Supplementary Materials

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Supplementary File 1. Instructions for Guideline Appraisal Using the AGREE II Instrument

Supplementary Table 1. Search strategy in PubMed

1	urate* OR uric acid OR gout OR hyperuricemia OR hyperuricaemia
2	guideline OR guideline* OR consensus OR policy OR polic* OR statement* OR
	recommendation*
3	1 AND 2

1	exp hyperuricemia/
2	exp gout/
3	exp uric acid/
4	exp urate/
5	gout.m_titl.
6	uric acid.m_titl.
7	urate\$.m_titl.
8	hyperuric?emia.m_titl.
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	exp practice guideline/
11	guideline\$.m_titl.
12	consensus.m_titl.
13	position statement\$.m_titl.
14	exp health care policy/ or exp policy/
15	recommendation\$.m_titl.
16	10 or 11 or 12 or 13 or 14 or 15
17	9 and 16

Supplementary Table 2. Search strategy in EMBASE using the OVID interface

Databases	Date of	Search strategy	Results	Full text	Included	URL
	search		found	screened	documents	
National Guideline	2017/07/24	hyperuricaemia OR hyperuricemia OR gout	27	6	4	www.guideline.gov
Clearinghouse						
Guidelines International	2017/07/24	hyperuricaemia OR hyperuricemia OR gout,	11	5	5	www.g-i-n.net
Network		Search mode: Guidelines				
National Institute for Health	2017/07/24	hyperuricaemia OR hyperuricemia OR gout	25	2	0	www.nice.org.uk
and Care Excellence						
National Health Service	2017/07/24	hyperuricaemia OR hyperuricemia OR gout,	498	5	3	www.evidence.nhs.uk
		filter type: guidance and policy				
Scottish Intercollegiate	2017/07/24	NA	53	0	0	www.sign.ac.uk/our-guidelines.html
Guidelines Network						
Guidelines and Audit	2017/07/24	"hyperuricaemia" OR "hyperuricemia" OR	0	0	0	rqia.org.uk/search-result
Implementation Network		"gout"				
Turning Research Into	2017/07/24	hyperuricaemia OR hyperuricemia OR gout,	155	9	3	www.tripdatabase.com
Practice Database		filter: all secondary evidence				
Epistemonikos database	2017/07/24	hyperuricaemia OR hyperuricemia OR gout,	38	2	1	www.epistemonikos.org
		filter: Broad syntheses OR Structured summaries				
Chinese Biomedical	2017/07/22	[Original search term in Chinese]	423	7	5	202.115.54.56/index.jsp
Literature Database		(hyperuricaemia OR gout) AND (guideline OR				
		consensus OR statement OR recommendation)				
Wanfang Data	2017/07/22	[Original search term in Chinese]	1331	19	4	www.wanfangdata.com.cn/
		(hyperuricaemia OR gout) AND (guideline OR				
		consensus OR statement OR recommendation)				

Supplementary Table 3. Searches in guideline databases

Abbreviations: NA: Not applicable.

Supplementary Table 4. Excluded studies and reasons for		
First author	Year	Reason for exclusion
Wuthrich [68]	2016	Review
Ceriotti [69]	2016	Primary study
Liote [70]	2016	Editorial
de Lautour [71]	2016	Primary study
de Lautour [72]	2014	Conference abstract
Dalbeth [73]	2015	Review
Terslev [74]	2015	Primary study
Turk [75]	2016	Not providing specific recommendations for hyperuricemia or gout
Stewart Coats [76]	2016	Editorial
Sullivan [77]	2015	Review
Gutierrez [78]	2015	Primary study
Grainger [79]	2015	Primary study
Robinson [80]	2015	Review
Chaudhary [81]	2013	Review
Bakris [82]	2014	Multimedia section
Terkeltaub [83]	2013	Review
Lyseng-Williamson [84]	2013	Review
Deodhar [85]	2013	Review
Simao [86]	2012	Review
Stamp [87]	2011	Review
Jansen [88]	2010	Not produced by related professional associations, institutes, societies, or communities
Grainger [89]	2009	Review
Grainger [90]	2008	Review
Dalbeth [91]	2007	Review
Jordan [92]	2007	Replaced by updated versions from the same organization
Becker [93]	2007	Not providing specific recommendations for hyperuricemia or gout

Supplementary Table 4. Excluded studies and reasons for exclusion

Zhang [55]	2006	Replaced by updated versions from the same organization
Caramia [94]	2004	Review
Terkeltaub [95]	2003	Case report
Cleland [96]	1995	Review
Hande [97]	1984	Case series
Committee on the Review of Medicines [98]	1978	Not providing specific recommendations for hyperuricemia or gout
Mourgues [99]	2016	Conference abstract
Bakris [100]	1970	Not providing specific recommendations for hyperuricemia or gout
Pai [101]	2015	Review
Vargas-Santos [102]	2016	Review
Filiopoulos [103]	2016	Comment letter
Chinchilla [104]	2016	Review
Rimler [105]	2016	Review
Saito [106]	2016	Not providing specific recommendations for hyperuricemia or gout
Mody [107]	2015	Review
Richette [108]	2014	Conference abstract
Richette [109]	2014	Conference abstract
Gutierrez [110]	2014	Conference abstract
Furst [111]	2013	Not providing specific recommendations for hyperuricemia or gout
Hershfield [112]	2013	Not providing specific recommendations for hyperuricemia or gout
Andres [113]	2012	Conference abstract
Stevenson [114]	2011	Technology appraisal
Diaz-Borjon [115]	2009	Review
Furst [116]	2010	Not providing specific recommendations for hyperuricemia or gout
Taylor [117]	2009	Primary study
Taylor [118]	2008	Primary study
Bussieres [119]	2008	Not providing specific recommendations for hyperuricemia or gout
Brooks [120]	2007	Review

Bestermann [121]	2005	Not providing specific recommendations for hyperuricemia or gout
Schumacher Jr [122]	2004	Review
Bartlett [123]	2002	Not providing specific recommendations for hyperuricemia or gout
Furst [124]	2013	Not providing specific recommendations for hyperuricemia or gout
Newberry [125]	2017	Review
Shekelle [126]	2017	Review
Sandberg [127]	2015	Not providing specific recommendations for hyperuricemia or gout
Kallinich [128]	2007	Not providing specific recommendations for hyperuricemia or gout
Preminger [129]	2007	Not providing specific recommendations for hyperuricemia or gout
TA164 [130]	2008	Technology appraisal
Phoon [131]	2012	Not providing specific recommendations for hyperuricemia or gout
Li [132]	2011	Review
Zhang [133]	2013	Review
Deng [134]	2016	Primary study
Chinese Rheumatology Association [135]	2004	Replaced by updated versions from the same organization
Chinese College of Cardiovascular Physicians [136]	2010	Replaced by updated versions from the same organization
Chinese Rheumatology Association [137]	2011	Replaced by updated versions from the same organization
National Department of Health, Pretoria, South Africa	2006	Not providing specific recommendations for hyperuricemia or gout
[138]		
European Medicines Agency [139]	2012	Not providing specific recommendations for hyperuricemia or gout
Agency for Healthcare Research and Quality [140]	2017	Review
Agency for Healthcare Research and Quality [141]	2017	Review
National Institute for Health and Care Excellence [142]	2013	Technology appraisal
Agency for Healthcare Research and Quality [143]	2016	Review
National Health System, United Kingdom [144]	2013	Not providing specific recommendations for hyperuricemia or gout
Canadian Expert Drug Advisory Committee [145]	2011	Not providing specific recommendations for hyperuricemia or gout
CME Academic Detailing Service [146]	2013	Presented as a 'handout', not a clinical practice guideline.
Henderson [147]	2015	Not released by a professional association

