8. Evidence table

KQ1	*Should we use NSAIDs over colchicine/corticosteroids in patients experiencing a gout flare to reduce the duration of the flare?*

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Billy 2017	Systematic Review	Acute gout patients	NSAIDs	Steroid	Pain, Acute gout duration
Roddy2019	RCT	Acute gout patients	NSAIDs	Colchicine	Pain, Acute gout duration

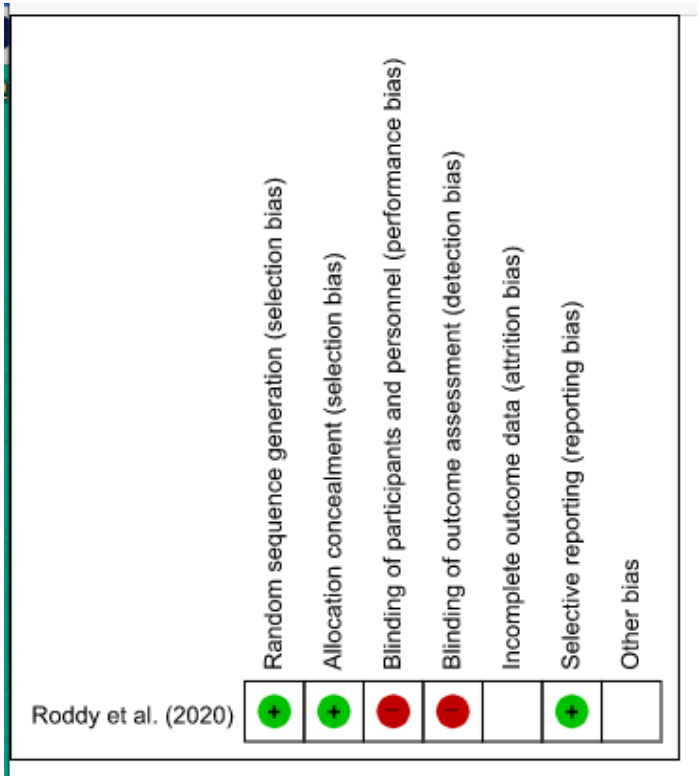
2) Assessment of risk of bias

Billy (Amstar: 8)

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			

5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

Roddy


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Roddy et al. (2020)

3) GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAIDs	steroid	Relative (95% CI)	Absolute (95% CI)		
Pain												
2	randomised trials	not serious	not serious	serious	not serious	none	267	267	-	SMD **0.09 SD lower** (0.26 lower to 0.08 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
Duration of flare												
1	randomised trials	serious	not serious	not serious	serious	none	-/10	-/10	not estimable		⨁⨁◯◯ LOW	critical

CI: Confidence interval; **SMD:** Standardised mean difference

Explanations

a. short-term pain (7 days)

b. Time to disease resolution

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	colchicine	Relative (95% CI)	Absolute (95% CI)		
Pain[a]												
1	randomised trials	serious [b]	not serious	not serious	not serious	none	200	199	-	not estimable	⨁⨁⨁◯ MODERATE	IMPORTANT
Duration (follow up: median 28 days)[c]												
1	randomised trials	serious [b]	not serious	not serious	not serious	none	200	199	-	median **1 days lower** (0 to 0)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval

Explanations

a. mean change in worst pain intensity over days 1–7

b. This is an open label study without blinded outcome assessment or placebo tablets, and collection of solely self-reported outcomes.

c. Days to complete pain resolution

KQ2	*Should we start ULT during a gout flare vs. after a gout flare has resolved when initiating ULT?*

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Fatma 2016	Systematic Review	Initiation of any ULT in patients with acute gout	Allopurinol	Placebo	Gout attack :Pain severity and Duration of gout attack

2) Assessment of risk of bias

AMSTAR: 8

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in	o			

formulating conclusions?				
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

3) GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**With ULT be used during a gout flare**	**With after a gout flare has resolved**	**Relative (95% CI)**	**Absolute (95% CI)**		
Gout flares												
2	randomized trials	not serious	not serious	not serious	very serious [a,b]	none	5/53 (9.4%)	8/49 (16.3%)	not estimable		⊕⊕◯◯ LOW	
Duration of gout attack												
1	randomized trials	serious [c]	not serious	not serious	very serious [a,b]	none	14	17	not estimable		⊕◯◯◯ VERY LOW	
Pain												
2	randomized trials	serious [c]	not serious	not serious	serious [a]	none	41	45	not estimable		⊕⊕◯◯ LOW	

