

Supplement: Safety of Anti-Osteoarthritis Medications

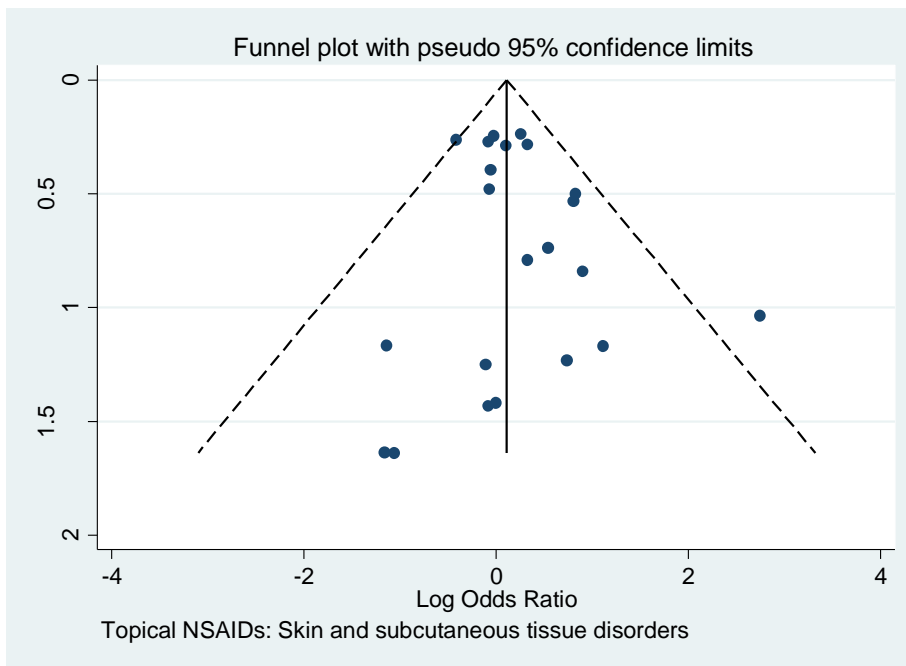
Safety of topical non-steroidal anti-inflammatory drugs in osteoarthritis: Outcomes of a systematic review and meta-analysis

Germain Honvo, Victoria Leclercq, Anton Geerinck, Thierry Thomas, Nicola Veronese, Alexia Charles, Véronique Rabenda, Charlotte Beaudart, Cyrus Cooper, Jean-Yves Reginster, Olivier Bruyère

ELECTRONIC SUPPLEMENTARY MATERIAL 3

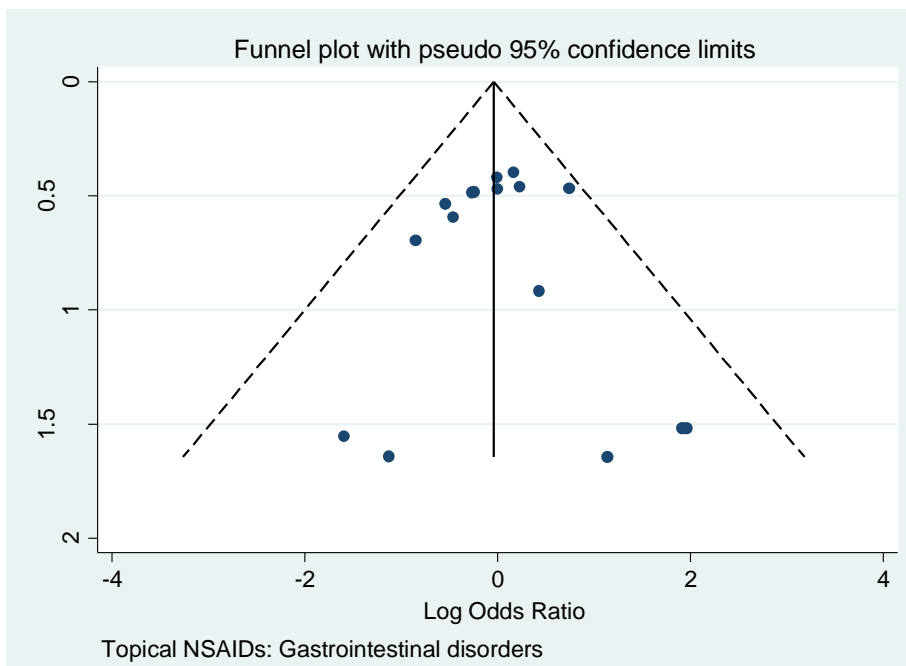
1. Assessment of publication bias by safety outcome in studies on topical non-steroidal anti-inflammatory drugs (NSAIDs) (overall)

Figure 38: Funnel plot using data for skin and subcutaneous tissue disorders with all topical NSAIDs versus placebo in patients with osteoarthritis (OA).



Harbord's test: $p = 0.663$

Figure 39: Funnel plot using data for gastrointestinal disorders with all topical NSAIDs versus placebo in patients with OA.



Harbord's test: $p = 0.802$

Figure 40: Funnel plot using data for cardiac disorders with all topical NSAIDs versus placebo in patients with OA.

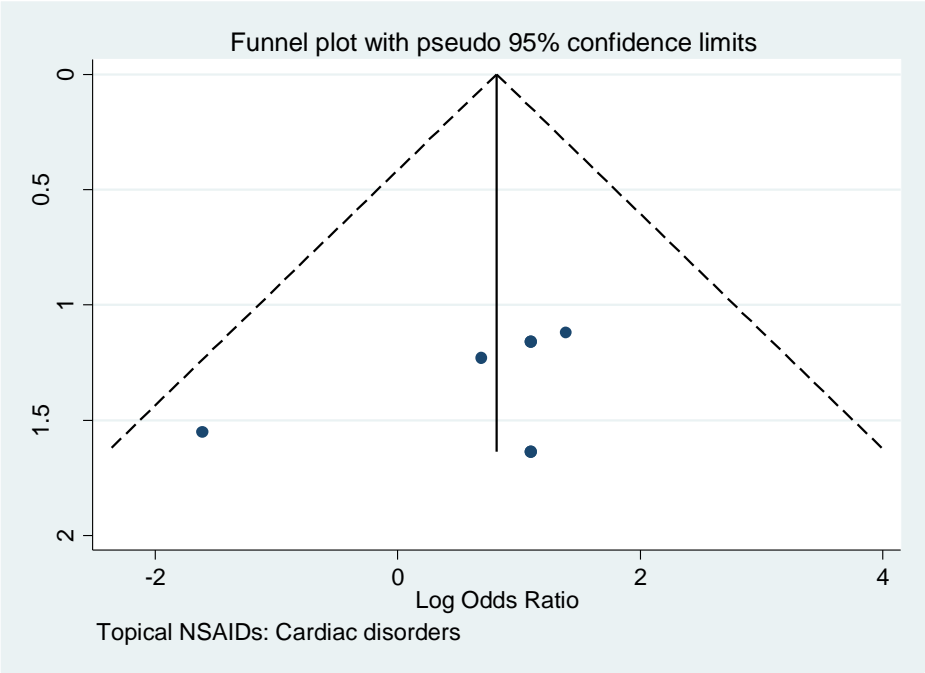


Figure 41: Funnel plot using data for vascular disorders with all topical NSAIDs versus placebo in patients with OA.