Document	Domain 1, %	Domain 2, %	Domain 3, %	Domain 4, %	Domain 5, %	Domain 6, %
3e_2013 [36]	95.8	34.7	65.6	77.8	42.7	72.9
3e_AU_NZ_2015 [43]	84.7	34.7	71.4	73.6	27.1	0.0
3e_PT_2014 [40]	95.8	22.2	42.7	70.8	27.1	0.0
ACP_2017 [19, 20]	93.1	70.8	80.2	86.1	27.1	70.8
ACR_2012 [14, 15]	86.1	81.9	73.4	84.7	1.0	45.8
ACR_EULAR_2015 [42]	86.1	50.0	71.4	98.6	27.1	50.0
BSR_2017 [21]	100.0	80.6	78.1	77.8	66.7	83.3
CCCP_2012 [47]	76.4	9.7	8.3	62.5	0.0	0.0
CRA_2016 [41]	84.7	48.6	50.5	70.8	2.1	33.3
CRA_multi_2017 [22]	79.2	54.2	13.0	63.9	2.1	0.0
CSE_2013 [37]	66.7	38.9	15.6	81.9	9.4	0.0
EULAR_2006 [18]	86.1	23.6	65.1	90.3	24.0	16.7
EULAR_2011 [17]	86.1	48.6	61.5	90.3	13.5	52.1
EULAR_2016 [16]	83.3	79.2	67.7	94.4	26.0	29.2
FMOH_2014 [44]	70.8	50.0	3.1	48.6	6.3	0.0
JSGNAM_2011 [48]	81.9	38.9	37.0	87.5	0.0	0.0
MOH_MSR_AMM_2008 [49]	98.6	61.1	46.4	94.4	11.5	31.3
PRA_2008 [50]	79.2	70.8	63.5	76.4	10.4	12.5
SAMA_2003 [51]	75.0	37.5	28.1	80.6	5.2	50.0
SER_2013 [46]	95.8	72.2	56.8	70.8	22.9	54.2
SIR_2013 [45]	97.2	55.6	56.8	77.8	20.8	0.0
T2T_2016 [39]	95.8	47.2	61.5	81.9	4.2	50.0
TRA_2016 [38]	73.6	40.3	14.1	86.1	7.3	0.0
UTAustin_2009 [52]	76.4	27.8	42.2	68.1	4.2	27.1
Median	85.4	48.6	56.8	79.2	10.9	28.1
Minimum	66.7	9.7	3.1	48.6	0.0	0.0
Maximum	100.0	81.9	80.2	98.6	66.7	83.3

Supplementary Table 5. Domain score for each included guidance document

Document	Don	nain 1			nain 2			ain 3							Dom	ain 4		Dom	nain 5			Dom 6	ain
Item	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
3e_2013 [36]	6.8	6.5	7.0	7.0	1.3	1.0	6.3	3.8	6.3	5.8	5.8	6.8	4.0	1.0	6.0	7.0	4.0	6.8	1.0	5.3	1.3	7.0	3.8
3e_AU_NZ_2015 [43]	6.0	5.5	6.8	5.8	1.0	2.5	6.5	6.8	7.0	6.5	6.5	6.8	1.3	1.0	5.8	6.0	4.5	5.8	1.0	2.8	1.0	1.0	1.0
3e_PT_2014 [40]	6.5	7.0	6.8	4.8	1.3	1.0	2.8	2.3	5.5	3.5	5.5	6.8	1.3	1.0	5.5	6.3	4.0	4.5	1.3	2.8	2.0	1.0	1.0
ACP_2017 [19, 20]	6.0	6.8	7.0	6.3	5.3	4.3	6.8	6.8	6.5	5.0	6.5	5.3	4.8	5.0	5.3	6.8	6.5	2.5	1.8	5.3	1.0	4.0	6.5
ACR_2012 [14, 15]	6.5	5.5	6.5	7.0	5.3	5.5	7.0	7.0	6.8	6.0	5.8	6.0	1.5	3.3	5.8	7.0	5.5	1.0	1.0	1.0	1.3	3.3	4.3
ACR_EULAR_2015 [42]	6.5	5.0	7.0	5.3	4.8	2.0	7.0	6.8	5.3	6.0	7.0	5.5	1.8	3.0	6.8	7.0	7.0	3.8	4.0	1.8	1.0	3.8	4.3
BSR_2017 [21]	7.0	7.0	7.0	5.5	5.3	6.8	7.0	6.0	6.5	6.8	6.3	6.0	5.0	2.0	6.8	6.8	3.5	4.8	4.8	6.5	4.0	7.0	5.0
CCCP_2012 [47]	6.8	3.0	7.0	2.0	1.0	1.8	1.0	1.0	1.0	1.0	3.8	2.0	1.3	1.0	4.5	5.8	4.0	1.0	1.0	1.0	1.0	1.0	1.0
CRA_2016 [41]	6.3	5.0	7.0	5.5	1.0	5.3	5.0	3.3	6.3	3.5	6.0	5.5	1.8	1.0	5.3	6.5	4.0	1.3	1.0	1.3	1.0	1.0	5.0
CRA_multi_2017 [22]	7.0	3.5	6.8	4.8	1.3	6.8	1.0	1.0	1.0	1.3	5.0	2.8	1.3	1.0	5.0	6.5	3.0	1.0	1.3	1.0	1.3	1.0	1.0
CSE_2013 [37]	7.0	1.8	6.3	3.0	1.0	6.0	1.0	1.0	2.0	1.0	5.0	3.5	1.0	1.0	5.5	5.5	6.8	3.0	1.0	1.0	1.3	1.0	1.0
EULAR_2006 [18]	6.0	5.5	7.0	5.0	1.0	1.3	7.0	7.0	5.8	4.3	6.0	5.8	1.3	2.3	6.0	6.8	6.5	1.0	2.5	5.3	1.0	3.0	1.0
EULAR_2011 [17]	6.5	5.0	7.0	5.0	1.0	5.8	4.0	4.5	6.8	6.0	7.0	7.0	1.3	1.0	5.8	6.8	6.8	1.3	1.3	3.8	1.0	3.8	4.5
EULAR_2016 [16]	6.3	4.8	7.0	5.8	5.0	6.5	5.0	2.0	6.3	6.8	6.0	6.5	6.0	2.0	6.5	6.8	6.8	3.0	1.3	5.0	1.0	1.5	4.0
FMOH_2014 [44]	6.5	2.8	6.5	5.3	1.0	5.8	1.0	1.0	1.0	1.0	2.0	1.5	1.0	1.0	3.0	4.5	4.3	1.0	1.3	2.3	1.0	1.0	1.0
JSGNAM_2011 [48]	5.3	5.5	7.0	1.8	4.3	4.0	1.3	1.0	6.8	3.3	6.3	3.8	2.5	1.0	6.8	6.3	5.8	1.0	1.0	1.0	1.0	1.0	1.0
MOH_MSR_AMM_2008 [49]	6.8	7.0	7.0	5.5	1.5	7.0	4.3	1.0	5.8	1.5	5.8	4.8	2.5	4.8	6.5	6.8	6.8	1.8	3.0	1.0	1.0	4.0	1.8
PRA_2008 [50]	6.5	5.5	5.3	3.8	5.0	7.0	5.0	4.3	7.0	4.8	6.5	4.8	1.3	5.0	5.3	6.5	5.0	1.8	1.3	2.5	1.0	1.0	2.5
SAMA_2003 [51]	6.5	3.0	7.0	4.0	1.3	4.5	1.0	1.0	1.0	4.0	6.5	2.8	2.5	2.8	5.0	6.5	6.0	1.0	2.0	1.3	1.0	7.0	1.0
SER_2013 [46]	7.0	6.3	7.0	6.8	5.0	4.3	3.3	1.0	7.0	4.0	6.8	4.8	2.0	6.5	5.8	6.8	4.3	3.5	2.3	2.8	1.0	6.5	2.0
SIR_2013 [45]	6.8	6.8	7.0	6.3	1.0	5.8	4.0	6.8	6.3	4.3	6.3	5.5	1.3	1.0	6.3	6.8	4.0	2.5	1.0	4.5	1.0	1.0	1.0
T2T_2016 [39]	6.3	7.0	7.0	5.3	5.0	1.3	7.0	6.5	6.5	6.5	3.3	4.0	1.8	2.0	5.0	6.3	6.5	2.0	1.0	1.0	1.0	3.5	4.5
TRA_2016 [38]	5.8	3.5	7.0	5.0	1.5	3.8	1.0	1.3	1.0	1.3	5.5	2.5	1.3	1.0	5.5	6.5	6.5	1.0	1.5	2.3	1.0	1.0	1.0
UTAustin_2009 [52]	7.0	2.8	7.0	3.0	1.0	4.0	4.3	2.0	7.0	2.5	4.3	5.3	2.0	1.0	4.8	5.3	5.3	1.3	1.5	1.3	1.0	4.0	1.3

Supplementary Table 6. Mean scores across reviewers for the individual AGREE II domain items

