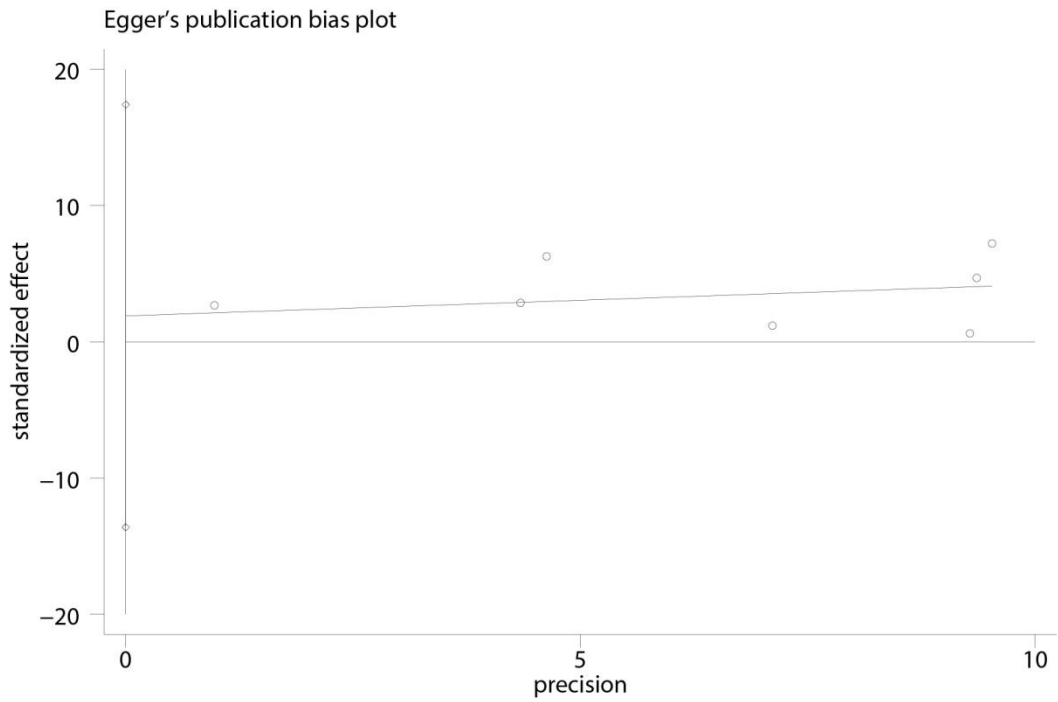


**Supplementary Figure 1:** Methodological quality assessment of included randomized controlled trials treating hyperuricemia and gout with urate-lowering therapies.

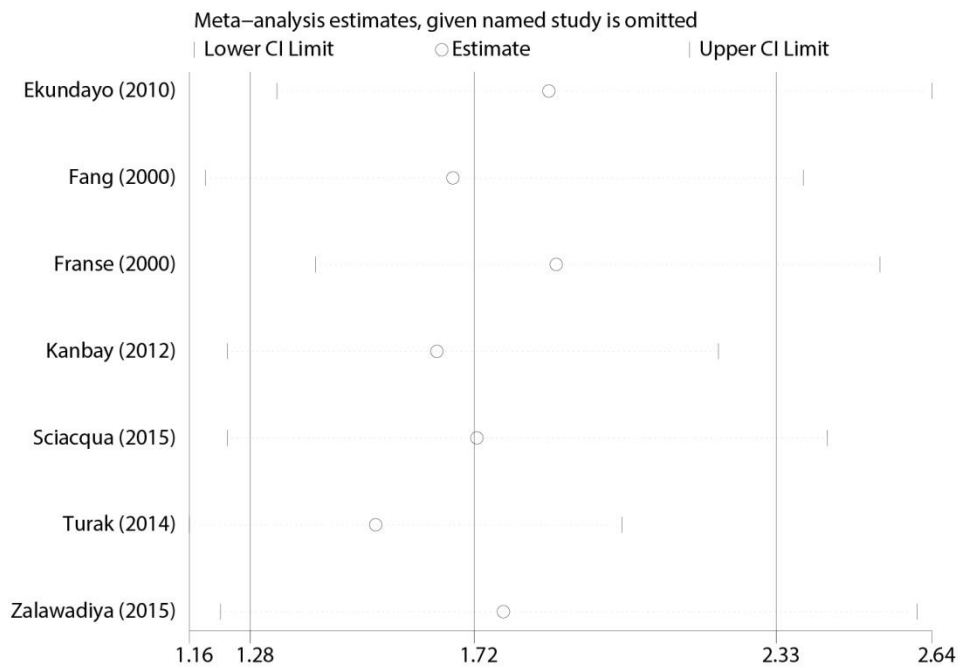
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Becker,2009	?	?	?	?	+	?	+
Becker,2010	?	?	+	+	+	?	+
Dalbeth,2017	?	?	+	+	+	?	+
Givertz,2015	+	?	+	+	+	?	+
Goicoechea,2015	?	?	+	?	+	?	+
Huang,2014	+	+	+	+	+	?	+
Jiang,2014	?	?	+	+	?	?	?
Kimura,2018	+	+	+	+	+	+	?
Lu,2016	+	?	?	?	+	?	?
Nong,2018	?	?	?	?	+	?	?
Saag,2016	+	+	+	+	+	+	?
Saag,2019	+	+	+	+	+	+	?
Schumacher,2008	-	?	+	+	+	?	+
Tang,2017	-	?	?	?	+	?	?
Tuta,2014	?	?	?	?	?	?	?
Wang,2013	?	?	+	+	+	?	+
White,2018	?	?	+	+	+	+	+

