-NSAID 4% (4475/100000) Celecoxib 6% (1170/18908) Rofecoxib 6% (857/14583) Non-selective NSAIDS 5% (542/11606) **CHF admission rates slightly higher for celecoxib and rofecoxib users relative to non-NSAID users. Additional analysis with age-matched and sex-matched controls showed similar patterns.
Levesques, et al. <sup>10</sup>	2006	Population-based, retrospective, matched, nested case-control	First hospitalization of acute MI, non-fatal or fatal	3423 individuals with a mean age of 75.3 years. 68456 controls matched on month and year of cohort entry and age, randomly selected from the case's risk-set and assigned the same index date	3,423 of 122079 were hospitalized for MI during study Period (2.8%) Adjusted Rate ratios contrasted no previous MI and Previous MI for each drug NSAIDS-1.10 Naproxen-1.54 Rofecoxib-1.43 Celecoxib-1.19
Rodriguez et al. <sup>11</sup>	2004	Nested case-control cohort	MI associated with NSAID use	404183 subjects 50-84 years old. 20000 Controls were randomly sampled and frequency was matched to cases by age, sex, and calendar year.	Multivariate Adjusted Odds ratio Current use of NSAIDS 1.07 The incidence rate of MI was higher among people with history of CHD. Estimates for Naproxen, ibuprofen, and diclofenac were comparable with no major effects on the risk of MI.
McGetting PM et al. <sup>12</sup>	2006	Observational	Serious CVD and MI	Case-control or Cohort design	Multivariate Adjusted Odds ratio Current use of rofecoxib 1.33 and 2.19 for high dose. Current user of Diclofenac was 1.40 The incidence rate of MI was higher among people with history of CHD. Estimates for Naproxen, ibuprofen, and diclofenac were comparable with no major effects on the risk of MI.
Helin-almivaara, et al. <sup>13</sup>	2006	Observational	Serious CVD and MI	33 309 persons with MI and 138 949 individually matched controls	For combined NSAIDs, the adjusted OR 1.40 (95% CI, 1.33–1.48). The risk was similar for conventional (1.34; 1.26–1.43), semi-selective (etodolac, nabumetone, nimesulide, and meloxicam) (1.50; 1.32–1.71), and cyclo-oxygenase-2 (COX-2) selective NSAIDs (rofecoxib, celecoxib, valdecoxib, and etoricoxib) (1.31; 1.13–1.50).

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