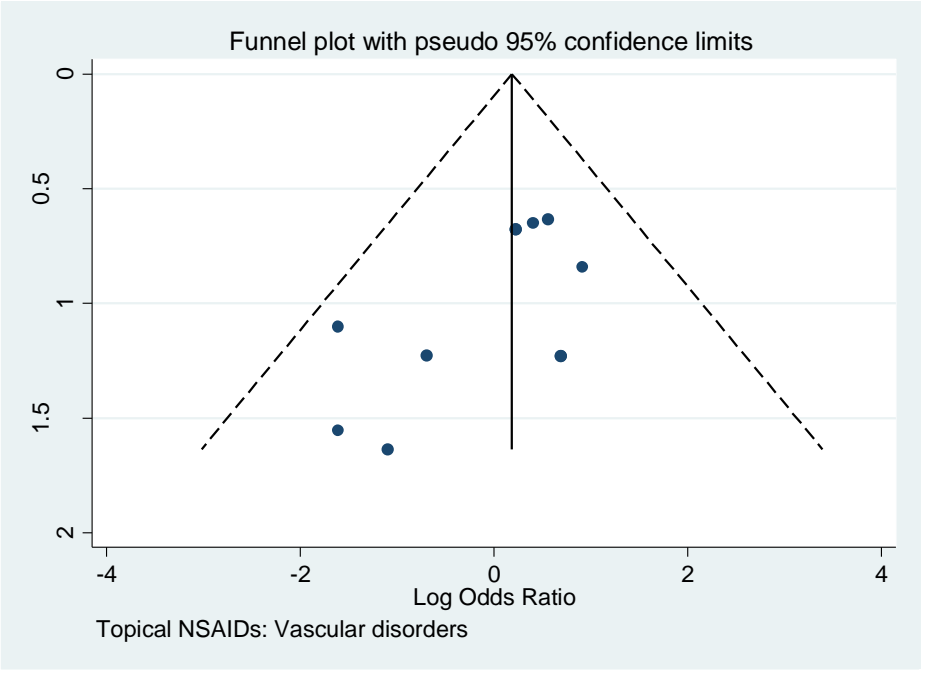
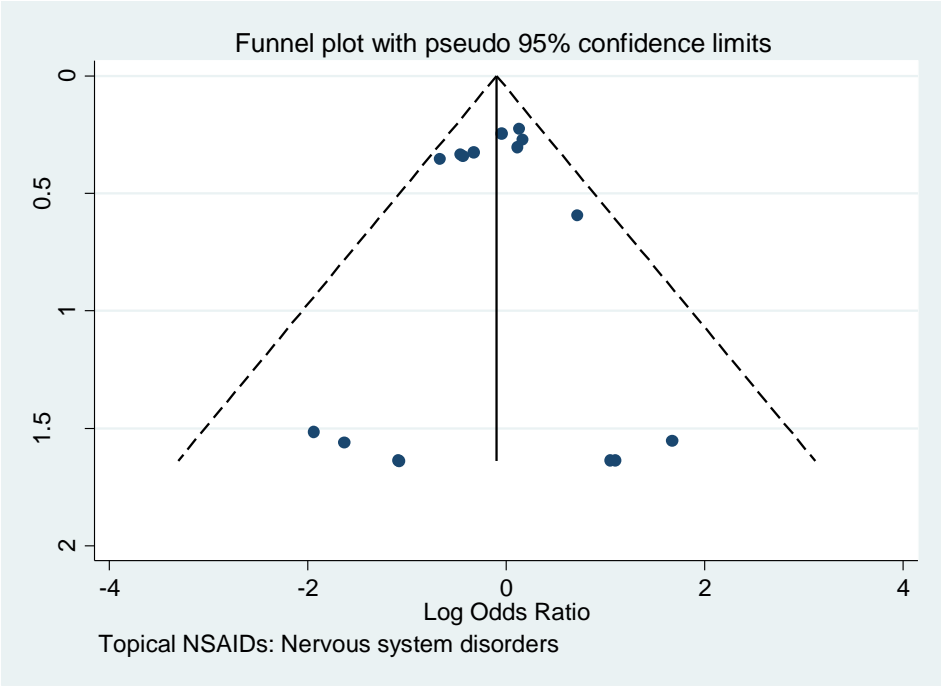
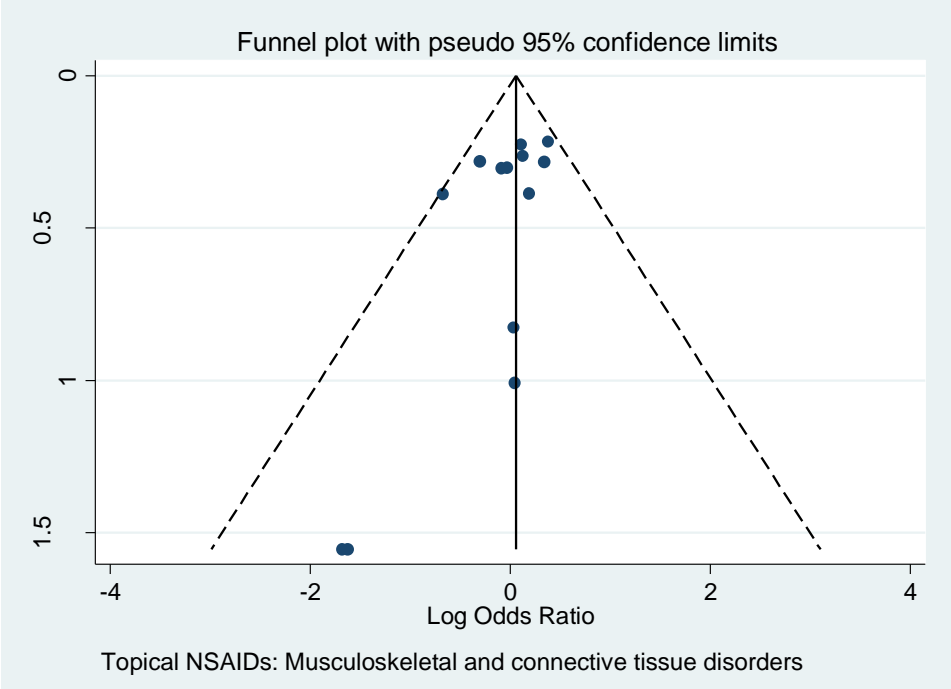


Figure 42: Funnel plot using data for nervous system disorders with all topical NSAIDs versus placebo in patients with OA.



Harbord's test: P = 0.652

Figure 43: Funnel plot using data for musculoskeletal and connective tissue disorders with all topical NSAIDs versus placebo in patients with OA.



Harbord's test: P = 0.038

Figure 44: Funnel plot using data for severe adverse events with all topical NSAIDs versus placebo in patients with OA.