**Supplementary Figure 2:** Egger publication bias plot (A) and sensitivity analysis result (B) of comparison between hyperuricemia and non-hyperuricemia in MACE. Egger publication bias plot (C) and sensitivity analysis result (D) of comparison between hyperuricemia and non-hyperuricemia in CVE. CVE: Cardiovascular events; MACE: Major adverse cardiovascular events.

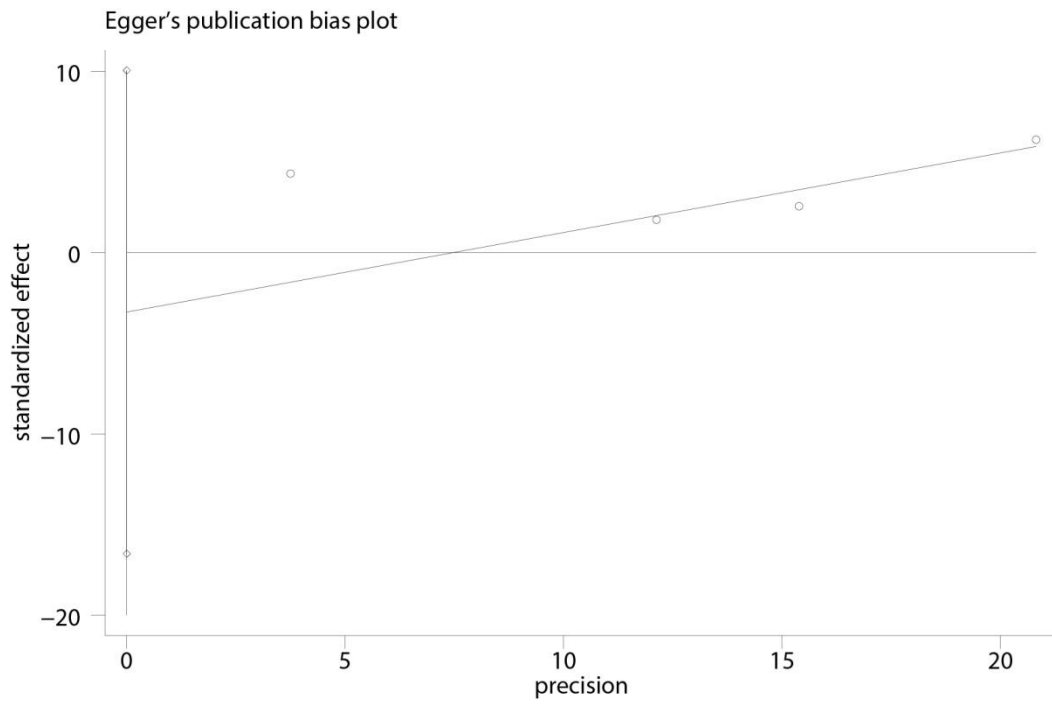
A



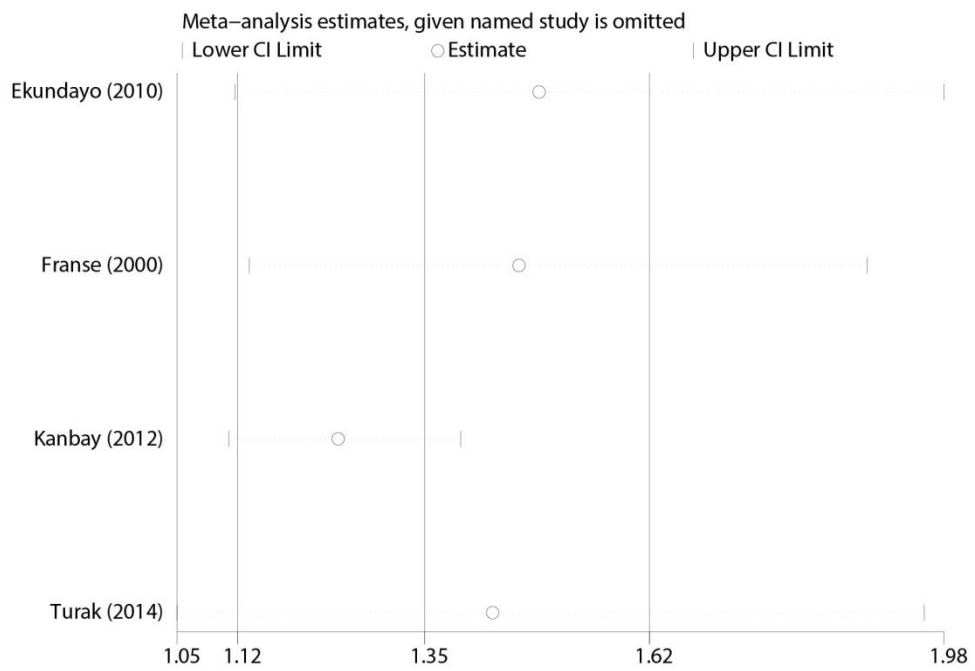
B



C

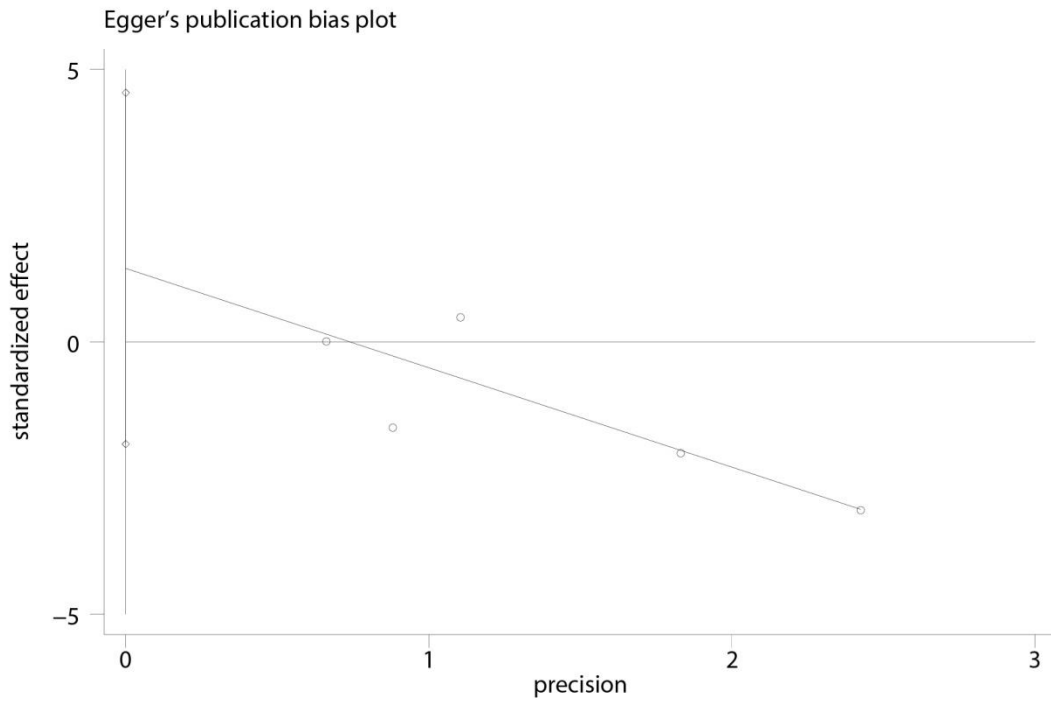


D

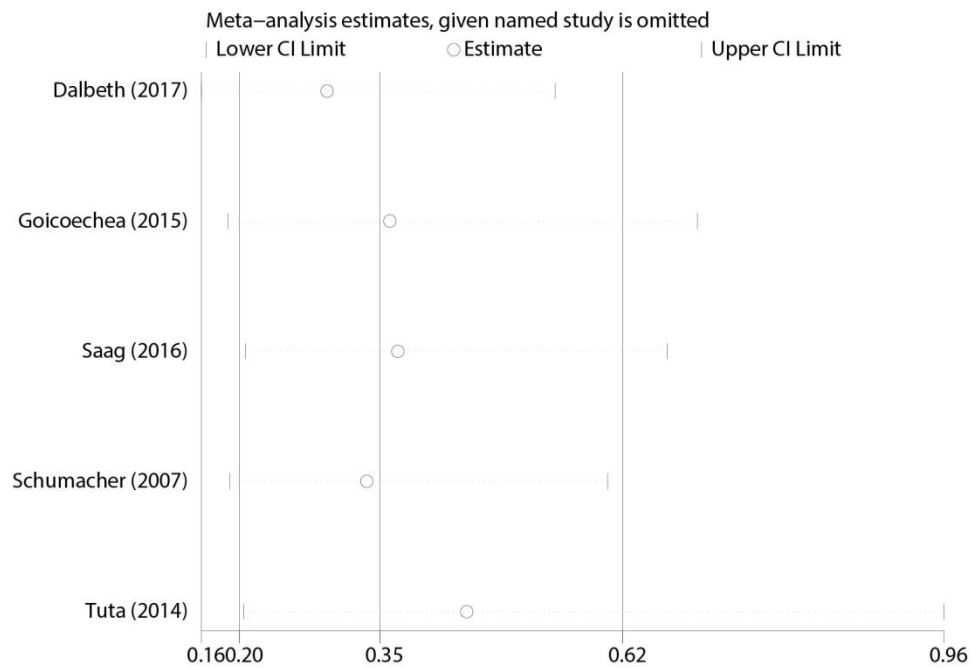


**Supplementary Figure 3:** Egger publication bias plot (A) and sensitivity analysis result (B) of comparison between XOIs and non-XOIs/placebo