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Meta-Analysis of Assay Sensitivity and Study Features in Clinical Trials of Pharmacologic Treatments for Osteoarthritis Pain

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Objective. **To identify patient, study, and site factors associated with assay sensitivity in clinical trials of pharmacologic treatments for osteoarthritis (OA) pain.**

Methods. **We examined associations between study characteristics and the standardized effect size (SES) in a database of 171 publicly available randomized clinical trials of pharmacologic treatment for OA pain. The included trials 1) evaluated oral, topical, or transdermal treatments, 2) had treatment durations of ≥7 days, 3) used parallel-group or crossover designs, 4) included patients with OA of the knee, hip, and/or hand, and 5) were placebo controlled and double blind. Crossover trials were excluded, because complete information was available for only 2 of 20 treatment conditions.**

Results. **There was considerable heterogeneity in the SES among the examined trials. A multiple meta-regression analysis indicated that trials with shorter treatment period durations and those that did not permit concomitant analgesics had significantly greater assay sensitivity. In univariate analyses of efficacious treatments, trials conducted outside North America and those with a minimum baseline pain inclusion criterion of ≥40 (0–100 scale) had significantly larger s, although these relationships were not significant in the multiple meta-regression analysis.**

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Conclusion. **The analyses examined potentially modifiable correlates of study SES and showed that longer treatment durations and allowing concomitant analgesics in randomized clinical trials of OA pain are associated with reduced assay sensitivity. These data provide a foundation for investigating strategies to improve assay sensitivity and thereby decrease the likelihood of false-negative outcomes in randomized clinical trials of efficacious treatments for OA pain.**

Multiple efficacious medications for the treatment of osteoarthritis (OA)–associated pain, including nonsteroidal antiinflammatory drugs (NSAIDs), duloxetine, tramadol, and opioid analgesics, have been identified. These treatments, however, have significant limitations. In many patients, pain is refractory to existing medications or the side effects are intolerable, and those who do have a response to treatment typically experience partial rather than complete pain relief (1–3). In addition to modest efficacy and tolerability, opioid analgesics are associated with appreciable safety risks, including cardiovascular, gastrointestinal, renal, and hepatic

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