CI: Confidence interval

Explanations

a. wide confidence intervals

b. small sample sizes in each arm

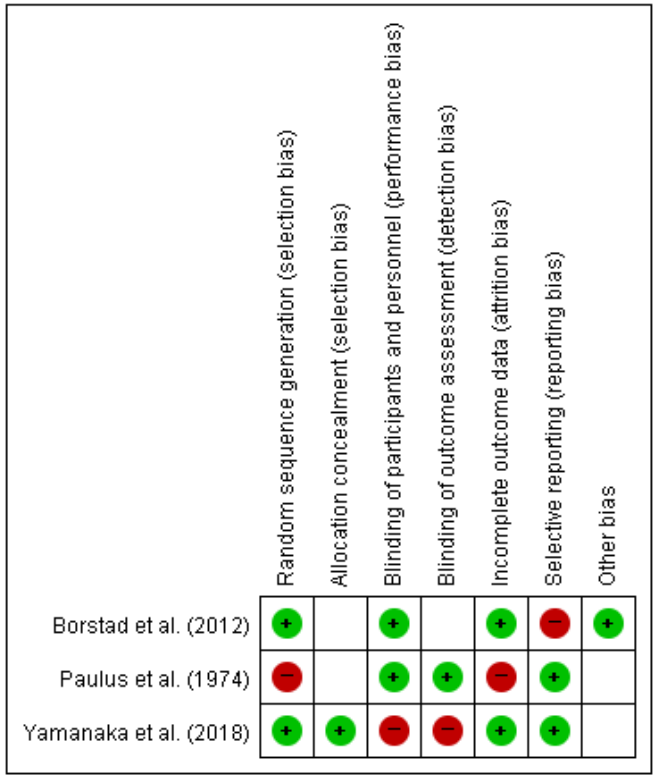
c. RCT with two domains with high RoB

KQ3	*Should prophylaxis vs. no prophylaxis be used in patients with gout starting ULT?*

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Paulus 1974	Placebo controlled trial	Gout	Prophylactic colchicine therapy	placebo	Gout flare
Borstad 2004	Randomised clinical trial	Gout	Prophylactic colchicine therapy	none	Gout flare
Yamanaka 2018	Randomised clinical trial	Gout	Prophylactic colchicine therapy	Step wise febuxostat dose increase	Gout flare

2) Assessment of risk of bias



3) GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)		
Gout flare												
3	randomised trials	not serious	not serious	not serious	serious ⇨	none	48/143 (33.6%)	90/193 (46.6%)	not estimable		⊕⊕⊕◯ MODERATE	

CI: Confidence interval

KQ4	*Should prescribing ULT to achieve serum urate <6mg/dL be used in gout on ULT in order to prevent gout flares and bone erosion?*

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Shiozawa 2017	Systematic Review	Individuals with preexisting gout	SUA levels at baseline Stratified by urate-lowering therapy use	none	Gout flare
Dalbeth 2019	Randomised clinical trial	Gout patients with serum uric acid level over 6mg/dL	Dose escalation with serum uric acid target below 6	none	CT erosion score

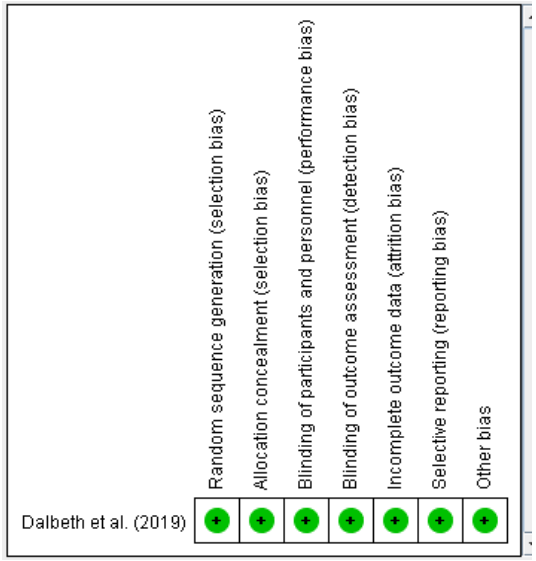
2) Assessment of risk of bias

Shiozawa AMSTAR: 5

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?	o			
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?		o		
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?		o		
9. Were the methods used to combine the findings of studies appropriate?		o		
10. Was the likelihood of publication bias assessed?		o		