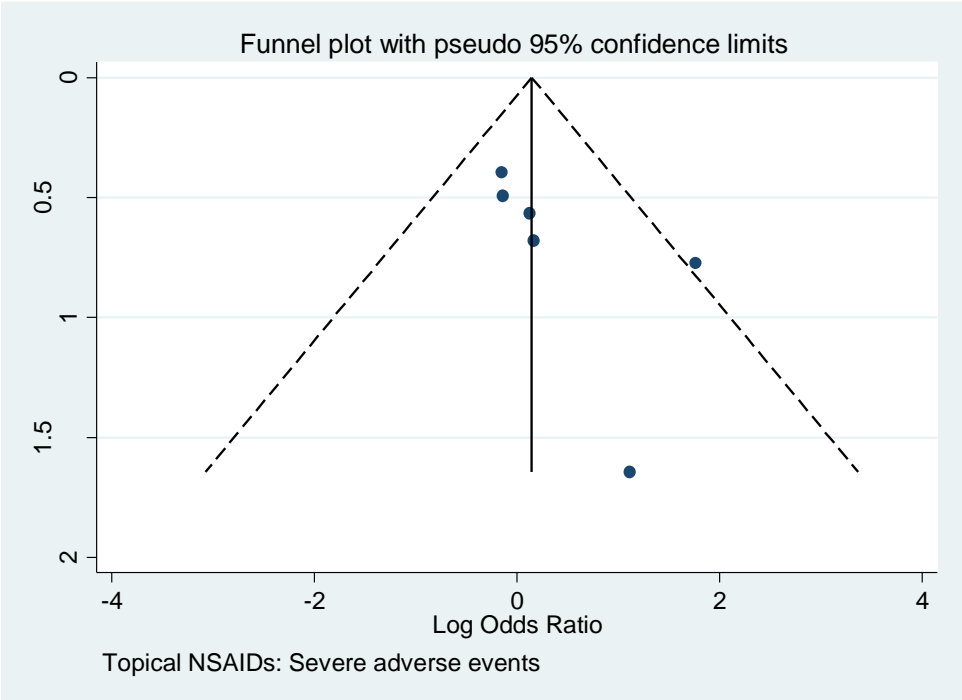


Figure 45: Funnel plot using data for serious adverse events with all topical NSAIDs versus placebo in patients with OA.

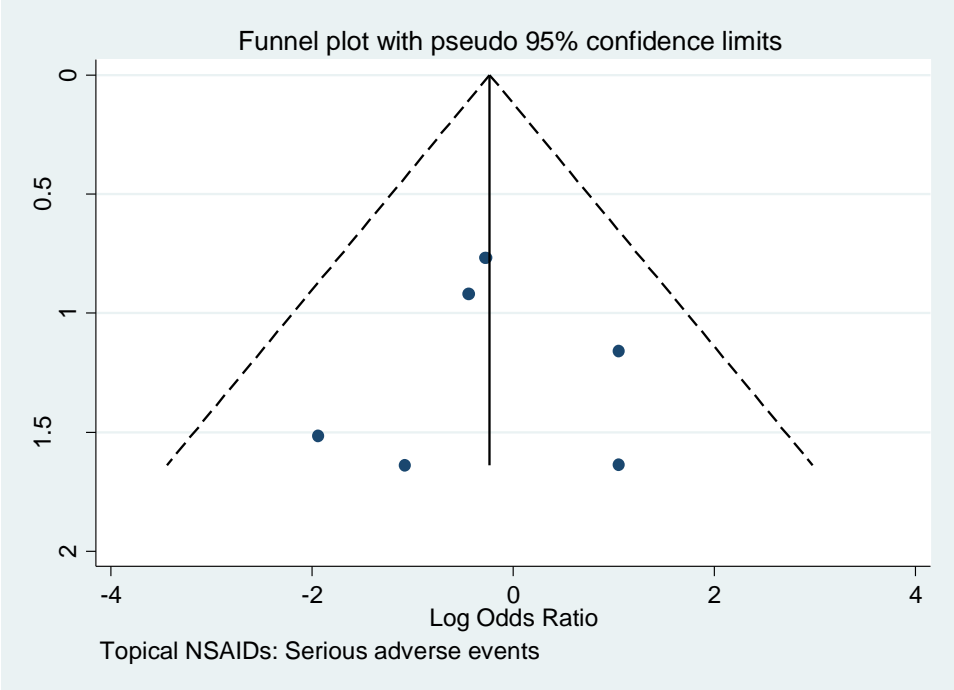
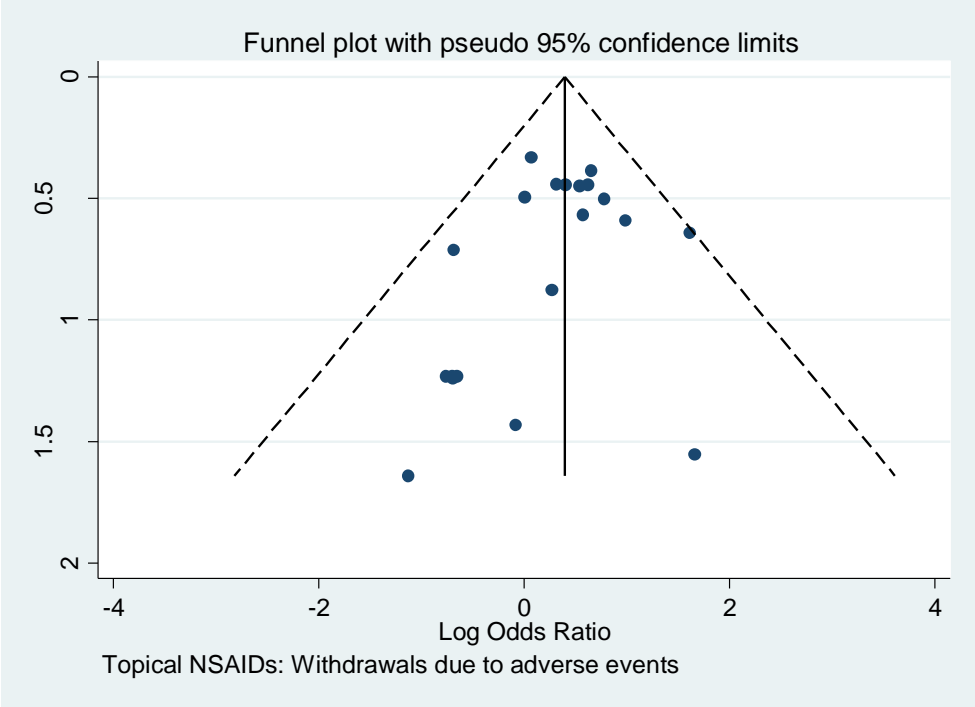


Figure 46: Funnel plot using data for dropouts due to adverse events with all topical NSAIDs versus placebo in patients with OA.



Harbord's test: P = 0.111

2. Assessment of publication bias by safety outcome in studies on topical diclofenac

Figure 47: Funnel plot using data for skin and subcutaneous tissue disorders with topical diclofenac versus placebo in patients with OA.

