

SUPPLEMENTARY MATERIAL

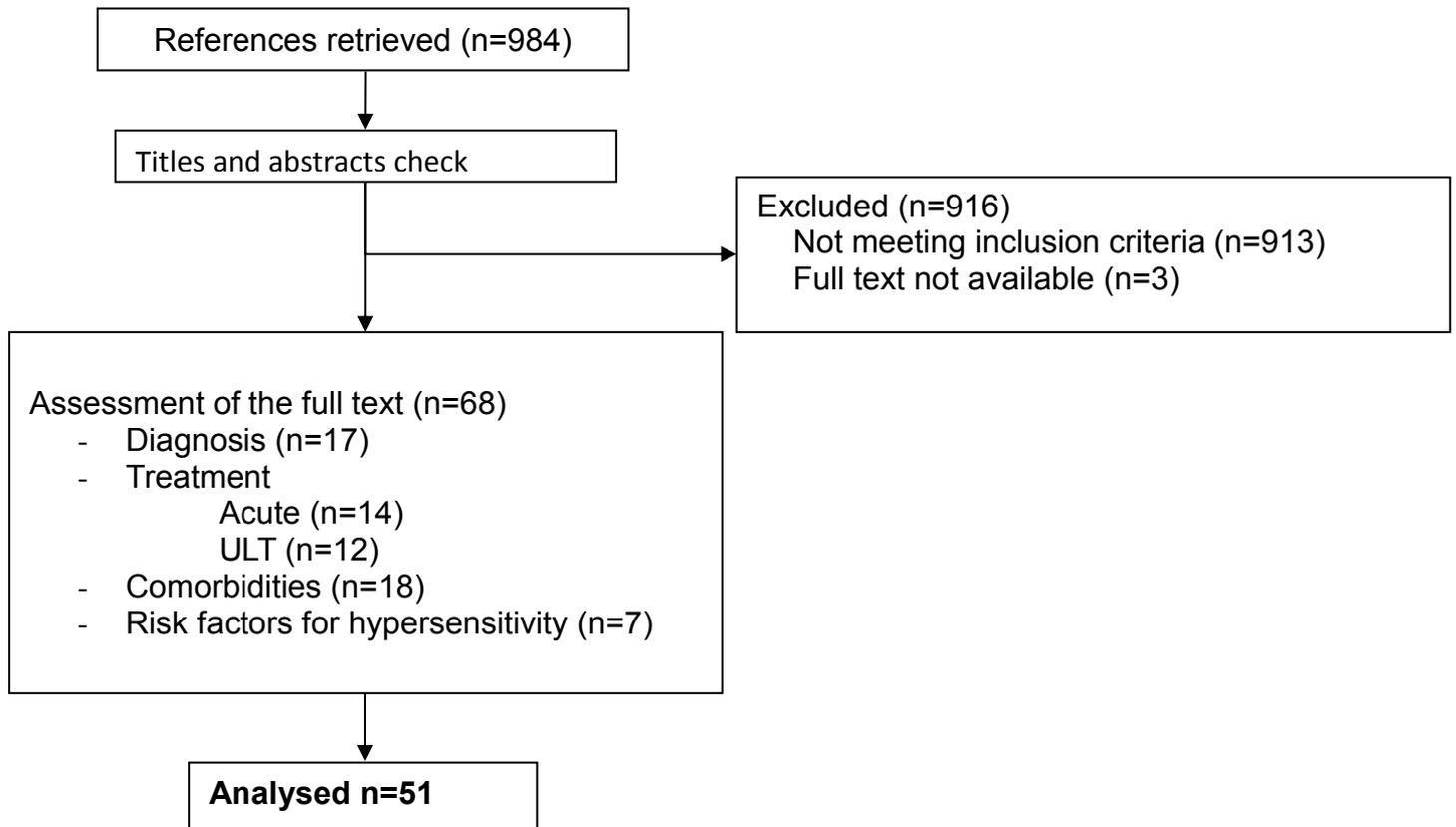
Notes for the 12 items from 2006 recommendations

1) Optimal treatment of gout requires both non-pharmacological and pharmacological modalities and should be tailored according to: (a) specific risk factors (levels of serum urate, previous attacks, radiographic signs) (b) clinical phase (acute/recurrent gout, intercritical gout, and chronic tophaceous gout) (c) general risk factors (age, sex, obesity, alcohol consumption, urate raising drugs, drug interactions, and comorbidity)	
<i>To keep</i>	7.0 [5.0-9.0]
<i>To modify (if to keep >=5)</i>	6.5 [5.0-8.0]
2) Patient education and appropriate lifestyle advice regarding weight loss if obese, diet, and reduced alcohol (especially beer) are core aspects of management	
<i>To keep</i>	8.0 [7.0-9.0]
<i>To modify (if to keep >=5)</i>	7.0 [5.5-8.0]
3) Associated comorbidity and risk factors such as hyperlipidaemia, hypertension, hyperglycaemia, obesity, and smoking should be addressed as an important part of the management of gout	
<i>To keep</i>	7.0 [6.0-9.0]
<i>To modify (if to keep >=5)</i>	6.0 [2.0-7.0]

