

**Acute gout: Oral steroids work as well as NSAIDs. *J Fam Pract.* 2008;57:655-657.**

**Potential PURL Review Form: Randomized controlled trials**

**SECTION1: IDENTIFYING INFORMATION**

<b>1.0</b> Citation	Janssens HJ, Janssen M, van de Lisdonk EH, van Riel PL, van Weel C. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial. <i>Lancet.</i> 2008;371:1854-1860.
<b>1.1</b> Editors classification of nominated study	Potential PURL
<b>1.3</b> Hypertext link to PDF of full article	<a href="http://www.thelancet.com/journals/lancet/article/PIIS0140673608607990/fulltext">http://www.thelancet.com/journals/lancet/article/PIIS0140673608607990/fulltext</a>
<b>1.4</b> First date published study available to readers	5/31/08
<b>1.5</b> PubMed ID	18514729
<b>1.6</b> Nominated By	Sarah-Anne Schumann
<b>1.7</b> Institutional Affiliation of Nominator	University of Chicago
<b>1.8</b> Date Nominated	5/31/08
<b>1.9</b> Identified Through	<i>Lancet</i>
<b>1.10</b> PURLS Editor	Bernard Ewigman
<b>1.11</b> Nomination Decision Date	6/2/08
<b>1.12</b> Potential PURL Review Form (PPRF) type	RCTs
<b>1.13</b> Other comments, materials or discussion	
<b>1.14</b> Assigned Potential PURL Reviewer	Bernard Ewigman
<b>1.15</b> Reviewer Affiliation	University of Chicago
<b>1.16</b> Date Review Due	6/19/08

<p><b>1.17 Abstract</b></p>	<p><b>BACKGROUND:</b> Nonsteroidal anti-inflammatory drugs and colchicine used to treat gout arthritis have gastrointestinal, renal, and cardiovascular adverse effects. Systemic corticosteroids might be a beneficial alternative. We investigated equivalence of naproxen and prednisolone in primary care. <b>METHODS:</b> We did a randomised clinical trial to test equivalence of prednisolone and naproxen for the treatment of monoarticular gout. Primary care patients with gout confirmed by presence of monosodium urate crystals were eligible. 120 patients were randomly assigned with computer-generated randomisation to receive either prednisolone (35 mg once a day; n=60) or naproxen (500 mg twice a day; n=60), for 5 days. Treatment was masked for both patients and physicians. The primary outcome was pain measured on a 100-mm visual analogue scale and the a priori margin for equivalence set at 10%. Analyses were done per protocol and by intention to treat. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN14648181. <b>FINDINGS:</b> Data were incomplete for 1 patient in each treatment group, so per-protocol analyses included 59 patients in each group. After 90 h, the reduction in the pain score was 44.7 and 46.0 mm for prednisolone and naproxen, respectively (difference 1.3 mm; 95% CI, -9.8 to 7.1), suggesting equivalence. The difference in the size of change in pain was 1.57 mm (95% CI, -8.65 to 11.78). Adverse effects were similar between groups, minor, and resolved by the 3-week follow-up. <b>INTERPRETATION:</b> Oral prednisolone and naproxen are equally effective in the initial treatment of gout arthritis over 4 days. <b>FUNDING:</b> Rheumatology Research Fund, Arnhem, Netherlands.</p>
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**SECTION 2: DETAILED STUDY DESCRIPTION**

<p><b>2.1</b> Number of patients starting each arm of the study?</p>	<p>60</p>
<p><b>2.2</b> Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)?</p>	<p>Dutch primary care patients with acute gout and confirmed urate crystals</p>
<p><b>2.3</b> Intervention(s) being investigated?</p>	<p>Prednisolone (35 mg once a day; n=60) or naproxen (500 mg twice a day; n=60), for 5 days</p>
<p><b>2.4</b> Comparison treatment(s), placebo, or nothing?</p>	<p>Above</p>
<p><b>2.5</b> Length of follow up? Note specified end points e.g. death, cure, etc.</p>	<p>3 weeks</p>