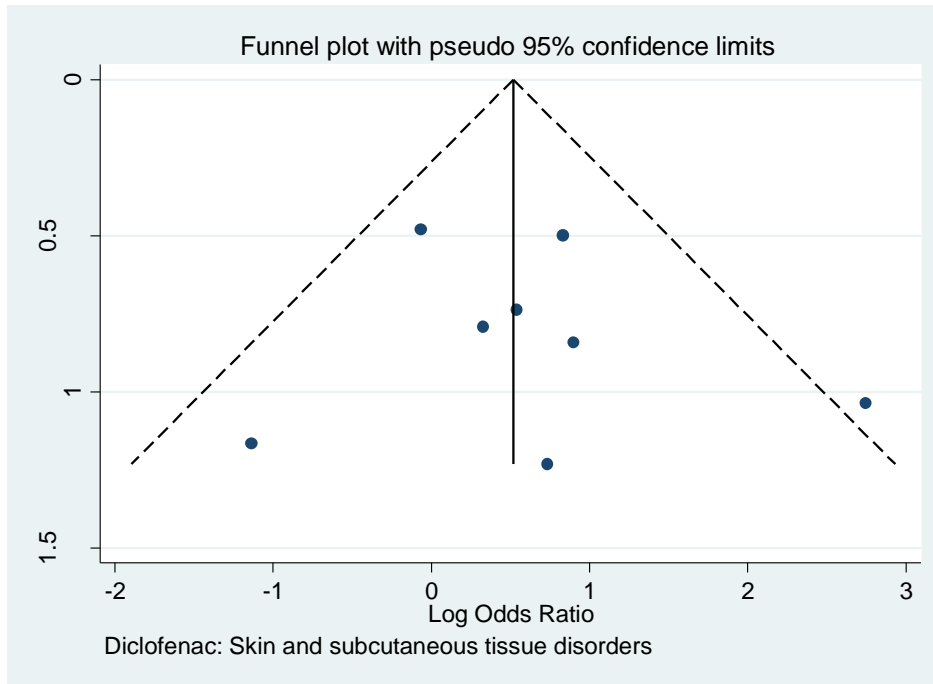


Figure 48: Funnel plot using data for gastrointestinal disorders with topical diclofenac versus placebo in patients with OA.

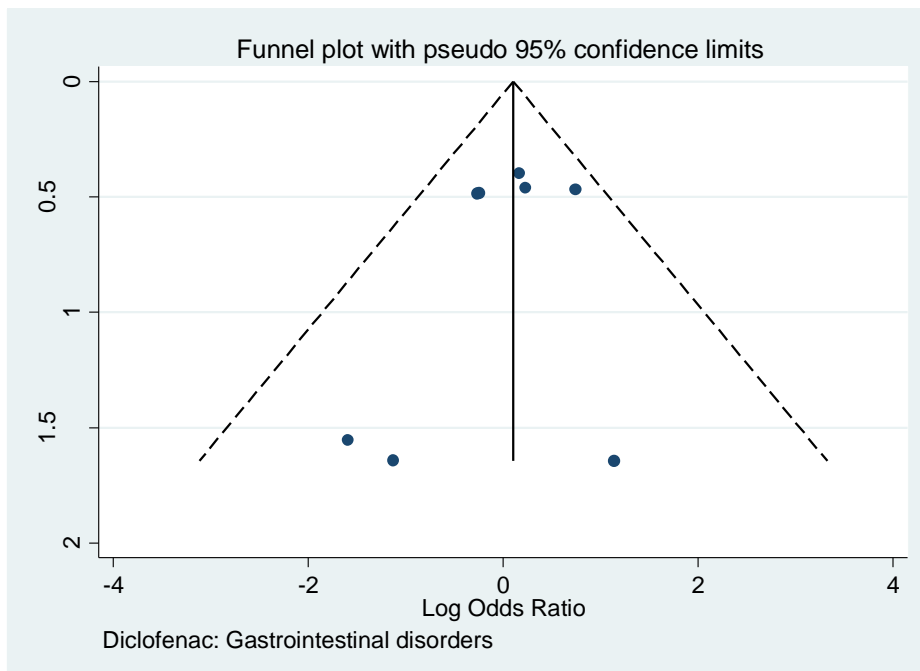


Figure 49: Funnel plot using data for cardiac disorders with topical diclofenac versus placebo in patients with OA.

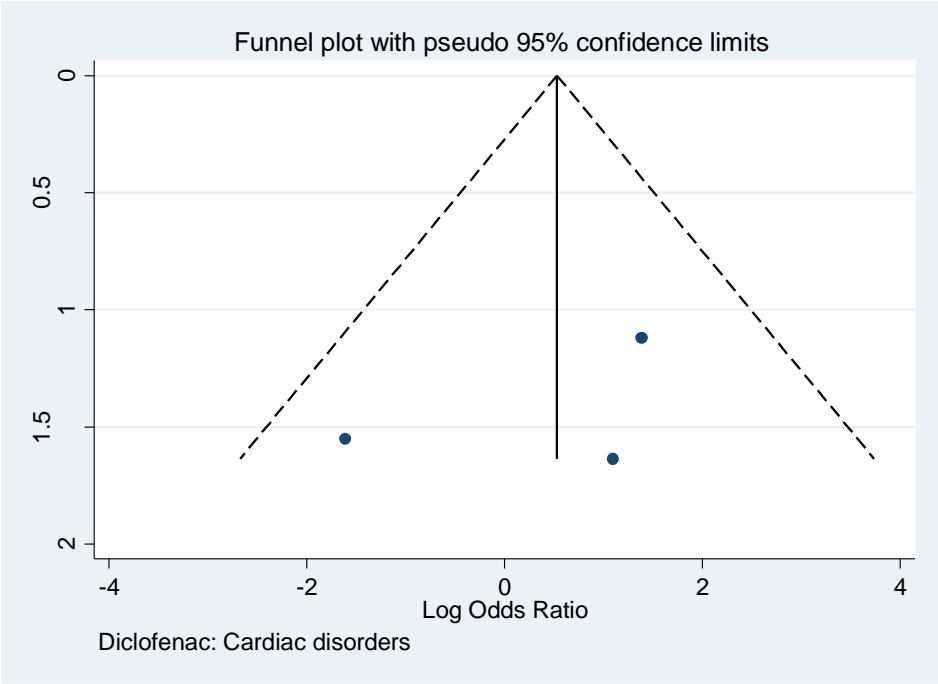


Figure 50: Funnel plot using data for vascular disorders with topical diclofenac versus placebo in patients with OA.

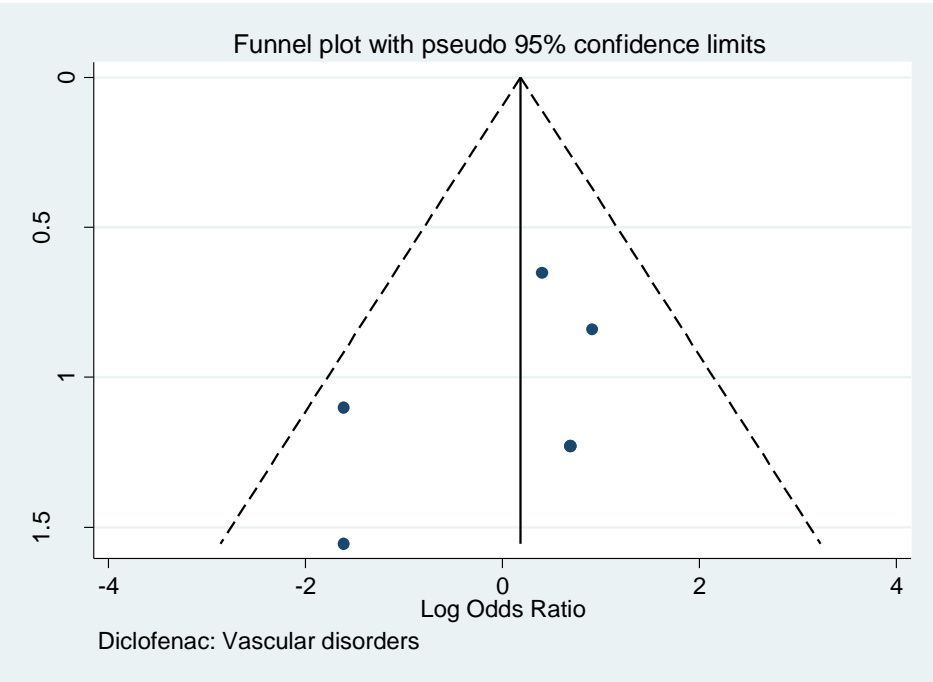


Figure 51: Funnel plot using data for nervous system disorders with topical diclofenac versus placebo in patients with OA.