11. Was the conflict of interest stated?		o		0

Dalbeth



3) GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[uric acid level below 6]	[uric acid over 6]	Relative (95% CI)	Absolute (95% CI)		
Bone erosion												
1	randomised trials	not serious	not serious	serious [a]	serious [b]	none			-		⨁⨁◯◯ LOW	
Gout flare												
17	observational studies	not serious	not serious	serious [c]	not serious	dose response gradient			not estimable		⨁⨁◯◯ LOW	

CI: Confidence interval

Explanations

a. not comparing according to the serum uric acid level, but according to the use of treatment serum uric acid target or not

b. results are based on group using serum uric acid target and group using fixed dose regimen without serum uric acid target

c. multiple comparators based on serum uric acid category

KQ5	*Should stopping ULT vs. continuing ULT be used for patients with gout on ULT?*

1) Characteristics of selected studies

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Belsion 2018	Systematic Review	Gout patients with urate lowering therapy	Discontinuation of urate lowering therapy	none	Relapse

2) Assessment of risk of bias

AMSTAR: 7

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	o			
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			

7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?		o		
10. Was the likelihood of publication bias assessed?		o		
11. Was the conflict of interest stated?		o		0

3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
relapse (follow up: range 12 months to 96 months)									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
5	observational studies	serious	not serious	not serious	serious	none	Continuation of urate lowering therapy vs. discontinuation Loebl (1974): RR 0.36(0.20-0.53) Sample size 33 Gast (1986): RR 0.5 (0.19-0.81) Sample size 10 Van Lieshout-Zuidema (1992): RR 0.81 (0.64-0.97) Sample size 21 Darmawan (2002): RR 0.59 (0.52-0.66) Sample size 206 Perez-Ruiz (2011): RR 0.39 (0.32-0.45) Sample size 211 *RR: relative risk	⊕◯◯◯ VERY LOW	

CI: Confidence interval

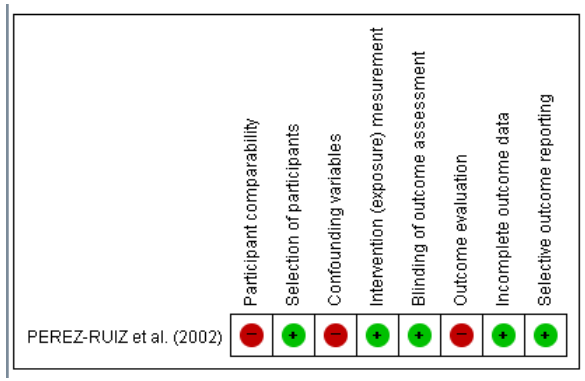
KQ6	*Should prescription of xanthine oxidase inhibitors over uricosuric agents be used in chronic tophaceous gout?*

1) Characteristics of selected studies

Study	Design	Characteristics	Intervention	Control	Outcome
Perez-Ruiz 2002	Observational prospective study	Patients with tophaceous gout	Xathine oxidase inhibitor (allopurinol)	Uricosuric agent (benzbromarone)	Tophi size reduction

2) Assessment of risk of bias

Risk of Bias for Nonrandomized studies (RoBANS)



3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
tophi reduction									
1	observational studies	serious [a]	not serious	not serious	serious	none	Allopurinol and benzbromarone are equally effective when optimal serum urate levels are achieved during therapy.	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

Explanations

a. Risk of bias determined by ROBANS is considered to be serious.