	Ite	Ite	Ite	Ite	Ite	Ite	Ite	Ite	Ite	Item	Ite	Item											
	m1	m2	m3	m4	m5	m6	m7	m8	m9	10	m11	12	13	14	15	16	17	18	19	20	21	22	23
3e_2013	[36]																						
Rev1	7	7	7	7	1	1	6	4	4	5	7	7	2	1	6	7	4	7	1	5	1	7	4
Rev2	6	7	7	7	1	1	6	2	7	5	6	7	4	1	6	7	4	7	1	6	1	7	4
Rev3	7	5	7	7	2	1	7	5	7	6	5	6	5	1	5	7	4	7	1	5	2	7	3
Rev4	7	7	7	7	1	1	6	4	7	7	5	7	5	1	7	7	4	6	1	5	1	7	4
3e_AU_N	NZ_201	15 [43]	l																				
Rev1	5	5	7	7	1	2	7	7	7	7	7	7	2	1	5	6	4	6	1	2	1	1	1
Rev2	7	5	7	7	1	1	5	7	7	6	6	7	1	1	6	7	4	6	1	4	1	1	1
Rev3	5	7	7	4	1	4	7	7	7	7	7	7	1	1	6	5	6	6	1	2	1	1	1
Rev4	7	5	6	5	1	3	7	6	7	6	6	6	1	1	6	6	4	5	1	3	1	1	1
3e_PT_2	014 [4	0]																					
Rev1	6	7	7	5	1	1	3	1	7	3	6	7	2	1	5	6	4	4	1	5	1	1	1
Rev2	6	7	7	5	1	1	3	1	7	3	6	7	1	1	6	7	4	6	1	3	1	1	1
Rev3	7	7	6	5	2	1	2	1	6	5	4	6	1	1	5	6	4	4	2	2	5	1	1
Rev4	7	7	7	4	1	1	3	6	2	3	6	7	1	1	6	6	4	4	1	1	1	1	1
ACP_20	17 [19,	20]																					
Rev1	6	7	7	6	5	4	7	7	7	5	7	5	5	5	5	7	7	2	2	4	1	4	7
Rev2	6	7	7	6	5	4	7	7	7	5	7	5	5	4	6	7	7	4	3	7	1	4	7
Rev3	6	7	7	6	6	3	6	6	6	6	6	5	4	5	5	6	6	2	1	5	1	4	6
Rev4	6	6	7	7	5	6	7	7	6	4	6	6	5	6	5	7	6	2	1	5	1	4	6
ACR_20	12 [14,	, 15]																					
Rev1	6	5	7	7	5	7	7	7	6	6	6	5	2	3	5	7	4	1	1	1	1	3	4
Rev2	6	7	7	7	7	4	7	7	7	6	6	5	2	3	6	7	7	1	1	1	1	4	4
Rev3	7	5	7	7	5	7	7	7	7	6	5	7	1	3	5	7	7	1	1	1	2	3	4
Rev4	7	5	5	7	4	4	7	7	7	6	6	7	1	4	7	7	4	1	1	1	1	3	5
ACR_EU	JLAR_	2015	[42]																				
Rev1	6	5	7	6	6	2	7	7	7	7	7	5	2	3	7	7	7	3	3	1	1	4	4

Supplementary Table 7. Scores for each individual AGREE II domain items by each reviewer

Rev2	6	5	7	5	6	1	7	7	6	6	7	5	2	3	7	7	7	5	7	1	1	4	4
Rev3	7	5	7	5	6	2	7	7	7	6	7	5	2	3	7	7	7	3	3	1	1	3	4
Rev4	7	5	7	5	1	3	7	6	1	5	7	7	1	3	6	7	7	4	3	4	1	4	5
BSR_201	7 [21]										1												L
Rev1	7	7	7	6	5	7	7	6	6	7	6	6	5	2	7	7	4	5	4	7	2	7	5
Rev2	7	7	7	6	5	7	7	6	6	6	7	5	5	2	7	7	3	5	5	7	5	7	5
Rev3	7	7	7	4	5	6	7	7	7	7	5	6	5	1	6	6	3	4	5	6	2	7	5
Rev4	7	7	7	6	6	7	7	5	7	7	7	7	5	3	7	7	4	5	5	6	2	7	5
CCCP_2	012 [4	7]																					·
Rev1	6	3	7	2	1	2	1	1	1	1	3	1	2	1	3	6	4	1	1	1	1	1	1
Rev2	7	3	7	2	1	1	1	1	1	1	4	3	1	1	4	5	4	1	1	1	1	1	1
Rev3	7	3	7	2	1	1	1	1	1	1	4	2	1	1	6	6	4	1	1	1	1	1	1
Rev4	7	3	7	2	1	3	1	1	1	1	4	2	1	1	5	6	4	1	1	1	1	1	1
CRA_20	16 [41]]																					
Rev1	5	5	7	6	1	4	5	3	7	3	7	5	2	1	5	7	4	1	1	1	1	1	4
Rev2	7	5	7	6	1	5	4	3	6	4	6	5	3	1	6	7	4	1	1	1	1	1	4
Rev3	7	5	7	5	1	6	5	3	6	1	5	6	1	1	5	6	4	1	1	2	1	1	6
Rev4	6	5	7	5	1	6	6	4	6	6	6	6	1	1	5	6	4	2	1	1	1	1	6
CRA_mu	ılti_20	017 [22]																				
Rev1	7	3	7	5	1	7	1	1	1	1	5	3	2	1	5	7	2	1	1	1	1	1	1
Rev2	7	3	7	5	1	7	1	1	1	2	5	2	1	1	5	7	3	1	1	1	1	1	1
Rev3	7	3	7	4	2	6	1	1	1	1	5	5	1	1	5	5	3	1	1	1	2	1	1
Rev4	7	5	6	5	1	7	1	1	1	1	5	1	1	1	5	7	4	1	2	1	1	1	1
CSE_201	13 [37]						-					-						-			-		
Rev1	7	1	6	3	1	6	1	1	2	1	5	5	1	1	5	6	7	3	1	1	1	1	1
Rev2	7	3	6	4	1	6	1	1	3	1	5	3	1	1	6	6	7	3	1	1	1	1	1
Rev3	7	1	7	2	1	7	1	1	2	1	5	3	1	1	6	6	6	3	1	1	2	1	1
Rev4	7	2	6	3	1	5	1	1	1	1	5	3	1	1	5	4	7	3	1	1	1	1	1
EULAR_	-																						
Rev1	5	5	7	5	1	1	7	7	5	3	6	5	2	1	5	7	7	1	2	5	1	4	1

Rev2	6	5	7	5	1	1	7	7	6	5	6	6	1	1	6	7	6	1	4	6	1	4	1
Rev3	7	7	7	5	1	1	7	7	6	5	7	6	1	1	7	7	7	1	1	5	1	1	1
Rev4	6	5	7	5	1	2	7	7	6	4	5	6	1	6	6	6	6	1	3	5	1	3	1
EULAR	2011	[17]				1		1		1											1		<u> </u>
Rev1	6	5	7	4	1	7	4	1	7	7	7	7	2	1	5	7	7	2	1	2	1	4	4
Rev2	6	5	7	5	1	3	4	7	7	4	7	7	1	1	6	7	7	1	1	5	1	4	4
Rev3	7	5	7	6	1	7	4	4	7	7	7	7	1	1	6	7	7	1	1	4	1	4	6
Rev4	7	5	7	5	1	6	4	6	6	6	7	7	1	1	6	6	6	1	2	4	1	3	4
EULAR_2016 [16]																							
Rev1	7	7	7	6	5	7	5	2	7	7	7	7	6	1	7	7	7	2	2	5	1	1	4
Rev2	7	1	7	6	5	7	5	2	7	7	6	7	6	3	7	7	7	4	1	6	1	1	4
Rev3	5	5	7	5	5	5	5	1	6	6	5	6	6	2	5	6	6	4	1	4	1	1	4
Rev4	6	6	7	6	5	7	5	3	5	7	6	6	6	2	7	7	7	2	1	5	1	3	4
FMOH_	FMOH_2014 [44]																						
Rev1	7	3	7	6	1	4	1	1	1	1	2	1	1	1	3	1	4	1	1	2	1	1	1
Rev2	7	3	7	5	1	7	1	1	1	1	2	1	1	1	4	4	4	1	2	3	1	1	1
Rev3	6	2	5	5	1	6	1	1	1	1	1	2	1	1	2	7	6	1	1	1	1	1	1
Rev4	6	3	7	5	1	6	1	1	1	1	3	2	1	1	3	6	3	1	1	3	1	1	1
JSGNAM		1 [48]			-	-		-		-		-					-				-	-	
Rev1	5	5	7	2	4	4	1	1	6	3	6	3	2	1	7	7	4	1	1	1	1	1	1
Rev2	6	5	7	2	4	4	1	1	7	4	6	4	3	1	7	6	7	1	1	1	1	1	1
Rev3	5	7	7	1	4	4	1	1	7	1	7	4	2	1	7	6	7	1	1	1	1	1	1
Rev4	5	5	7	2	5	4	2	1	7	5	6	4	3	1	6	6	5	1	1	1	1	1	1
MOH_M	ISR_A	MM_2	2008 [4	-	-	-		-		-											-		_
Rev1	6	7	7	5	1	7	4	1	5	1	6	5	2	4	7	7	7	2	3	1	1	4	1
Rev2	7	7	7	5	3	7	4	1	6	2	6	4	3	5	6	7	7	3	5	1	1	4	2
Rev3	7	7	7	7	1	7	4	1	6	1	6	5	2	5	7	7	7	1	1	1	1	4	2
Rev4	7	7	7	5	1	7	5	1	6	2	5	5	3	5	6	6	6	1	3	1	1	4	2
PRA_20	08 [50]]			-					-											-		
Rev1	5	3	5	4	5	7	5	1	7	4	7	5	1	5	5	7	4	2	1	2	1	1	2