4) Oral colchicine and/or NSAID are first line agents for systemic treatment of acute attacks, in the absence of contraindications, an NSAID is a convenient and well accepted option	
<i>To keep</i>	7.0 [6.0-8.0]
<i>To modify (if to keep ≥ 5)</i>	8.0 [4.0-9.0]
5) High doses of colchicines lead to side effects, and low doses (for example, 0.5 mg three times daily) may be sufficient for some patients with acute gout	
<i>To keep</i>	8.0 [7.0-8.0]
<i>To modify (if to keep ≥ 5)</i>	3.5 [2.0-8.0]
6) Intra-articular aspiration and injection of long acting steroid is an effective and safe treatment for an acute attack	
<i>To keep</i>	7.0 [6.0-9.0]
<i>To modify (if to keep ≥ 5)</i>	8.0 [4.0-9.0]
7) Urate lowering therapy is indicated in patients with recurrent acute attacks, arthropathy, tophi, or radiographic changes of gout	
<i>To keep</i>	8.0 [8.0-9.0]
<i>To modify (if to keep ≥ 5)</i>	7.0 [5.0-9.0]
8) The therapeutic goal of urate lowering therapy is to promote crystal dissolution and prevent crystal formation. This is achieved by maintaining the serum uric acid below the saturation point for monosodium urate (<360 µmol/l)	
<i>To keep</i>	8.0 [6.0-9.0]
<i>To modify (if to keep ≥ 5)</i>	6.0 [5.0-9.0]

<p>9) Allopurinol is an appropriate long term urate lowering drug. It should be started at a low dose (for example, 100 mg daily) and increased by 100 mg every 2–4 weeks if required. The dose must be adjusted in patients with renal impairment. If allopurinol toxicity occurs, options include other xanthine oxidase inhibitors, a uricosuric agent, or allopurinol desensitisation (the latter only in cases of mild rash)</p>	
<p><i>To keep</i></p>	<p>6.0 [2.0-8.0]</p>
<p><i>To modify (if to keep >= 5)</i></p>	<p>4.5 [2.0-8.5]</p>
<p>10) Uricosuric agents such as probenecid and sulphinyprazole can be used as an alternative to allopurinol in patients with normal renal function but are relatively contraindicated in patients with urolithiasis. Benzbromarone can be used in patients with mild to moderate renal insufficiency on a named patient basis but carries a small risk of hepatotoxicity</p>	
<p><i>To keep</i></p>	<p>6.5 [4.0-8.0]</p>
<p><i>To modify (if to keep >= 5)</i></p>	<p>6.5 [3.0-8.0]</p>
<p>11) Prophylaxis against acute attacks during the first months of urate lowering therapy can be achieved by colchicine (0.5–1 mg daily) and/or an NSAID (with gastro-protection if indicated)</p>	
<p><i>To keep</i></p>	<p>8.0 [7.0-8.0]</p>
<p><i>To modify (if to keep >= 5)</i></p>	<p>5.5 [2.0-8.0]</p>
<p>12) When gout associates with diuretic therapy, stop the diuretic if possible. For hypertension and hyperlipidaemia consider use of losartan and fenofibrate, respectively (both have modest uricosuric effects)</p>	
<p><i>To keep</i></p>	<p>8.0 [6.0-8.0]</p>
<p><i>To modify (if to keep >= 5)</i></p>	<p>3.0 [2.0-7.0]</p>

Flowchart of the systematic literature review (January 2005-June 2013)



Updated systematic literature review (January 2005-May 2016)

- Randomized controlled trials = 37
- Systematic literature review/Meta-analysis: n= 46

Level of agreement from external GPs (n=8) and Rheumatologists (n=5)

Item	Level of agreement (mean±SD)
A	8.3±2.1
B	8.0±1.0
C	8.0±1.5
1	7.82±1.5
2	8.5±0.5
3	8.4±0.8
4	7.9±1.4
5	8.2±0.9
6	8.1±1.5
7	8.1±1.6
8	8.0±1.3
9	8.5±0.9
10	8.0±1.7
11	8.2±1.3

Categories of evidence (Ref. 19)

Category	Evidence
1A	From meta-analysis of randomised controlled trials
1B	From at least one randomised controlled trial
2A	From at least one controlled study without randomisation
2B	From at least one type of quasi-experimental study
3	From descriptive studies, such as comparative studies, correlation studies or case-control studies
4	From expert committee reports or opinions and/or clinical experience of respected authorities

Strength of recommendations (Ref. 19)

Strength	Directly based on
A	Category I evidence
B	Category II evidence or extrapolated recommendations from category I evidence
C	Category III evidence or extrapolated recommendation from category I or II evidence
D	Category IV evidence or extrapolated recommendation from category II or III evidence

Percentage of patients achieving target serum uric acid of <6.0 mg/dl (360 µmol/L) in pivotal trials of febuxostat versus allopurinol.

	Duration	Randomized patients (n)	Allopurinol 300 mg	Febuxostat 80 mg	Febuxostat 120 mg	Febuxostat 240 mg
Fact (151)	52 weeks	762	21%	53%	62%	
Apex (97)	28 weeks	1072	41%	76%	87%	94%
Confirm (149)	6 months	2269	42%	67%		