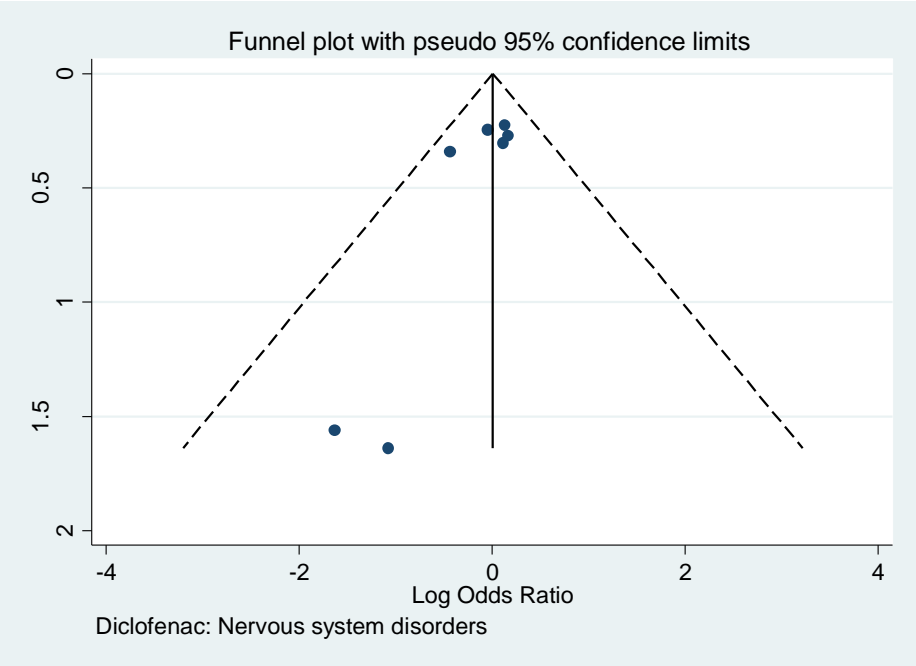


Figure 52: Funnel plot using data for musculoskeletal and connective tissue disorders with topical diclofenac versus placebo in patients with OA.

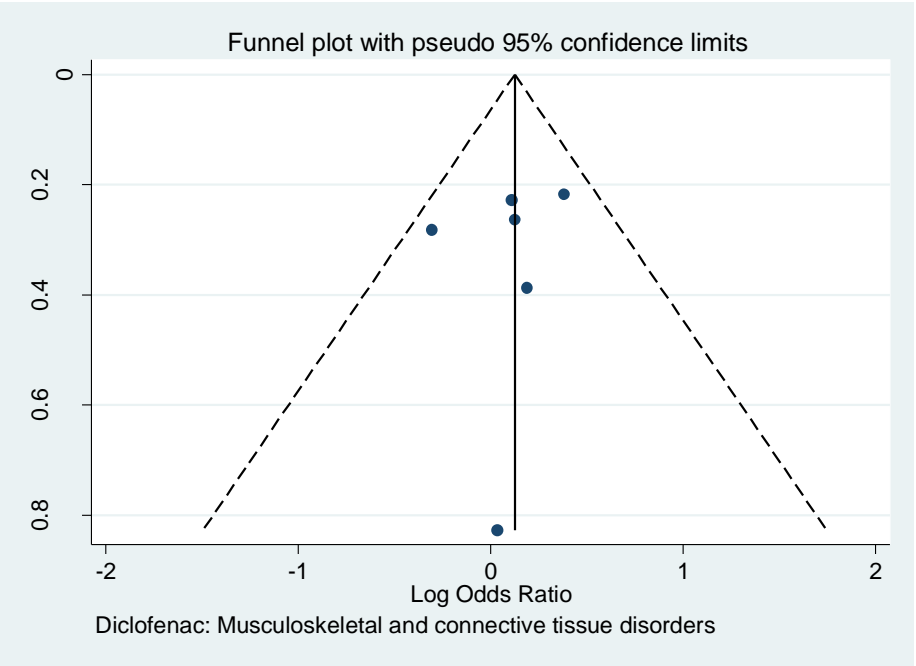


Figure 53: Funnel plot using data for severe adverse events with topical diclofenac versus placebo in patients with OA.

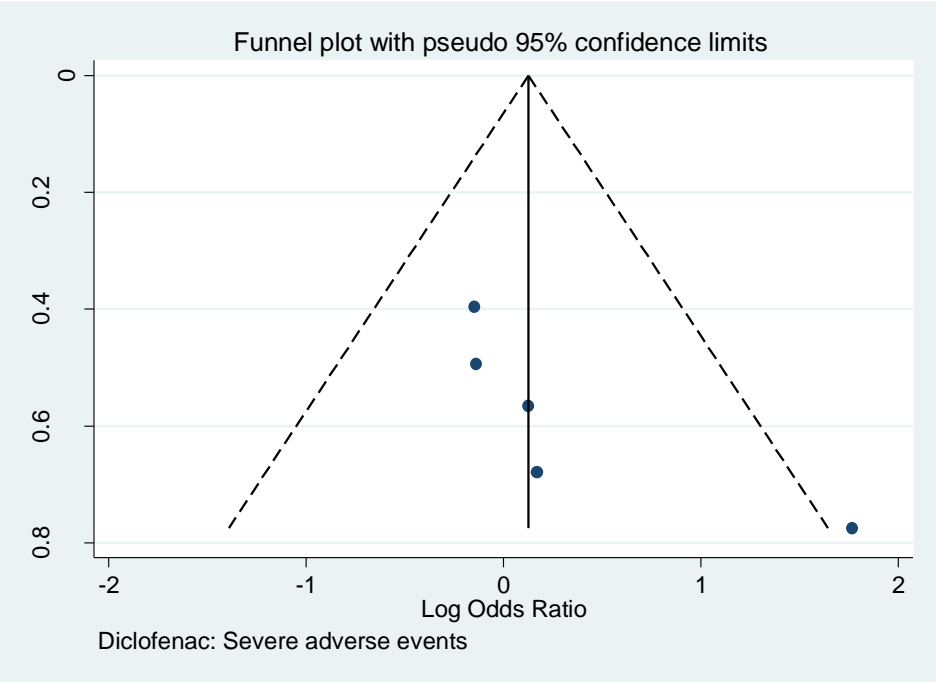


Figure 54: Funnel plot using data for serious adverse events with topical diclofenac versus placebo in patients with OA.