<b>2.6</b> What outcome measures are used? List all that assess effectiveness.	The primary outcome was pain measured on a 100-mm visual analogue scale and the a priori margin for equivalence set at 10%.
<b>2.7</b> What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, <i>P</i> values, etc.	Equivalence of pain control at 90 hr as measured on a visual analogue scale. After 90 h the reduction in the pain score was 44.7 and 46.0 mm for prednisolone and naproxen, respectively (difference 1.3 mm; 95% CI, -9.8 to 7.1), suggesting equivalence. The difference in the size of change in pain was 1.57 mm (95% CI, -8.65 to 11.78). Adverse effects were similar between groups, minor, and resolved by the 3-week follow-up.
<b>SECTION 3: INTERNAL VALIDITY</b>	
<b>3.1</b> Study addresses an appropriate and clearly focused question	Well addressed
<b>3.2</b> Random allocation to comparison groups	Well addressed
<b>3.3</b> Concealed allocation to comparison groups	Well addressed
<b>3.4</b> Subjects and investigators kept "blind" to comparison group allocation	Well addressed
<b>3.5</b> Comparison groups are similar at the start of the trial	Well addressed
<b>3.6</b> Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias.	Well addressed
<b>3.7</b> Were all relevant outcomes measured in a standardized, valid, and reliable way?	Well addressed
<b>3.8</b> Are patient-oriented outcomes	Yes. Pain.

included? If yes, what are they?	
<b>3.9</b> What percent dropped out, and were lost to follow up? Could this bias the results? How?	Only 1 patient
<b>3.10</b> Was there an intention-to-treat analysis? If not, could this bias the results? How?	Yes.
<b>3.11</b> If a multi-site study, are results comparable for all sites?	N/A
<b>3.12</b> Is the funding for the trial a potential source of bias? If yes, what measures were taken to ensure scientific integrity?	Funding was through the Rheumatology Research Fund, Arnhem, Netherlands.
<b>SECTION 4: EXTERNAL VALIDITY</b>	
<b>4.1</b> To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized.	Primary care patients with acute gout.
<b>4.2</b> In what care settings might the findings apply, or not apply?	Primary care, emergency care
<b>4.3</b> To which clinicians or policy makers might the findings be relevant?	Family physicians, other primary care providers, emergency physicians.
<b>SECTION 5: REVIEW OF SECONDARY LITERATURE</b>	
<b>5.1</b> DynaMed excerpts	Corticosteroids and adrenocorticotrophic hormone (ACTH) may be used in patients in whom NSAIDs and colchicine are contraindicated or ineffective. The following studies are quoted for

	evidence <a href="#">Lancet 2008 May 31;371(9627):1854</a> <a href="#">Ann Emerg Med 2007 May;49(5):670</a>
5.2 DynaMed citation/access date	<a href="http://dynaweb.ebscohost.com/Detail.aspx?id=115215&amp;sid=d7881a8a-e99d-491d-b4c3-1b635f8ad12b@SRCSM1">http://dynaweb.ebscohost.com/Detail.aspx?id=115215&amp;sid=d7881a8a-e99d-491d-b4c3-1b635f8ad12b@SRCSM1</a> Accessed June 18, 2008
5.3 UpToDate excerpts	<b>Systemic glucocorticoids</b> are an alternative to NSAIDs or colchicine for the treatment of acute gout. These agents can be used particularly when NSAIDs and colchicine are contraindicated or when intraarticular glucocorticoids are not an option, as in polyarticular disease.  The data on oral glucocorticoids efficacy are limited. Clinical experience has shown that short-course glucocorticoids are effective in decreasing pain.
5.4 UpToDate citation/access date	<a href="http://www.uptodate.com/online/content/topic.do?topicKey=crystald/2460&amp;selectedTitle=5~150&amp;source=search_result">http://www.uptodate.com/online/content/topic.do?topicKey=crystald/2460&amp;selectedTitle=5~150&amp;source=search_result</a> ; accessed on June 18, 2008
5.5 PEPID PCP excerpts	<ol style="list-style-type: none"> <li>1. Acute treatment <ul style="list-style-type: none"> <li>○ Aggressively treat pain during acute attack <ul style="list-style-type: none"> <li>▪ Usually will need opioid</li> </ul> </li> <li>○ <a href="#">NSAIDs</a> <ul style="list-style-type: none"> <li>▪ Any and all</li> <li>▪ <a href="#">Indocin</a> traditionally most used</li> <li>▪ Avoid in renal impairment</li> </ul> </li> <li>○ <a href="#">Colchicine</a> <ul style="list-style-type: none"> <li>▪ 0.5- or 0.6-mg tabs, 1-2 initially followed by 1-2 tabs every hour. until resolved or GI problems develop (very common) or max dose 8 mg</li> <li>▪ May be given IV 1-2 mg with additional dose of 1 mg in 12-24 h</li> </ul> </li> <li>○ <a href="#">Steroids</a> <ul style="list-style-type: none"> <li>▪ Consider oral, IV, IM or intraarticular <ul style="list-style-type: none"> <li>▪ <a href="#">Prednisone</a> 40 mg PO daily until response</li> </ul> </li> </ul> </li> </ul> </li> </ol>
5.6 PEPID citation/access data	<a href="http://www.pepidonline.com/Main.aspx">http://www.pepidonline.com/Main.aspx</a> Accessed June 18, 2008
5.7 Other excerpts (USPSTF; other guidelines; etc.)	
5.8 Citations for other excerpts	
<b>SECTION 6: CONCLUSIONS</b>	