Rev2	7	7	4	3	5	7	5	6	7	4	6	4	2	5	5	6	7	3	2	3	1	1	4
Rev3	7	7	7	4	5	7	5	5	7	6	7	5	1	5	6	7	5	1	1	2	1	1	2
Rev4	7	5	5	4	5	7	5	5	7	5	6	5	1	5	5	6	4	1	1	3	1	1	2
SAMA_2	2003 [5	-	-	-	-		-	-		-	Ť	-		-	-	Ť		-	-	-	_	-	<u> </u>
Rev1	6	3	7	5	1	4	1	1	1	5	7	3	2	3	3	6	7	1	1	2	1	7	1
Rev2	7	3	7	4	1	5	1	1	1	5	7	2	4	2	5	7	4	1	5	1	1	7	1
Rev3	7	3	7	2	1	5	1	1	1	1	7	3	1	1	6	7	7	1	1	1	1	7	1
Rev4	6	3	7	5	2	4	1	1	1	5	5	3	3	5	6	6	6	1	1	1	1	7	1
SER_2013 [46]														<u> </u>									
Rev1	7	6	7	7	5	4	3	1	7	3	7	5	2	5	5	6	4	2	2	2	1	7	2
Rev2	7	6	7	6	5	3	3	1	7	5	6	4	2	7	6	7	4	4	5	3	1	5	2
Rev3	7	7	7	7	5	5	3	1	7	3	7	6	2	7	7	7	4	4	1	4	1	7	2
Rev4	7	6	7	7	5	5	4	1	7	5	7	4	2	7	5	7	5	4	1	2	1	7	2
SIR_201	3 [45]		•						•			•						•		•		•	
Rev1	7	7	7	6	1	7	4	7	5	3	7	5	2	1	7	7	4	2	1	4	1	1	1
Rev2	7	7	7	6	1	4	4	7	7	5	6	5	1	1	6	7	4	4	1	6	1	1	1
Rev3	7	7	7	6	1	6	4	7	7	6	7	6	1	1	6	7	4	1	1	4	1	1	1
Rev4	6	6	7	7	1	6	4	6	6	3	5	6	1	1	6	6	4	3	1	4	1	1	1
T2T_201	16 [39]																						
Rev1	6	7	7	5	5	1	7	7	7	7	3	3	2	1	4	6	7	3	1	1	1	4	2
Rev2	7	7	7	6	5	1	7	7	7	7	4	5	2	5	6	7	7	1	1	1	1	4	4
Rev3	5	7	7	5	5	2	7	6	6	6	2	3	2	1	5	6	6	3	1	1	1	3	6
Rev4	7	7	7	5	5	1	7	6	6	6	4	5	1	1	5	6	6	1	1	1	1	3	6
TRA_20	16 [38]]																					
Rev1	5	3	7	5	1	4	1	1	1	1	6	2	2	1	6	7	7	1	1	2	1	1	1
Rev2	6	3	7	5	1	7	1	1	1	2	6	2	1	1	6	7	7	1	3	3	1	1	1
Rev3	6	3	7	5	3	1	1	2	1	1	5	4	1	1	5	6	6	1	1	2	1	1	1
Rev4	6	5	7	5	1	3	1	1	1	1	5	2	1	1	5	6	6	1	1	2	1	1	1
UTAusti	n_2009	9 [52]																					
Rev1	7	3	7	4	1	4	4	1	7	3	4	5	2	1	3	4	4	1	1	1	1	4	2

Rev2	7	3	7	2	1	4	4	1	7	2	4	5	2	1	5	6	7	2	3	1	1	4	1
Rev3	7	2	7	2	1	4	4	1	7	1	6	5	2	1	6	6	7	1	1	1	1	4	1
Rev4	7	3	7	4	1	4	5	5	7	4	3	6	2	1	5	5	3	1	1	2	1	4	1

Supplementary material

Suppl	ementary Table	8. Summary	of recom	nendations for	r the diagno	sis of gout	and hyper	uricemia	by included guidance document	
TE •	CC 1 1) (CII	1.		1. 1.1	a	OTTA		• 1	

IE: insufficient evidence; MSU: monosodium urate; NA: not applicable; NG: not given; SUA: serum uric acid.

	SAMA_2003 [51]	EULAR_2006 [18]	MOH_MSR_AMM_2008 [49]	PRA_2008 [50]	EULAR_2011 [17]	JSGNAM_2011 [48]	CCCP_2012 [47]	3e_2013 [36]	CSE_2013 [37]	SER_2013 [46]	SIR_2013 [45]	3e_PT_2014 [40]	3e_AU_NZ_2015 [43]	ACR_EULAR_2015 [42]	CRA_2016 [41]	TRA_2016 [38]	ACP_2017 [19, 20]	CRA_multi_2017 [22]
Diagnosis of gout	+	+	+	NG	+	NG	NG	+	NG	+	NG	+	+	+	+	+	+	+
_Clinical manifestations	+	+	+	NA	+	NA	NA	+	NA	+	NA	+	+	+	+	+	+	+
_Laboratory results	+	+	-	NA	+	NA	NA	+	NA	+	NA	+	+	+	+	+	+	+
_Imaging results	-	+*	-	NA	-	NA	NA	+	NA	+	NA	+	+	+	+	+	IE	+
_MSU crystal as definitive diagnosis	+	+	+	NA	+	NA	NA	+	NA	+	NA	+	+	+	+	+	+	+
Monitor urate deposits clearance by imaging	-	-	-	-	-	-	-	-	-	IE	-	-	-	+	-	-	-	+
Is the timing to assess urate deposits with imaging techniques provided?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SUA for hyperuricemia, µmol/L [mg/dL]	+	NG	+	+	+	+	+	NG	+	+	+	NG	NG	NG	NG	+	NG	+
_All gender	420	NG	NG	NG	[6.8]	[7.0]	420 [7.0]	NG	NG	NG	404 [6.8]	NG	NG	NG	NG	[7.0]	NG	NG
_Female	NG	NG	360 [6.0]	357 [6.0]	NG	NG	NG	NG	360	[6.0]	NG	NG	NG	NG	NG	NG	NG	360
_Male	NG	NG	420 [7.0]	416 [7.0]	NG	NG	NG	NG	420	[7.0]	NG	NG	NG	NG	NG	NG	NG	420
Diagnosis of asymptomatic hyperuricemia	NG	NG	+	+	NG	+	+	+.	NG	+	NG	NG	NG	NG	NG	+	NG	NG
_Gout flare	NA	NA	-	+	NA	+	+	+	NA	+	NA	NA	NA	NA	NA	+	NA	NA
_Tophi	NA	NA	-	-	NA	+	-	+	NA	-	NA	NA	NA	NA	NA	-	NA	NA
_Additional medical conditions†	NA	NA	+	+	NA	+	+	-	NA	-	NA	NA	NA	NA	NA	+	NA	NA

*Imaging results are considered for chronic gout, but not for early/acute gout.

†Additional medical conditions considered in the definition of asymptomatic hyperuricemia included complications of gout [47], renal disorder [48], signs or symptoms of

urate deposition [49], and uric acid nephrolithiasis [50]. One document provided a general statement of any clinical presentations [38]. One document explicitly stated that the inclusion of patients with pre-existing renal or cardiovascular disease was allowed [36].

Supplementary Table 9. Summary of recommendations for the treatment of hyperuricemia by included guidance documents

A: allopurinol; Aft: (to initiate ULT) after an acute attack; B: benzbromarone; CCr: creatinine clearance rate; Cr: serum creatinine; CKD: chronic kidney disease; D: (to initiate ULT) during an acute attack; eGFR: estimated glomerular filtration rate; F: febuxostat; IE: insufficient evidence; m: month(s); NA: not applicable; NG: not given; P: probenecid; RF: renal function; SUA: serum uric acid; U: uricosurics without specification; ULT: urate lowering therapy; w: week(s); y: year.