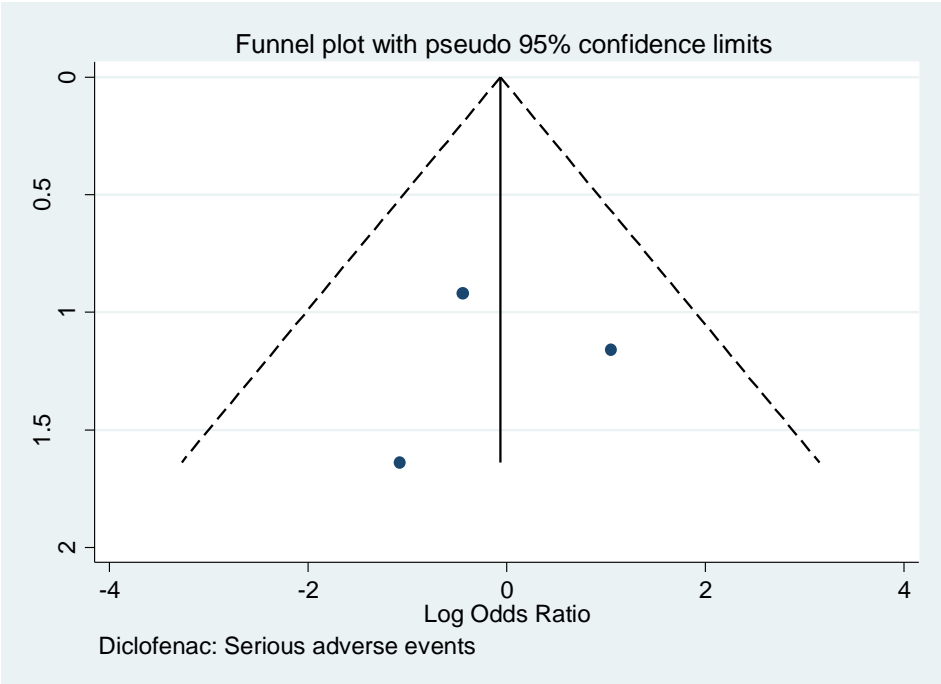
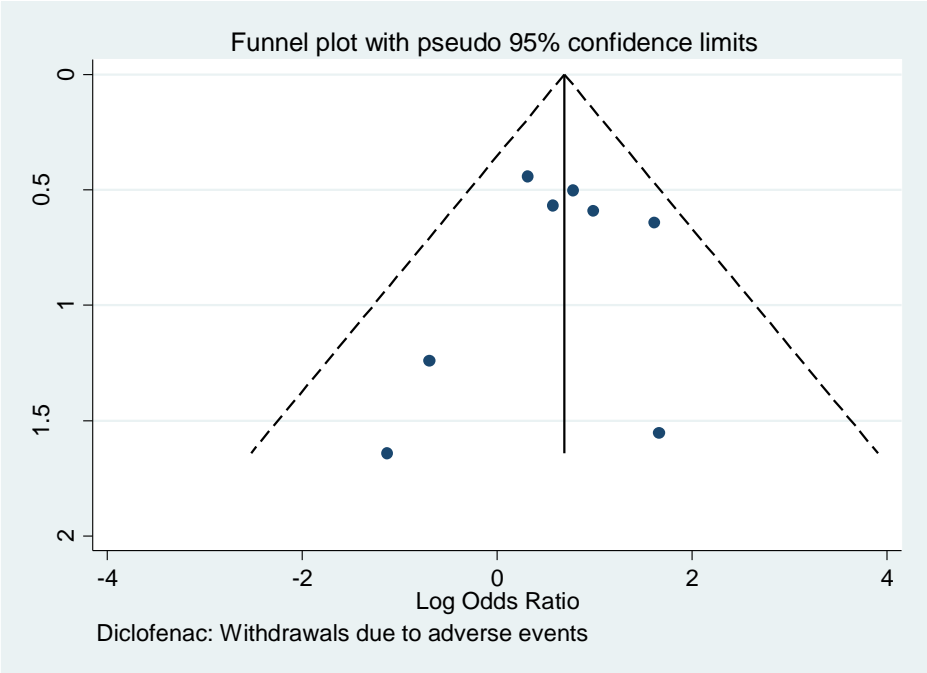


Figure 55: Funnel plot using data for dropouts due to adverse events with topical diclofenac versus placebo in patients with OA.



3. Assessment of publication bias by safety outcome in studies on topical ketoprofen

Figure 56: Funnel plot using data for skin and subcutaneous tissue disorders with topical ketoprofen versus placebo in patients with OA.

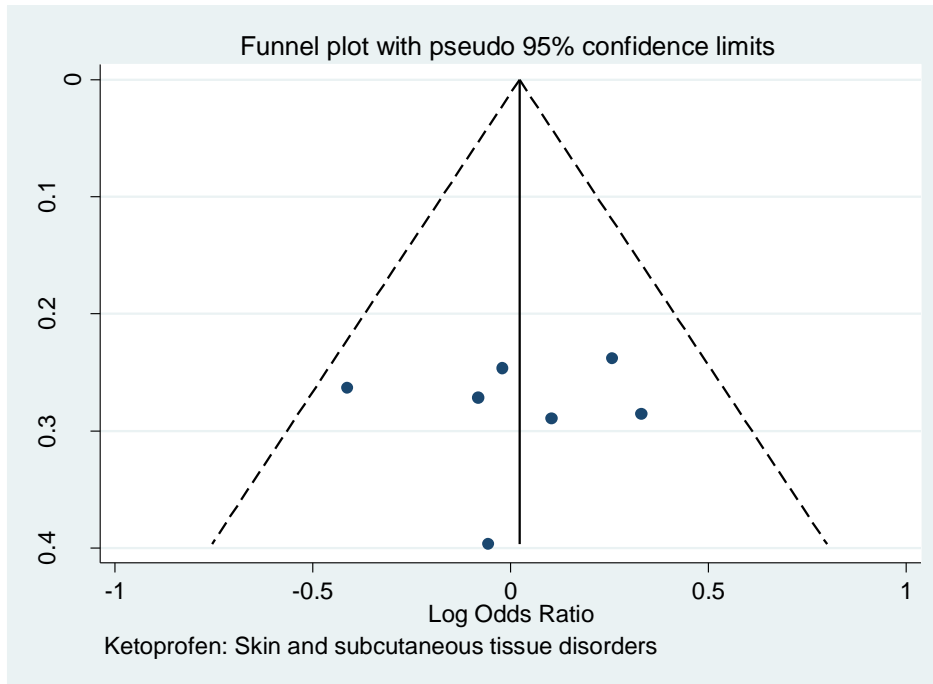


Figure 57: Funnel plot using data for gastrointestinal disorders with topical ketoprofen versus placebo in patients with OA.

