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Supplement: Safety of Anti-Osteoarthritis Medications

Safety of symptomatic slow-acting drugs in osteoarthritis: outcomes of a systematic review and meta-analysis

Germain Honvo, Jean-Yves Reginster, Véronique Rabenda, Anton Geerinck, Ouafa Mkinsi, Alexia Charles, Rene Rizzoli, Cyrus Cooper, Bernard Avouac, Olivier Bruyère

ELECTRONIC SUPPLEMENTARY MATERIAL 3
1. Publication bias in studies on Glucosamine sulfate

**Figure 48**: Funnel plot using data for the meta-analysis comparing gastrointestinal disorders with glucosamine sulfate versus placebo in patients with OA

Funnel plot with pseudo 95% confidence limits

- With concomitant anti-OA medication
- Without concomitant anti-OA medication

Glucosamine sulfate: Gastrointestinal disorders
**Figure 49:** Funnel plot using data for the meta-analysis comparing nervous system disorders with glucosamine sulfate versus placebo in patients with OA.

**Figure 50:** Funnel plot using data for the meta-analysis comparing skin and subcutaneous tissue disorders with glucosamine sulfate versus placebo in patients with OA.
Figure 51: Funnel plot using data for the meta-analysis comparing musculoskeletal and connective tissue disorders with glucosamine sulfate versus placebo in patients with OA.
**Figure 52:** Funnel plot using data for the meta-analysis comparing dropouts due to adverse events with glucosamine sulfate versus placebo in patients with OA

Note: Very few studies of glucosamine sulfate versus placebo (<5) were available for the meta-analyses for cardiac disorders, vascular disorders, severe adverse events, and serious adverse events; therefore, the funnel plots for these outcomes are not displayed. For renal and urinary disorders, all studies were with null events in both the GS and placebo groups.
2. Publication bias in studies on Chondroitin sulfate

Figure 53: Funnel plot using data for the meta-analysis comparing gastrointestinal disorders with chondroitin sulfate versus placebo in patients with OA

Harbord’s test: $p = 0.29$
**Figure 54:** Funnel plot using data for the meta-analysis comparing cardiac disorders with chondroitin sulfate versus placebo in patients with OA

**Figure 55:** Funnel plot using data for the meta-analysis comparing vascular disorders with chondroitin sulfate versus placebo in patients with OA
Figure 56: Funnel plot using data for the meta-analysis comparing nervous system disorders with chondroitin sulfate versus placebo in patients with OA.
**Figure 57:** Funnel plot using data for the meta-analysis comparing skin and subcutaneous tissue disorders with chondroitin sulfate versus placebo in patients with OA

Harbord’s test: $p = 0.21$
Figure 58: Funnel plot using data for the meta-analysis comparing musculoskeletal and connective tissue disorders with chondroitin sulfate versus placebo in patients with OA

Figure 59: Funnel plot using data for the meta-analysis comparing renal and urinary system disorders with chondroitin sulfate versus placebo in patients with OA
Figure 60: Funnel plot using data for the meta-analysis comparing severe adverse events with chondroitin sulfate versus placebo in patients with OA.

Figure 61: Funnel plot using data for the meta-analysis comparing serious adverse events with chondroitin sulfate versus placebo in patients with OA.
**Figure 62:** Funnel plot using data for the meta-analysis comparing dropouts due to adverse events with chondroitin sulfate versus placebo in patients with OA.

Harbord’s test: p = 0.98
3. Publication bias in studies on Diacerein

Figure 63: Funnel plot using data for the meta-analysis comparing gastrointestinal disorders with diacerein versus placebo in patients with OA
**Figure 64:** Funnel plot using data for the meta-analysis comparing cardiac disorders with diacerein versus placebo in patients with OA

**Figure 65:** Funnel plot using data for the meta-analysis comparing vascular disorders with diacerein versus placebo in patients with OA
Figure 66: Funnel plot using data for the meta-analysis comparing nervous system disorders with diacerein versus placebo in patients with OA

![Funnel plot with pseudo 95% confidence limits](image)

Diacerein: Nervous system disorders

Figure 67: Funnel plot using data for the meta-analysis comparing skin and subcutaneous tissue disorders with diacerein versus placebo in patients with OA

![Funnel plot with pseudo 95% confidence limits](image)

Diacerein: Skin and subcutaneous tissue disorders
**Figure 68:** Funnel plot using data for the meta-analysis comparing musculoskeletal and connective tissue disorders with diacerein versus placebo in patients with OA.

**Figure 69:** Funnel plot using data for the meta-analysis comparing renal and urinary disorders with diacerein versus placebo in patients with OA.
**Figure 70**: Funnel plot using data for the meta-analysis comparing serious adverse events with diacerein versus placebo in patients with OA.
**Figure 71**: Funnel plot using data for the meta-analysis comparing dropouts due to adverse events with diacerein versus placebo in patients with OA

Note: Very few studies of diacerein versus placebo (<5) were available for the meta-analysis for severe adverse events; therefore, the funnel plot for this outcome is not displayed.
4. Publication bias in studies on Avocado/soybean unsaponifiables

**Figure 72:** Funnel plot using data for the meta-analysis comparing gastrointestinal disorders with avocado/soybean unsaponifiables versus placebo in patients with OA.
Figure 73: Funnel plot using data for the meta-analysis comparing nervous system disorders with avocado/soybean unsaponifiables versus placebo in patients with OA.
**Figure 74**: Funnel plot using data for the meta-analysis comparing severe adverse events with avocado/soybean unsaponifiables versus placebo in patients with OA.
**Figure 75:** Funnel plot using data for the meta-analysis comparing dropouts due to adverse events with avocado/soybean unsaponifiables versus placebo in patients with OA.

Note: Very few studies of avocado/soybean unsaponifiables versus placebo (<5) were available for the meta-analyses for cardiac disorders, vascular disorders, skin and subcutaneous tissue disorders, musculoskeletal and connective tissue disorders, renal and urinary disorders, and serious adverse events; therefore, the funnel plots for these outcomes are not displayed.