<u>`</u>																						
	SAMA_2003 [51]	MOH_MSR_AMM _2008 [49]	PRA_2008 [50]	UTAustin_2009 [52]	EULAR_2011 [17]	JSGNAM_2011 [48]	ACR_2012 [14, 15]	CCCP_2012 [47]	3e_2013 [36]	CSE_2013 [37]	SER_2013 [46]	SIR_2013 [45]	3e_PT_2014 [40]	FMOH_2014 [44]	3e_AU_NZ_2015 [43]	CRA_2016 [41]	EULAR_2016 [16]	T2T_2016 [39]	TRA_2016 [38]	ACP_2017 [19, 20]	BSR_2017 [21]	CRA_multi_2017 [22]
Upper limit for target SUA, µmol/L [mg/dL]																						
_General target*	300	360 [6.0]	[6.0]	NG	[6.0]	[6.0]	[6.0]	357 [6.0]	360 [6.0]	360	[6.0]	360 [6.0]	360 [6.0]	NG	360	360 [6.0]	360 [6.0]	360 [6.0]	360 [6.0]	NG	360	360 [6.0]
_Target for serve cases†	NG	NG	NG	NG	[4.0]	NG	[5.0]	NG	300	300	NG	NG	300 [5.0]	NG	300	NG	300 [5.0]	300 [5.0]	300 [5.0]	NG	300	300 [5.0]
Lower limit for target SUA, µmol/L [mg/dL]	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	[3.0]	NG	NG	NG	NG	180
Drinking water	-	+	+	-	-	+	-	+	-	+	+	-	-	+	-	+	-	-	+	-	+	+
Urine alkalinisation	+	+	-	-	+	-	+	+	-	+	+	-	+	+	-	+	-	-	+	-	+	+
Indications for ULT	+	+	+	-	+	+	+	+	-	+	+	+	-	NG	-	+	+	-	+	+	+	+
_Recurrent attacks	+, >2	+, >3/y	+	NA	+, >1/y	+	+, ≥2/y	-	NA	-	-	+	NA	NG	-	+, >2/y	+, ≥2/y	NA	-	+, ≥2/y	+, ≥2/y	+
_Tophi	+	+	+	NA	+	+	+	-	NA	-	-	+	NA	NG	NA	+	+	NA	+	+	+	+
_Urate nephrolithiasis	-	+	+	NA	+	-	+	-	NA	+	-	-	NA	NG	NA	-	+	NA	+	+	+	+
_Arthropathy	-	+	-	NA	+	-	-	-	NA	-	-	+	NA	NG	NA	+	+	NA	+	-	+	+
_Comorbidities‡	-	+	+	NA	-	-	+	+	NA	+	-	-	NA	NG	NA	-	+	NA	-	+	+	+
_Others§	+	+	+	NA	-	-	-	+	NA	-	+	-	NA	NG	NA	-	+	NA	-	-	+	+
Initiate ULT during or after an acute attack (Aft[time after attack])	Aft	Aft	NG	Aft (4-6 w)	Aft	Aft (2w)	D	NA	Aft	D/ Aft (2w)	NG	NG	Aft	NG	NG	NG	IE	IE	Aft	NG	Aft	Aft
First line ULT drug(s)	NG	А	А	NG	A, F	A, B	A, F	NG	А	NG	A, F,	А	А	NG	А	NG	А	NG	NG	NG	А	NG

BMJ	Open

											В											
Second line ULT	NG	Р	NG	NG	Р	NG	Р	NG	U, F	NG	NG	F, P,	F, B,	NG	P, B,	NG	F, U	NG	NG	NG	F	NG
drug(s)												В	P, U		F							
Allopurinol use																						
_Maximum dose (mg/d)	300	NG	NG	NG	800	NG	800	600	NG	600	800-	800	NG	NG	900	NG	NG	NG	800	NG	900	600
											900											ļ
_RF to initiate dose	CCr	CCr	NG	NG	NG	NG	СК	NG	NG	CCr	CCr	CCr	NG	NG	NG	NG	NG	NG	NG	NG	eGFR	1.5mg/
adjustment (eGFR in	60	80					D4			60	140	20									130	eGFR∥
ml/min/1.73m ² , CCr in																						
mL/min)																						
_Starting dose in	50-1	100-	NG	NG	100	50	≤ 100	50	NG	100-	NG	100	NG	NG	NG	100	100	NG	100	50-1	200	50-100
normal RF (mg/d)	00	150								150										00		
_HLA-B*5801 gene	-	-	-	-	-	-	+	-	-	+	-	-	-	NG	-	-	-	-	+	-	+	+
screening																						
Prophylaxis before ULT	+	NG	NG	NG	+	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
Prophylaxis with ULT	+	+	NG	NG	+	+	+	NG	+	+	+	+	+	NG	+	+	+	+	+	+	+	+
Duration for	1-3	1-6	NG	NG	NG	NG	3-6	NG	Un-	6m	>6m	NG	>6m	NG	Vari-	3-6	NG	>6m	3-6	>8w	<6m	3-6m
prophylaxis	m¶	m**					m††		clear						ed‡‡	m			m			
Pharmacological ULT	-	+	NG	-	-	+	IE	+	IE	IE	NG	NG	-§§	NG	IE	NG	NG	IE	-	NG	-	NG
for asymptomatic																						
hyperuricemia?																						
_Comorbidities	NA	-	NA	NA	NA	+	NA	+	NA	NA	NA	NA	-	NG	NA	NA	NA	NA	NA	NA	NA	NA
_SUA cut-offs, µmol/L	NA	[10-1	NA	NA	NA	[8.0-	NA	[8.0-	NA	NA	NA	NA	[9.0]	NG	NA	NA	NA	NA	NA	NA	NA	NA
[mg/dL]		3]				9.0]		9.0]														
						11		***														

* The general target was the target serum uric acid level for long term control recommended for all patients on pharmacological urate lowering therapy.

† The intensive target the intensive target was the target serum uric acid level for long term control recommended for patients with tophi [16, 17, 22, 36, 38, 40, 43], with recurrent attacks [16, 21, 22], or with chronic gouty arthritis [16, 22], or to prevent crystal formation [21], or to improve gout signs and symptoms [14, 15]. One document provided stricter target for any patient with gout [37], and one for patients with severe gout without clear definition [39].

‡ Comorbidities considered as the indication for ULT include renal impairment [14-16, 19-22, 37, 49, 50], cardiovascular risk or cardiovascular diseases [16, 22, 47], glucose intolerance or DM, lipid disorder, and obesity [22].

§ Others indications considered for pharmacological ULT include joint damage [21], diuretic therapy use [21], young age [16, 21, 22] with some documents defined as less than 40 years old [16, 22], high SUA level defined as >8mg/dL (480 umol/L) [16] or >13mg/dl [50], impending cytotoxic chemotherapy or radiotherapy for lymphoma or

leukaemia [49], persistently raised uric acid levels and willingness to continue lifelong therapy [51]. Some documents evaluated SUA levels in patients after lifestyle modification and indicated pharmacological ULT in individuals with SUA above 6 mg/dL [46], or with SUA above 8mg/dl with CV risk or CVD and above 9mg/dl without CV risk or CVD [47].

|| The starting dose of allopurinol in patients with renal impairment should not exceed 1.5mg/eGFR.

¶ Prophylaxis should be continued until the serum urate is normal and the patient has not had any attacks for 1-3 months.

** Prophylaxis should be continued until 6 months free of acute attacks or until 1 month with target serum urate level achieved.

† Prophylaxis should be continued for 1) 6 months' duration, 2) 3 months after achieving the target serum urate level for the patient without tophi detected on physical

examination, or 3) 6 months after achieving the target serum urate level, where there has been resolution of tophi previously detected on physical examination.

The during for prophylaxis varied and depends on the presence of tophi and comorbidities and on serum urate response. But prophylaxis should be continued until the target SUA is reached or until the tophi has resolved.

§§ The recommendations provided were conflict within the same document.

Pharmacological urate lowering therapy is recommended in male patients with serum uric acid >13 mg/dL and in female patients with serum uric acid >10 mg/dL.

IN Pharmacological urate lowering therapy is recommended in patients with serum uric acid >8 mg/dL if with complications or >9 mg/dL in all patients.

*** Pharmacological urate lowering therapy is recommended in patients with serum uric acid >8 mg/dL if with cardiovascular disease or cardiovascular risk factors or >9 mg/dL if without cardiovascular disease or cardiovascular risk factors.

Supplementary Table 10. Summary of recommendations for the treatment of acute gout by included guidance documents

NG: not given; NSAIDs: non-steroidal anti-inflammatory drugs.

