

# General practitioners' advice to use topical rather than oral ibuprofen resulted in equivalent effects on chronic knee pain

## QUESTION

For older patients with chronic knee pain, should general practitioners advise use of topical or oral non-steroidal anti-inflammatory drugs (NSAIDs)?

## METHODS

**Design:** randomised controlled trial (Topical or Oral Ibuprofen [TOIB]).

**Allocation:** concealed.

**Blinding:** blinded (data collectors).

**Follow-up period:** 12 months.

**Setting:** 26 general practices in the UK.

**Patients:** 282 patients  $\geq 50$  years of age (mean age 63 y, 54% women) with knee pain (97% with osteoarthritis). Exclusion criteria included history of, or awaiting, knee replacement, and recent knee injury.

**Intervention:** the patient's general practitioner recommended preferential use of topical ibuprofen (n = 138) or oral ibuprofen (n = 144).

**Outcomes:** Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, adverse effects, and cost-effectiveness. The study had  $>80\%$  power to show equivalence in WOMAC scores to within 10 mm ( $\alpha = 0.05$ ).

**Patient follow-up:** 88% (intention-to-treat analysis).

## MAIN RESULTS

Groups did not differ for change in WOMAC scores (table). Proportions of patients with  $\geq 1$  unplanned hospital admission were similar (4.4% in the topical group v 1.4% in the oral group,  $p = 0.16$ ); no deaths or episodes of gastric bleeding occurred in either group. Patients in the topical group had a lower rate of minor respiratory adverse effects (7% v 17%,  $p = 0.02$ ), but groups did not differ for minor gastrointestinal (42% v 40%) or renovascular (16% v 15%) adverse effects. Total healthcare costs were £176 lower with topical ibuprofen, with a only a slight reduction in quality-adjusted life years (0.02). The incremental cost-effectiveness ratio for oral ibuprofen was £8810.

## CONCLUSION

In older patients with chronic knee pain, general practitioners' advice to use topical rather than oral ibuprofen resulted in equivalent effects on knee pain, with lower total healthcare costs.

A modified version of this abstract appears in *Evidence-Based Medicine*.

## ABSTRACTED FROM

**Underwood M**, Ashby D, Carnes D, *et al*. Topical or oral ibuprofen for chronic knee pain in older people. The TOIB study. *Health Technol Assess* 2008;**12**:1–176.

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**Sources of funding:** Health Technology Assessment Programme; Goldshield Pharmaceuticals supplied starter packs of topical ibuprofen.

► **Clinical impact ratings:** Elderly care 6/7; Family/general practice 6/7; Pain management 5/7

Advice from general practitioners to use topical v oral ibuprofen for chronic knee pain

WOMAC domain*	Baseline scores		12-month scores		Difference (95% CI)†
	Topical	Oral	Topical	Oral	
Pain	39	30	38	36	1 (–4 to 6)
Stiffness	50	47	46	43	0 (–6 to 5)
Disability	37	38	39	36	3 (–2 to 7)
Global assessment	38	39	40	37	2 (–2 to 6)

\*WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index (visual analogue scale, range 0 to 100 [worst]).

†Difference in change from baseline, adjusted for baseline values. A positive difference favours oral ibuprofen. CI defined in glossary.

Osteoarthritis of the knee is ubiquitous. Millions of people worldwide seek relief from its pain, stiffness, and functional deficits. As definitive treatment is elusive, symptom management remains the clinical challenge. For nearly 30 years, millions of people have used oral NSAIDs, including ibuprofen, to minimise the symptoms of osteoarthritis. More recently, topical NSAID therapy has been supported in many studies (as reviewed by Underwood *et al*) and is widely used in the UK. In contrast, the 2008 edition of Epocrates, a clinical decision support software programme popular in the USA, does not list topical NSAIDs of any kind as recommended treatment for osteoarthritis; only topical diclofenac is included in the Epocrates drug reference.

In this context, the findings of the equivalence trial of oral and topical ibuprofen by Underwood *et al* are important for nurses in the USA. The TOIB trial, funded by the UK Health Technology Assessment Programme, provides clear evidence of the equivalence and safety of advice to use topical ibuprofen compared with advice to use oral ibuprofen. Originally, the investigators aimed to enrol only patients  $\geq 65$  years of age, but when recruitment was slower than expected, enrolment age was lowered to  $\geq 50$  years; hence, this study of "older" patients had a relatively young mean age of 63 years.

Although the WOMAC scores did not improve from baseline to 12 months with either topical or oral

ibuprofen, the silver lining is that pain, stiffness, and disability did not progress. In the final cost analysis, although the acquisition costs of the topical preparation were higher, the overall costs were lower because of the avoidance of expenses related to minor side effects such as indigestion. Overall, nurses can now confidently educate patients and other professionals on the clinical equivalence of topical and oral ibuprofen for patients  $\geq 50$  years of age who have osteoarthritic knee pain.

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