KQ7	*Should ULT vs no treatment be used in gout patients in order to preserve renal function?*

1) Characteristics of selected studies

Study	Design	Characteristics	Intervention	Control	Outcome
Wang 2013	Systematic Review	Patients with hyperuricemia	ULT drugs 1) Benzbromarone and losartan 2) Allopurinol and febuxostat 3) Rasburicase and pegloticase	Placebo or no URT	Renal function: SCr, eGFR or CCr

2) Assessment of risk of bias

AMSTAR 10점

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	o			

2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?			o	
5. Was a list of studies (included and excluded) provided?	o			
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?	o			

3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Reduction of sCr									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
9	randomised trials	serious [a]	not serious	serious [b]	not serious	all plausible residual confounding would reduce the demonstrated effect dose response gradient	The ULT tended to be associated with reduction of SCr (SMD 5 21.253, 95% CI 21.985 to 20.520, I2593.0%; Fig. 3).	⊕⊕⊕⊕ HIGH	CRITICAL
Improvement in renal function (eGFR or CCr)									
3	randomised trials	serious [c]	not serious	serious [b]	not serious	all plausible residual confounding would reduce the demonstrated effect dose response gradient	The hypouricemic treatment was also found to have benefits on eGFR (SMD 5 0.412, 95% CI 0.142-0.682, I2 5 30.6%; Fig. 4).	⊕⊕⊕⊕ HIGH	CRITICAL

CI: Confidence interval

Explanations

a. Lack of allocation concealment 7/9 studies, lack of blinding 8/9 studies, Description of withdrawals 8/9 studies, Intention to treat analysis 3/9 studies

b. Population different from PICO. Intended population: gout patients. Studied population: hyperuricemia subjects

c. Lack of allocation concealment in 1/3 studies, lack of blinding in 3/3 studies, description of withdrawal in 1/3 studies, Intention to treat analysis in 2/3 studies

KQ8	*Should prescribing ULT vs. no treatment be used to improve cardiovascular outcomes in patients with gout?*

No evidence

KQ9	*Should prescribing ULT vs. no treatment be used in CKD 3,4 patients with asymptomatic hyperuricemia in order to protect renal function?*

1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Kanji, 2015	Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect
Xiang Xia Zeng, 2018	Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect
Tsu-Chen Lin, 2019	Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect

2) Assessment of risk of bias

Kanji, 2015, AMSTAR: 6

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			0	
2. Was there duplicate study selection and data extraction?	0			
3. Was a comprehensive literature search performed?	0			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		0		
5. Was a list of studies (included and excluded) provided?		0		
6. Were the characteristics of the included studies provided?	0			
7. Was the scientific quality of the included studies assessed and documented?	0			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	0			
9. Were the methods used to combine the findings of studies appropriate?		0		
10. Was the likelihood of publication bias assessed?	0			
11. Was the conflict of interest stated?		0		

Tsu-Chen Lin, 2019, AMSTAR : 7

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	o			
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		o		
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?		o		
11. Was the conflict of interest stated?		o		

Xiang Xia Zeng, 2018, AMSTAR : 6

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?		o		
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		o		
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?		o		
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

3) GRADE evidence profile

Certainty assessment							impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
13	randomised trials	serious	not serious	not serious	serious	none	urate lowering therapy vs. Placebo Shankar(2017): MD 0.21 (-0.17,0.59) Sample size 108 Kenneth(2016): MD 0.05 (-0.34,0.44) Sample size 106 Kenichi(2015): MD 0.11 (-0.47,0.69) Sample size 46 Chen(2016): MD 0.45 (-0.24,1.13) Sample size 34 Andrew(2013): MD 0.21 (-0.17,0.59) Sample size 320 Kimura(2018): MD 0.5 (-1.43, 2.43) Sample size 441 Mukri(2018): MD 0.7 (-4.58, 5.98) Sample size 93 Sircar(2015): MD 7.6 (1.89, 13.31) Sample size 93 Goicoechea (2010): MD 5.000 (2.725, 7.275) Sample size 113 Kao (2011): MD 0.00 (-3.367, 3.367) Sample size 67 Momeni(2010): MD 1.650 (-8.522, 11.8222) Sample size 44 Shi (2012): MD 1.600 (-9.263, 12.463) Sample size 40 Siu(2006): MD 7.1 (-0.375, 14.575) Sample size 54 *MD: Mean difference	⊕⊕◯◯ LOW	

CI: Confidence interval