	What is the first line pharmacological treatment option?	Is colchicine recommended to be given as a fixed dose or as a loading dose + followed doses?	Is intra-articular steroids recommended?	What are the indications for intra-articular steroids?	Which line is intra-articular steroids recommended to be?	Is systemic steroids recommended?	What are the indications for systemic steroids?	Which line of option is systemic steroids recommended to be?
SAMA_2003 [51]	NSAIDs	Loading dose + followed doses	Yes	Contraindicated to NSAIDs and joint accessible	NG	Yes	Contraindicated or not responding to NSAIDs or polyarthritis	NG
MOH_MSR_AMM_2008 [49]	NSAIDs	NG	Yes	NG	NG	Yes	Elderly people, renal insufficiency, hepatic dysfunction, cardiac failure, peptic ulcer disease, and hypersensitivity to NSAIDs	NG
PRA_2008 [50]	NSAIDs	NG	NG	NG	NG	Yes	Contraindicated to NSAIDs	NG
UTAustin_2009 [52]	NSAIDs	Loading dose + followed doses	Yes	Only 1-2 joints is involved	Third	Yes	Contraindicated or not responding to NSAIDs and colchicine and polyarthritis	Third
EULAR_2011 [17]	Colchicine, NSAIDs, glucocorticoids	Loading dose + followed doses	Yes	NG	NG	Yes	Contraindications to NSAIDs and colchicine	First
JSGNAM_2011 [48]	Colchicine, NSAIDs	Fixed	NG	NG	NG	Yes	Contraindicated or not responding to NSAIDs or polyarthritis	Second
ACR_2012 [14, 15]	NSAIDs, corticosteroids, colchicine	Loading dose + followed doses	Yes	Involvement of 1 or 2 large joints	First	Yes	Oral steroids for involvement of 1 or 2 joints or when intra-articular joint injection is impractical. Intravenous steroids for the nothing by mouth patients.	First
3e_2013 [36]	NSAIDs, colchicine, glucocorticoids	NG	Yes	NG	First	Yes	NG	First
CSE_2013 [37]	NSAIDs, colchicine,	NG	NG	NG	NG	NG	NG	NG

	corticosteroids							
SER_2013 [46]	NSAIDs	NG	Yes	Monoarthritis	NG	Yes	Contraindicated to NSAIDs	NG
SIR_2013 [45]	NSAIDs, colchicine	NG	Yes	NG	NG	Yes	Intolerance or contraindications to NSAIDs and colchicine	NG
3e_PT_2014 [40]	Colchicine, NSAIDs	Fixed low dose	Yes	NG	NG	Yes	NG	NG
FMOH_2014 [44]	NG	NG	NG	NG	NG	NG	NG	NG
3e_AU_NZ_2015 [43]	NSAIDs, colchicine, glucocorticoids	NG	Yes	NG	First	Yes	NG	First
CRA_2016 [41]	NSAIDs	NG	NG	NG	NG	Yes	Contraindications to NSAIDs and colchicine	NG
EULAR_2016 [16]	Colchicine, NSAIDs, corticosteroid	Loading dose + followed doses	Yes	NG	First	Yes	NG	First
T2T_2016 [39]	Anti-inflammatory medications	NG	NG	NG	NG	NG	NG	NG
TRA_2016 [38]	NSAIDs	Fixed or Loading dose + followed doses	Yes	Involvement of 1-2 major joints, contraindications to both colchicine and NSAIDs	NG	Yes	Contraindications to NSAIDs and colchicine	NG
ACP_2017 [19, 20]	Corticosteroids	Loading dose + followed doses	NG	NG	NG	Yes	If not contraindicated.	First
BSR_2017 [21]	NSAIDs, colchicine	NG	Yes	Patients with acute illness and comorbidity	First	Yes	Intolerance to NSAIDs and colchicine and intra-articular injection is not feasible.	Second
CRA_multi_2017 [22]	NSAIDs, colchicine	Loading dose + followed doses	Yes	Involvement of 1-2 major joints and not responding to systemic treatment	NG	Yes	Contraindicated to or not responding to NSAIDs and colchicine	NG

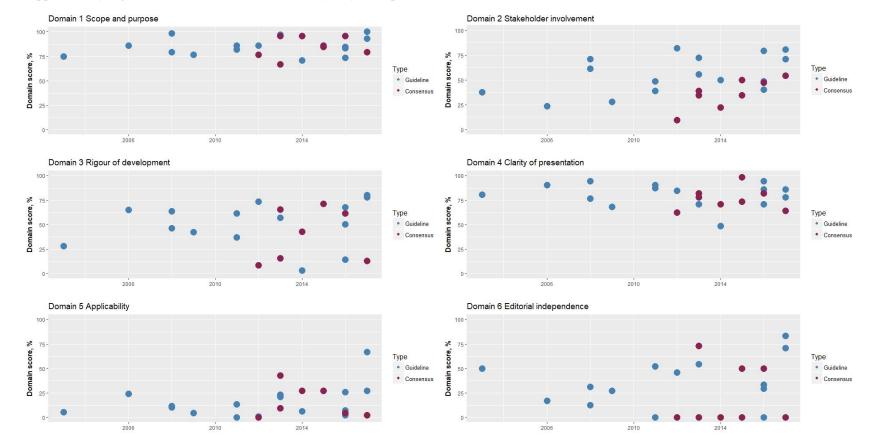
	SAMA_2003 [51]	MOH_MSR_AMM_2008 [49]	PRA_2008 [50]	UTAustin_2009 [52]	EULAR_2011 [17]	JSGNAM_2011 [48]	ACR_2012 [14, 15]	3e_2013 [36]	CSE_2013 [37]	SER_2013 [46]	SIR_2013 [45]	3e_PT_2014 [40]	FMOH_2014 [44]	3e_AU_NZ_2015 [43]	CRA_2016 [41]	EULAR_2016 [16]	T2T_2016 [39]	TRA_2016 [38]	ACP_2017 [19, 20]	BSR_2017 [21]	CRA_multi_2017 [22]
Is surgery recommended?	+	+	NG	NG	NG	+	NG	+	NG	NG	NG	+	NG	+	NG	NG	IE	+	NG	-	+
Indications for surgery	NG	+	NG	NG	NG	NG	NG	+	NG	NG	NG	NG	NG	+	NG	NG	NG	+	NG	NG	+
_Nerve compression	NA	-	NA	NA	NA	NA	NA	+	NA	NA	NA	NA	NA	+	NA	NA	NA	+	NA	NA	+
_Infection	NA	-	NA	NA	NA	NA	NA	+	NA	NA	NA	NA	NA	+	NA	NA	NA	+	NA	NA	-
_Mechanical impingement	NA	-	NA	NA	NA	NA	NA	+	NA	NA	NA	NA	NA	+	NA	NA	NA	-	NA	NA	-
_Loss of mobility	NA	+	NA	NA	NA	NA	NA	-	NA	NA	NA	NA	NA	-	NA	NA	NA	+	NA	NA	-
_Severe pain	NA	+	NA	NA	NA	NA	NA	-	NA	NA	NA	NA	NA	-	NA	NA	NA	+	NA	NA	-
_Tophaceous ulcer	NA	+	NA	NA	NA	NA	NA	-	NA	NA	NA	NA	NA	-	NA	NA	NA	-	NA	NA	+
_Others*	NA	+	NA	NA	NA	NA	NA	-	NA	NA	NA	NA	NA	-	NA	NA	NA	+	NA	NA	+
Risks of surgery	WH	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
Is long-term ULT recommended?	+	+	+	NG	+	+	+	+	+	+	+	+	NG	+	+	+	+	+	+	+	+
Is any ULT drug recommended?	А	-	-	-	Р	-	Р	-	В	F	NA	-	-	Р	-	Р	-	-	-	P, R	-

Supplementary Table 11. Summary of recommendations for the treatment of tophi by included guidance documents

A: allopurinol; B: benzbromarone; F: febuxostat; NA: not applicable; NG: not given; P: pegloticase; R: rasburicase; ULT: urate lowering therapy; WH: wound healing.

* Other indications for surgery include large tophi [22], persistent tophi [22], joint deformation [38], major joint destruction [49], pressure symptoms [49], and cosmetic

[49].



Supplementary Figure 1. Standardized domain scores by the year of publication

Supplementary File 1. Instructions for Guideline Appraisal Using the AGREE II Instrument

TRAINING MATERIALS

- o Online tutorial: http://www.agreetrust.org/resource-centre/agree-ii-training-tools/
- User's Manual: http://www.agreetrust.org/wp-content/uploads/2013/06/AGREE_II_Users_Manual_and_23-item_I nstrument_ENGLISH.pdf

PROLOGUE

- The Appraisal of Guidelines for REsearch & Evaluation (AGREE) Instrument is an international, validated and rigorously developed tool to evaluate the quality of clinical practice guidelines and consensus statements.
- The AGREE II instrument was published in 2010 and consists of 23 key items organized within 6 domains followed by 2 global rating items ("Overall Assessment"). Each domain captures a unique dimension of guideline quality.
 - Scope and purpose
 - Stakeholder involvement
 - Rigour of development
 - Clarity of presentation
 - Applicability
 - Editorial independence.
- o Reviewers score each item on a 7-point Likert Scale.
 - 1 Strongly disagree
 - 7 Strongly agree
 - For the majority of items, we use an 'add-up' strategy to score, that is, corresponding scores will be added to 1' if information on predefined aspects is provided. For only one item, we subtract scores from 7'.
- Domain scores will be calculated as: (obtained score-minimal possible score)/(maximal possible score)

DETAILED INSTRUCTIONS FOR SCORING

(adapted from AGREE II User's Manual [28])

Domain 1 Scope and Purpose

Item 1 Objectives: The overall objective(s) of the guideline is (are) specifically described. Instructions:

Information on three aspects should be provided (add corresponding scores for each aspect, 5' in total):

a) Health intent, i.e., prevention, screening, diagnosis, treatment, etc. (2');

b) Expected benefit or outcome (2');

- *Clarification*: If gout epidemiology is provided as background information (i.e., the importance or significance of the diagnosis and management of gout/hyperuricemia is stated), 1' will be given. If clear statements, such as "to prevent (long term) complications of patients with diabetes mellitus" "to lower the risk of subsequent vascular events in patients with previous myocardial infarction", are provided, 2' will be given.

c) Target, e.g., patient population, society (1').