<p><b>6.1</b> How well does the study minimize sources of internal bias and maximize internal validity? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)</p>	<p>1</p>
<p><b>6.2</b> If 6.1 was coded as 4 or greater, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results?</p>	
<p><b>6.3</b> Are the results of this study relevant to the health care needs of patients cared for by “full scope” family physicians, general internists, general pediatricians, or general OB/GYNs? Are they applicable without significant change in programs or policies such as the organization or financing of practice? Give one number on a scale of 1 to 7 (1=absolutely relevant; 4=neutral; 7=not at all relevant)</p>	<p>1</p>
<p><b>6.4</b> Please explain your response to item 6.3.</p>	<p>Gout is common and important; corticosteroids are cheap and easy to prescribe on a short-term basis.</p>
<p><b>6.5</b> What is the main recommendation for change in practice, if any? Include a description of the change in practice, the indications, and the target population.</p>	<p>Prescribe 5 days of oral corticosteroids to reduce pain from acute gout with fewer side effects than with nonsteroidal anti-inflammatory drugs.</p>
<p><b>SECTION 7: EDITORIAL DECISIONS</b></p>	
<p><b>7.1</b> FPIN PURLs editorial decision (select one)</p>	<p>Pending PURL</p>
<p><b>7.2</b> FPIN PURLS Editor</p>	<p>Bernard Ewigman</p>

7.3 Date of decision	June 19, 2008
7.4 Brief summary of decision	<p>This is the second RCT showing that control of pain from acute gout is controlled by oral corticosteroids equally as with NSAIDs with similar side effects. Two other nonrandomized studies had similar findings. This trial has the advantage of having recruited patients from primary care and confirming the diagnosis through aspiration of joint fluid and documentation of urate crystals. Oral corticosteroids are mentioned as an option in current recommendations, but not prominently. The main advantage would be for patients with contraindications to NSAIDs, such as those with renal impairment or a history of ulcer disease. Fifteen percent of patients screened for this trial were not eligible because of a contraindication to NSAIDs. Those patients, an important sub-group, could benefit from oral corticosteroids.</p> <p>Pending PURL Review: The main issue is whether this is a practice changer. Lisa Vargish estimates that about 20%-30% (of her patients) get prednisone and that is because they cannot tolerate or take other medicines for some reason, renal, GI etc. She says she would be more inclined to treat with prednisone because of this study. So she thinks this study would change her practice and she would prescribe steroids more frequently. She says she still treats some patients with colchicine, because prednisone also has side effects and because it is something she was taught to do and sees others doing.</p> <p>According to the National Ambulatory Medical Care Survey data, based on a representative sample of outpatients and emergency department patients of all ages with a diagnosis of gout, of those who received a drug:</p> <ul style="list-style-type: none"> <li>• 48% got an NSAID</li> <li>• 30% got colchicine</li> <li>• 22% got a corticosteroid</li> </ul> <p>Sermo survey: 84 people responded so far (July 2):</p> <ul style="list-style-type: none"> <li>• NSAIDs = 38%</li> <li>• Indocin = 29%</li> <li>• Colchicine = 12%</li> <li>• Steroids = 5%</li> <li>• Don't know, missing, and other = 16%</li> </ul> <p>Bottom line...looks like oral corticosteroids are used...but there may be more patients who would benefit.</p>

**7.5** Survey Question

What drugs do you most commonly use to treat the pain of acute gout?

- NSAIDs
- Colchicine
- Oral corticosteroids
- Intra-articular corticosteroids
- Other