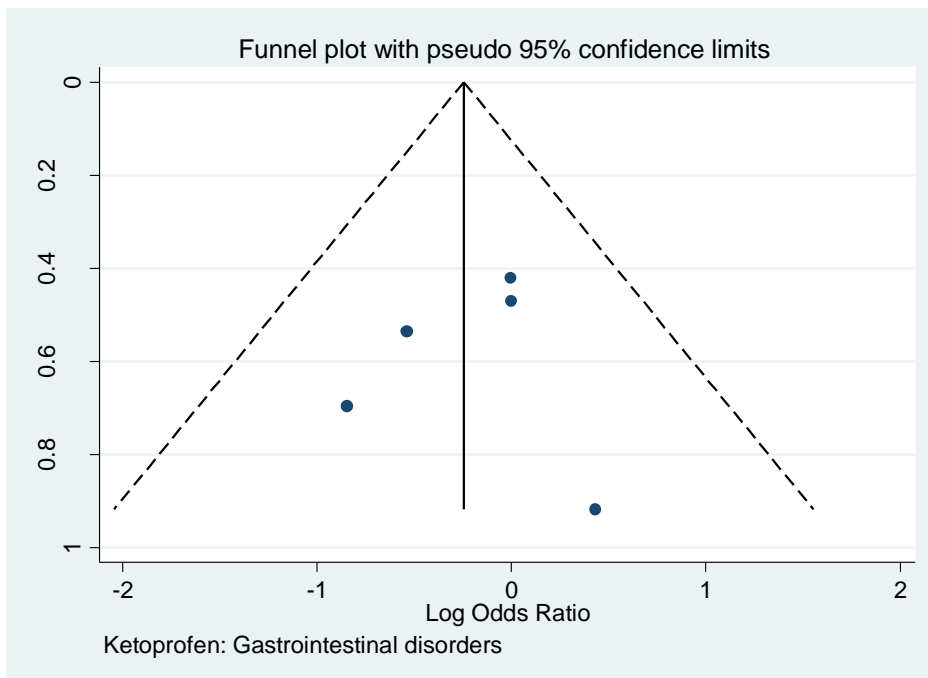


Figure 58: Funnel plot using data for cardiac disorders with topical ketoprofen versus placebo in patients with OA.

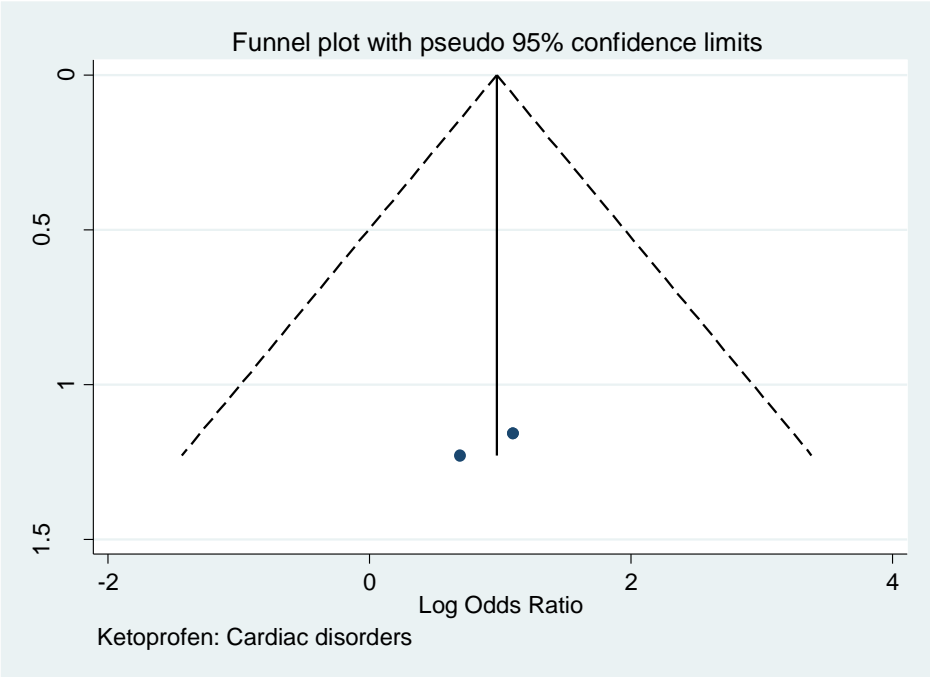


Figure 59: Funnel plot using data for vascular disorders with topical ketoprofen versus placebo in patients with OA.

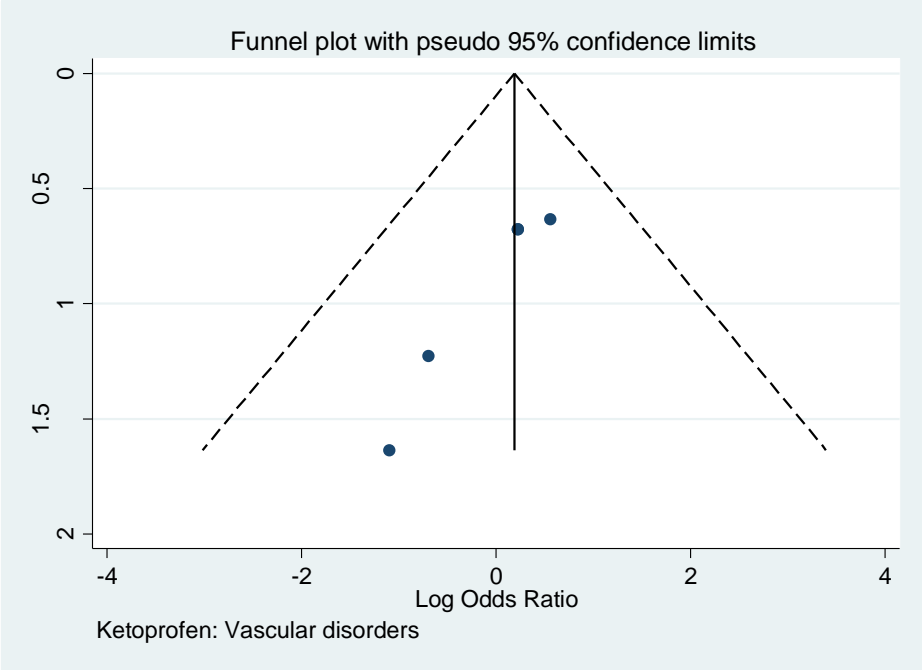


Figure 60: Funnel plot using data for nervous system disorders with topical ketoprofen versus placebo in patients with OA.

