

Title: Long-term effects of use of prescription non-steroidal anti-inflammatory agents on symptoms and disease progression among patients with radiographically confirmed osteoarthritis of the knee

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Abstract:

**Objective:** To estimate the extent to which long-term use of prescription non-steroidal anti-inflammatory agents (NSAIDs) relieve symptoms and delay disease progression among patients with radiographically confirmed osteoarthritis (OA) of the knee.

**Methods:** Using Osteoarthritis Initiative data, we identified participants with confirmed OA at enrollment and evaluated changes in symptoms measured using the Western Ontario and McMaster Universities Arthritis Index, WOMAC (n=1,846) and joint space width measured using serial x-rays and a customized software tool (n=1,116) over 4 years. Covariates included sociodemographics, OA clinical characteristics, indices of general health status, body mass index, and use of other treatments. We adjusted for baseline and time-varying confounders using marginal structural modeling.

**Results:** Six percent initiated NSAID treatment at year one, with half of the initiators being regular users. After adjusting for time-varying confounders with marginal structural models, we found that compared to participants who never reported use of prescription NSAIDs, those reporting use for 3 years had on average 0.88 point decrease (95% Confidence Interval (CI): -0.46 to 2.22) in WOMAC Pain, 0.72 point decrease (95% CI: -0.12 to 1.56) in WOMAC Stiffness, 4.27 points decrease (95% CI: 0.31 to -8.84) in WOMAC Function, and 0.28mm increase (95% CI: -0.06 to 0.62) in joint space width.

**Conclusions:** Long term NSAID use was associated with a priori defined minimally important clinical improvements in stiffness, function and structural degeneration, but not in pain.