Performance: Is the item well written and is the content easy to find? (1')

Related *Report Criteria* from *User's Manual*: • health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) • expected benefit or outcome • target(s) (e.g., patient population, society)

Item 2 Questions: The health question(s) covered by the guideline is (are) specifically described. Instructions:

Information on five aspects should be provided (add corresponding scores for each aspect, 5' in total):

a) Target population (2');

b) Intervention or exposure (if appropriate, 1');

- c) Comparisons (if appropriate, 1');
- d) Outcome (1');

e) Health care setting or context (1').

Performance: Is the item well written and is the content easy to find? (1')

Note:

- 1) If c) is not appropriate, no score will be subtracted.
- It is not necessary to have this information provided in questions. Reviewers can try to paraphrase
 2-3 key recommendations into questions to see the information above is provided and score based on paraphrased questions.

Related *Report Criteria* from *User's Manual*: • target population • intervention(s) or exposure(s) • comparisons (if appropriate) • outcome(s) • health care setting or context

Item 3 Population: The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

Instructions:

A default full score (7') should be considered. Subtract 1-2 points where the population is not clearly described or where the descriptions in the guideline is contradictory (e.g., a guideline stating "to treat asymptomatic hyperuricaemia" in the introduction, while stating "to treat hyperuricaemia and gout" in the title and providing no specific definition of patients' condition in recommendations).

Related *Report Criteria* from *User's Manual*: • target population, gender and age • clinical condition (if relevant) • severity/stage of disease (if relevant) • comorbidities (if relevant) • excluded populations (if relevant)

Domain 2 Stakeholder Involvement

Item 4 Group Membership: The guideline development group includes individuals from all relevant professional groups.

Instructions:

Information on two aspects should be provided (add corresponding scores for each aspect, 5' in total): a) The guideline development group is stated (1');

b) For each member of the guideline development group, the following information is included (1' each): name (1'), discipline/content expertise (e.g., neurosurgeon, methodologist, 1'), institution (e.g., St. Peter's hospital, 1'), a description of the member's role in the guideline development group (1')

- *Clarification*: Please subtract 1' if no methodologist (i.e., epidemiologist) is inferred from the discipline/content expertise.

Performance: Is the item well written and is the content easy to find? (1')

Note: Where the relation between the guideline development group and the authors is unclear, the authors of the guidance document will be considered as equivalent to the guideline development group.

Related *Report Criteria* from *User's Manual*: • For each member of the guideline development group, the following information is included: name, discipline/content expertise (e.g., neurosurgeon, methodologist), institution (e.g., St. Peter's hospital), geographical location (e.g., Seattle, WA), a description of the member's role in the guideline development group

Item 5 Target Population Preferences and Views: The views and preferences of the target population (patients, public, etc.) have been sought.

Instructions:

Information the following four aspects should be provided (add corresponding scores for each aspect, 6' in total):

a) Statement of type of strategy used to capture patients'/public's' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences, 2');

b) Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups, 1');

c) Outcomes/information gathered on patient/public information (2');

d) Description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations (1')

- *Clarification*: If a patient representative is included in the guideline development panel, scores on aspects a), b), and d) will be given as default.

Related *Report Criteria* from *User's Manual*: • statement of type of strategy used to capture patients'/public's' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) • methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) • outcomes/information gathered on patient/public information • description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations

Item 6 Target Users: The target users of the guideline are clearly defined.

Instructions:

Information on two aspects should be provided (add corresponding scores for each aspect, 6' in total): a) Clear description of intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators, 3');

b) Description of how the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care, 3')

Related *Report Criteria* from *User's Manual*: • clear description of intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) • description of how the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)

Domain 3 Rigour of Development

Item 7 Search Methods: Systematic methods were used to search for evidence.

Instructions:

Information on four aspects should be provided (add corresponding scores for each aspect, 6' in total):

a) Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL, 2');

b) Time periods searched (e.g., January 1, 2004 to March 31, 2008, 1');

c) Search terms used (e.g., text words, indexing terms, subheadings, 1');

d) Full search strategy included (e.g., possibly located in appendix, 2')

Related *Report Criteria* from *User's Manual*: • named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) • time periods searched (e.g., January 1, 2004 to March 31, 2008) • search terms used (e.g., text words, indexing terms, subheadings) • full search strategy included (e.g., possibly located in appendix)

Item 8 Evidence Selection Criteria: The criteria for selecting the evidence are clearly described. Instructions:

Information on both inclusion and exclusion criteria should be provided (add corresponding scores for each aspect, 6' in total):

a) Description of the inclusion criteria:

- a1) target population (patient, public, etc.) characteristics (2'),
- a2) study design (2),
- a4) outcomes (1'),

b) Description of the exclusion criteria (if relevant; e.g., French only listed in the inclusion criteria statement could logically preclude non-French listed in the exclusion criteria statement, 1'). Note: if a3), a5), a6), b) is not relevant, no score will be subtracted.

Related *Report Criteria* from *User's Manual*: • description of the inclusion criteria, including: target population (patient, public, etc.) characteristics, study design, comparisons (if relevant), outcomes, language (if relevant), context (if relevant) • description of the exclusion criteria (if relevant; e.g., French only listed in the inclusion criteria statement could logically preclude non-French listed in the exclusion criteria statement)

Item 9 Strengths and Limitations of The Evidence: The strengths and limitations of the body of evidence are clearly described.

Instructions:

For each evidence, information on two aspects should be provided. If only some of the evidences report the following information, please first calculate the score based on the most informative evidence (e.g., scored 5'), and then subtract 1' to get the final score (e.g., 5'-1'=4').

For each evidence, both a general statement of the method and detailed descriptions should be provided: a) A statement of the method used to evaluate the strengths and limitations of the evidence should be provided (3').

b) The stated method should evaluate at least three of the following aspects (add 1' for each aspect, maximum 3'):

b1) Study design(s);

b2) Study methodology limitations (e.g., sampling, blinding, allocation concealment, analytical methods);

b3) Appropriateness/relevance of primary and secondary outcomes considered;

- b4) Consistency of results across studies;
- b5) Direction of results across studies;
- b6) Magnitude of benefit versus magnitude of harm;

b7) Applicability to practice context

Related *Report Criteria* from *User's Manual:* • descriptions of how the body of evidence was evaluated for bias and how it was interpreted by members of the guideline development group • aspects upon which to frame descriptions include: study design(s) included in body of evidence, study methodology limitations (sampling, blinding, allocation concealment, analytical methods), appropriateness/relevance of primary and secondary outcomes considered, consistency of results across studies, direction of results across studies, magnitude of benefit versus magnitude of harm, applicability to practice context

Item 10 Formulation of Recommendations: The methods for formulating the recommendations are clearly described.

Instructions:

Information on three aspects should be provide (add 2' for each aspect, 6' in total):

a) Description of the recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered, 2');

b) Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures, 2');

c) Description of how the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote, 2')

Related *Report Criteria* from *User's Manual:* • description of the recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) • outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) • description of how the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)

Item 11 Consideration of Benefits and Harms: The health benefits, side effects, and risks have been considered in formulating the recommendations.

Instructions:

For each recommendation, information on four aspects should be provided. If only some of the recommendations report the following information, please first calculate the score based on the most informative recommendation (e.g., scored 5'), and subtract 1' to get the final score (e.g., 5'-1'=4').

For each recommendation, information on four aspects should be provided (add corresponding scores for each aspect, 6' in total):

a) Supporting data and report of benefits (2'); b) Supporting data and report of harms/side effects/risks (2');

- Clarification: Data on a) and b) can be provided as references.

c) Reporting of the balance/trade-off between benefits and harms/side effects/risks (1');

d) Recommendations reflect considerations of both benefits and harms/side effects/risks (1')

Related *Report Criteria* from *User's Manual:* • supporting data and report of benefits • supporting data and report of harms/side effects/risks • reporting of the balance/trade-off between benefits and harms/side effects/risks • recommendations reflect considerations of both benefits and harms/side effects/risks

Item 12 Link Between Recommendations and Evidence: There is an explicit link between the recommendations and the supporting evidence.