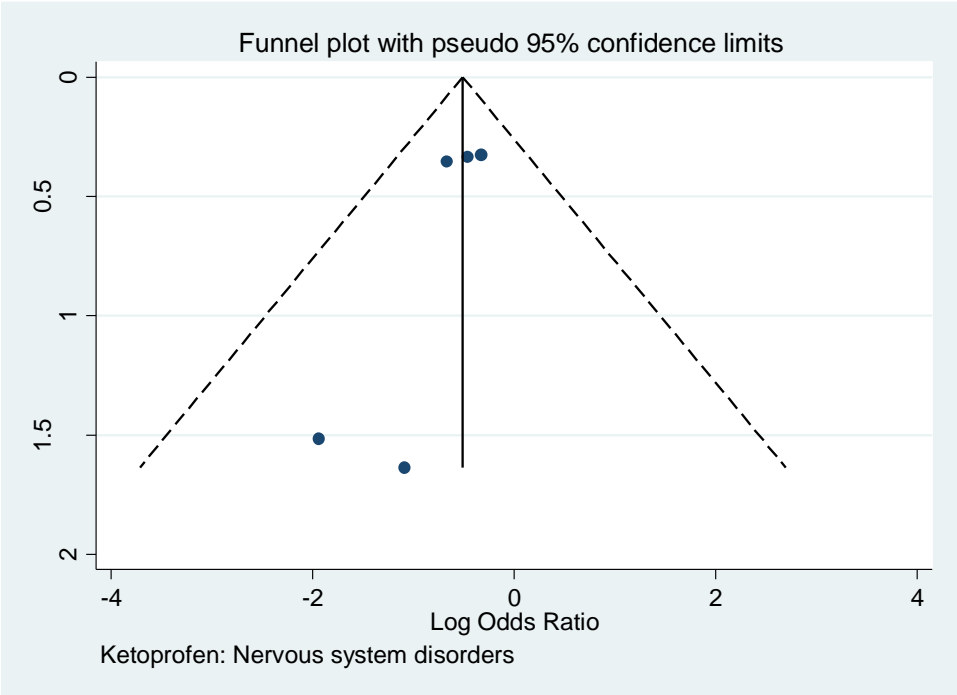
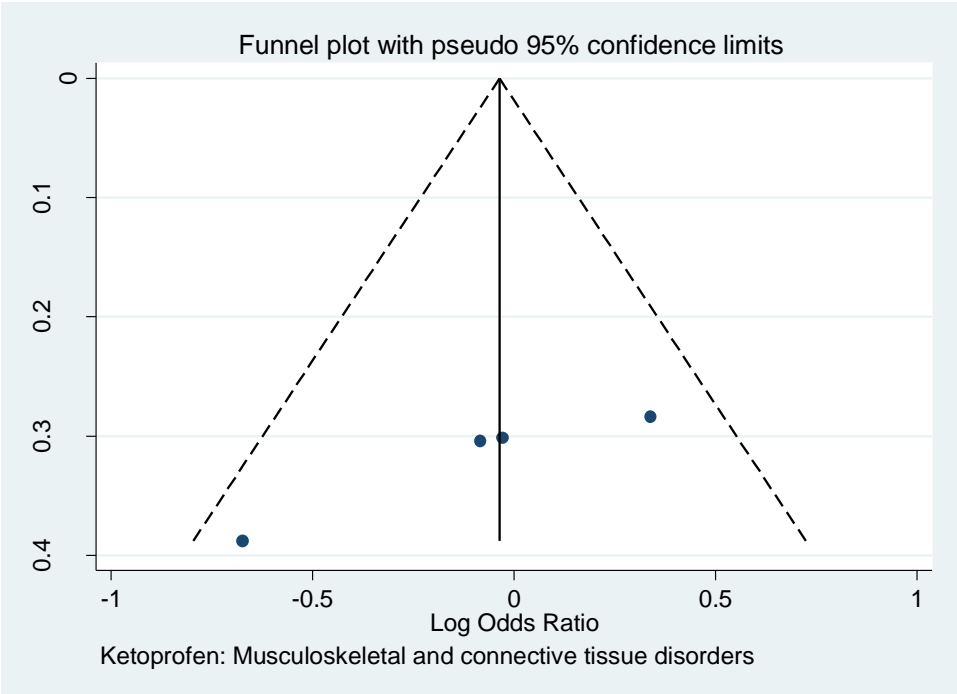


Figure 61: Funnel plot using data for musculoskeletal and connective tissue disorders with topical ketoprofen versus placebo in patients with OA.



Severe adverse events with topical ketoprofen: All studies were with null events; thus, the analysis for publication bias was not possible.

Figure 62: Funnel plot using data for serious adverse events with topical ketoprofen versus placebo in patients with OA.

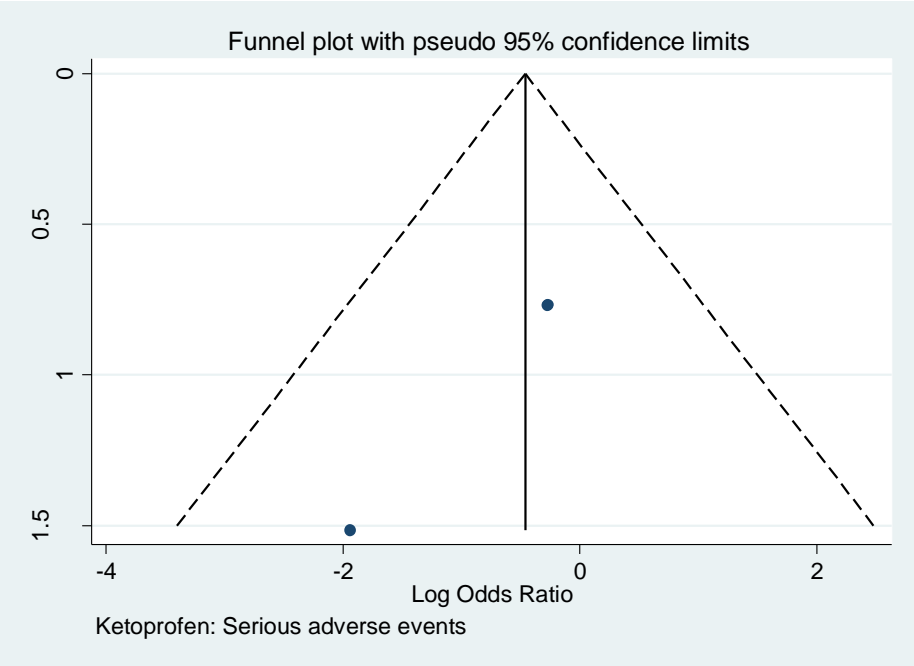
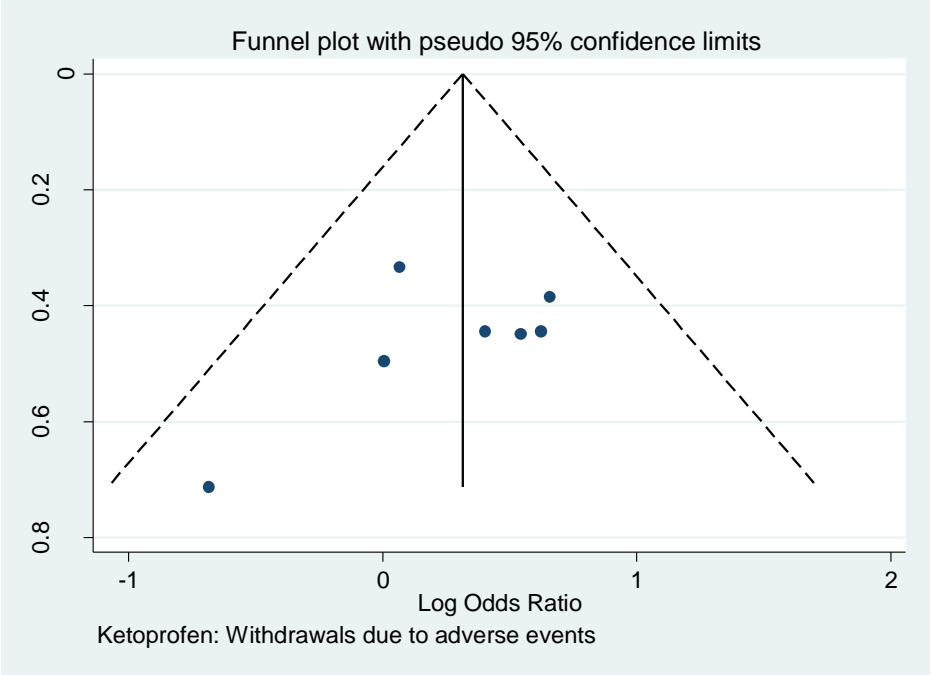


Figure 63: Funnel plot using data for dropouts due to adverse events with topical ketoprofen versus placebo in patients with OA.



4. Assessment of publication bias by safety outcome in studies on topical Ibuprofen

Only 3 studies were available for this meta-analysis, with several null events; thus, analyses for publication bias were not possible.