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Alimentary Pharmacology  
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Systematic Review with Meta-analysis

### Systematic review with network meta-analysis: comparative effectiveness and safety of strategies for preventing NSAID-associated gastrointestinal toxicity

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As part of AP&T's peer-review process, a technical check of this meta-analysis was performed by Dr Y. Yuan. This article was accepted for publication after full peer-review.

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## Summary

## Background

Many strategies are used to prevent nonsteroidal anti-inflammatory drug (NSAID)-associated gastrointestinal toxicity, but the comparative effectiveness remains unclear.

## Aim

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To evaluate the comparative effectiveness of clinical strategies for preventing gastrointestinal toxicity induced by NSAIDs.

## Methods

MEDLINE, EMBASE and the Cochrane Library (from their inception to May 2015) were searched for randomised controlled trials comparing the risk of gastrointestinal adverse events in patients taking nonselective NSAIDs, selective cyclooxygenase(COX)-2 inhibitors or nonselective NSAIDs/COX-2 inhibitors plus gastroprotective agents [proton pump inhibitors (PPIs), histamine-2 receptor antagonists, misoprostol]. Both pairwise meta-analysis and Bayesian network meta-analysis were performed.

## Results

Analyses were based on 82 trials including 125 053 participants. Network meta-analysis demonstrated that selective COX-2 inhibitors + PPIs [Risk ratio (RR), 95% Credible Interval (CrI): ulcer complications 0.07, 0.02–0.18], selective COX-2 inhibitors (RR, 95% CrI: ulcer complications 0.25, 0.15–0.38; symptomatic ulcer 0.12, 0.04–0.30), nonselective NSAIDs + PPIs (RR, 95% CrI: ulcer complications 0.28, 0.18–0.41; symptomatic ulcer 0.11, 0.04–0.23), nonselective NSAIDs + misoprostol (RR, 95% CrI: ulcer complications 0.47, 0.24–0.81; symptomatic ulcer 0.41, 0.13–1.00) were associated with significantly lower risk of clinical gastrointestinal events compared with nonselective NSAIDs. For all effectiveness endpoints, selective COX-2 inhibitors + PPIs was associated with the lowest absolute event probability and the highest rank, followed by selective COX-2 inhibitors and thirdly by nonselective NSAIDs + PPIs.

## Conclusion

The combination of selective COX-2 inhibitors plus PPIs provides the best gastrointestinal protection, followed by selective COX-2 inhibitors, and thirdly by nonselective NSAIDs plus PPIs.

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