Instructions:

Information on three aspects should be provided (add 2' for each aspect, 6' in total):

a) The guideline describes how the guideline development group linked and used the evidence to inform recommendations (2');

- Clarification: Can be provided as narrative summaries and/or discussions of evidences.

b) Each recommendation is linked to a key evidence description/paragraph and/or reference list (2');

- Note: Please subtract 1' if only some recommendations meet criterium b).

c) Recommendations linked to evidence summaries, evidence tables in the results section of the guideline (2')

Related *Report Criteria* from *User's Manual*: • the guideline describes how the guideline development group linked and used the evidence to inform recommendations • each recommendation is linked to a key evidence description/paragraph and/or reference list • recommendations linked to evidence summaries, evidence tables in the results section of the guideline

Item 13 External Review: The guideline has been externally reviewed by experts prior to its publication.

Instructions:

Information on five aspects should be provided (add corresponding scores for each aspect, 6' in total): a) Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence, 1');

b) Methods taken to undertake the external review (e.g., rating scale, open-ended questions, 1');

c) Description of the external reviewers (e.g., number, type of reviewers, affiliations, 1');

d) Outcomes/information gathered from the external review (e.g., summary of key findings, 1');

e) Description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations, 2')

- *Clarification*: Publication through a peer-reviewed journal can be considered as externally reviewed. Note: If dates of revision and acceptance is provided on the document, it is also considered externally reviewed.

Related *Report Criteria* from *User's Manual*: • purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) • methods taken to undertake the external review (e.g., rating scale, open-ended questions) • description of the external reviewers (e.g., number, type of reviewers, affiliations) • outcomes/information gathered from the external review (e.g., summary of key findings) • description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)

Item 14 Updating Procedure: A procedure for updating the guideline is provided. Instructions:

Information on three aspects should be provided (add 2' for each aspect, 6' in total):

a) A statement that the guideline will be updated (2');

b) Explicit time interval or explicit criteria to guide decisions about when an update will occur (2');

c) Methodology for the updating procedure is reported (2')

Related Report Criteria from User's Manual: • a statement that the guideline will be updated • explicit

time interval or explicit criteria to guide decisions about when an update will occur • methodology for the updating procedure is reported

Domain 4 Clarity of Presentation

Item 15 Specific and Unambiguous Recommendations: The recommendations are specific and unambiguous.

Instructions:

For each recommendation, information on four aspects should be provided. If only some of the recommendations report the following information, please first calculate the score based on the most informative recommendation (e.g., scored 5'), and then subtract 1' to get the final score (e.g., 5'-1'=4').

For each recommendation, information on four aspects should be provided (add corresponding scores for each aspect, 6' in total):

a) If a recommendation is uncertain, the uncertainty should be reflected in the recommendation and also be explicitly stated (2')

b) Identification of the intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects, 2');

- *Clarification*: If the benefit for uric acid lowering in patients with CVD is not clearly stated, the score for this aspect should not be added.

c) Identification of the relevant population (e.g., patients, public, 1');

d) Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply, 1').

Note: if c) is not relevant, no score will be subtracted.

Related *Report Criteria* from *User's Manual*: • statement of the recommended action • identification of the intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) • identification of the relevant population (e.g., patients, public) • caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply)

Item 16 Management Options: The different options for management of the condition or health issue are clearly presented.

Instructions:

Information on two aspects should be provided (add 3' for each aspect, 6' in total):

a) Description of options (3');

b) Description of population or clinical situation most appropriate to each option (3')

- *Note*: Please subtract 1' if only some options are provided with the most appropriate population or clinical situation.

Related *Report Criteria* from *User's Manual*: • description of options • description of population or clinical situation most appropriate to each option

Item 17 Identifiable Key Recommendations: Key recommendations are easily identifiable. Instructions:

Reporting style should follow two criteria (add 3' for each aspect, 6' in total):

a) Description of recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms (3');

b) Specific recommendations are grouped together in one section (3')

- *Clarification*: If recommendations are summarised in the abstract, scores for aspect b) can also be given.

Related *Report Criteria* from *User's Manual*: • description of recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms • specific recommendations are grouped together in one section

Domain 5 Applicability

Item 18 Facilitators and Barriers to Application: The guideline describes facilitators and barriers to its application.

Instructions:

Information on four aspects should be provided (add corresponding scores for each aspect, 6' in total): a) Identification of the types of facilitators and barriers that were considered (2');

- *Clarification*: Statements of that certain drugs are not available in certain regions can be considered as identification of the facilitators and barriers.

b) Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation, 2');

c) Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography, 1');

d) Description of how the information influenced the guideline development process and/or formation of the recommendations (1')

Related *Report Criteria* from *User's Manual*: • identification of the types of facilitators and barriers that were considered • methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) • information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) • description of how the information influenced the guideline development process and/or formation of the recommendations

Item 19 Implementation Advice or Tools: The guideline provides advice and/or tools on how the recommendations can be put into practice.

Instructions:

Information on three aspects should be provided (add corresponding scores for each aspect, 6' in total): a) An implementation section in the guideline (2');

b) Tools and resources to facilitate application (add 1' for each tool/resource, maximum 2'): guideline summary documents, links to check lists/algorithms, links to how-to manuals, solutions linked to barrier analysis (see Item 18), tools to capitalize on guideline facilitators (see Item 18), outcome of pilot test and lessons learned;

c) Directions on how users can access tools and resources (2')

Related *Report Criteria* from *User's Manual*: • an implementation section in the guideline • tools and resources to facilitate application: guideline summary documents, links to check lists/algorithms, links to how-to manuals, solutions linked to barrier analysis (see Item 18), tools to capitalize on guideline facilitators (see Item 18), outcome of pilot test and lessons learned • directions on how users can access

tools and resources

Item 20 Resource Implications: The potential resource implications of applying the recommendations have been considered.

- *Clarification*: The aim of this item is to the cost information considered by the guideline. <u>Instructions:</u>

Information on four aspects should be provided (add corresponding scores for each aspect, 6' in total): a) Identification of the types of cost information that were considered (e.g., economic evaluations, drug acquisition costs, 2');

b) Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc., 2');

c) Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course, 1');

d) Description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations (1')

Related *Report Criteria* from *User's Manual:* • identification of the types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) • methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) • information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) • description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations

Item 21 Monitoring or Auditing Criteria: The guideline presents monitoring and/or auditing criteria.

- *Clarification*: The aim of this item is to evaluate the adherence to guidelines, but not to provide follow up parameters for diseases. *Monitoring* in this item refers to the action to monitor physicians' adherence to the guideline in daily practice by a group of investigators, but not to monitor the management of the disease in an individual patient. And the *auditing criteria* are the criteria to assess how well the guideline affects the practice in a region, but not how well the patients achieve the treatment target.

Instructions:

Information on four aspects should be provided (add corresponding scores for each aspect, 6' in total):

- a) Identification of criteria to assess guideline implementation or adherence to recommendations (2');
- b) Criteria for assessing impact of implementing the recommendations (2');
- c) Advice on the frequency and interval of measurement (1');
- d) Descriptions or operational definitions of how the criteria should be measured (1')

Related *Report Criteria* from *User's Manual*: • identification of criteria to assess guideline implementation or adherence to recommendations • criteria for assessing impact of implementing the recommendations • advice on the frequency and interval of measurement • descriptions or operational definitions of how the criteria should be measured

Domain 6 Editorial Independence

Item 22 Funding Body: The views of the funding body have not influenced the content of the guideline.

Instructions:

Information on two aspects should be provided (add 3' for each aspect, 6' in total):

a) The name of the funding body or source of funding (or explicit statement of no funding, 3');b) A statement that the funding body did not influence the content of the guideline (3')

Related *Report Criteria* from *User's Manual*: • the name of the funding body or source of funding (or explicit statement of no funding) • a statement that the funding body did not influence the content of the guideline

Item 23 Competing Interests: Competing interests of guideline development group members have been recorded and addressed.

Instructions:

Information on four aspects should be provided (add corresponding scores for each aspect, 6' in total):

a) Description of the types of competing interests considered (2');

b) Methods by which potential competing interests were sought (1');

c) Description of the competing interests (1');

d) Description of how the competing interests influenced the guideline process and development of recommendations (2')

Related *Report Criteria* from *User's Manual*: • description of the types of competing interests considered • methods by which potential competing interests were sought • description of the competing interests • description of how the competing interests influenced the guideline process and development of recommendations

Overall Guideline Assessment

Question 1 Overall quality: Rate the overall quality of this guideline.

Instructions:

7' in total. Reviewer's impression on the overall quality of the guideline.

Question 2 Strength of recommendation: I would recommend this guideline for use.

<u>Instructions:</u> Three options to choose from: a) Yes; b) Yes, with modifications; c) No Reviewer's impression on whether the guideline is easy to be applied to clinical practice.

Related *Report Criteria* from *User's Manual*: The overall assessment requires the AGREE II user to make a judgment as to the quality of the guideline, taking into account the appraisal items considered in the assessment process.

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