in MACE with low CV risk. Egger publication bias plot (C) and sensitivity analysis result (D) of comparison between XOIs and non-XOIs/placebo in CVE with low CV risk. CV: Cardiovascular; CVE: Cardiovascular events; MACE: Major adverse cardiovascular events, XOIs: Xanthine oxidase inhibitors.

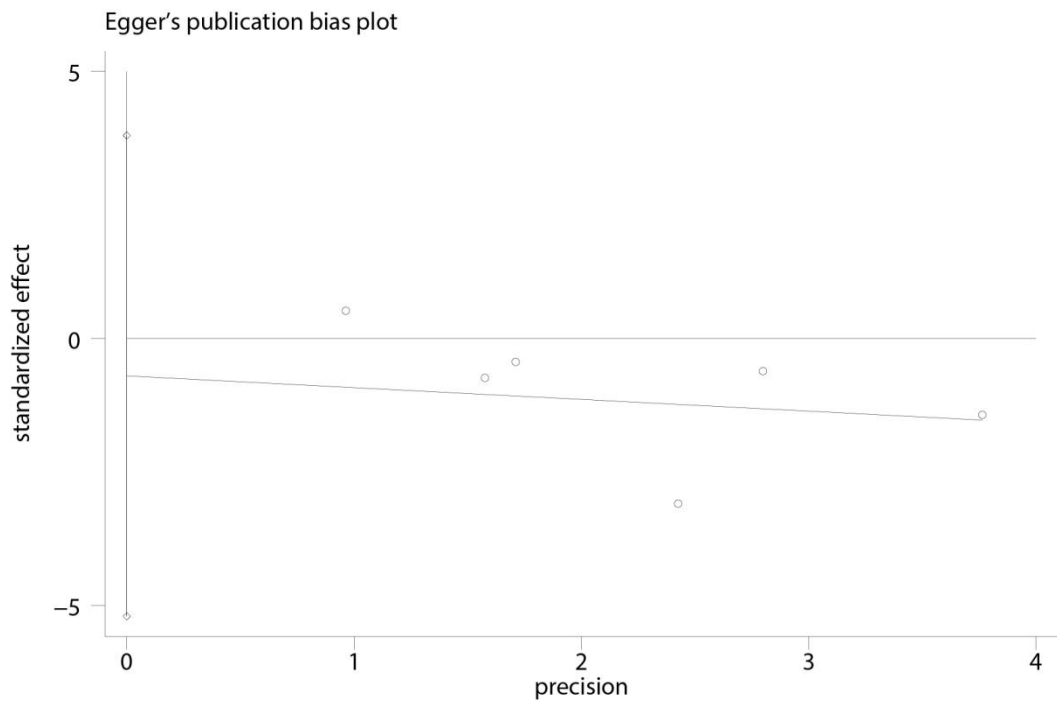
A



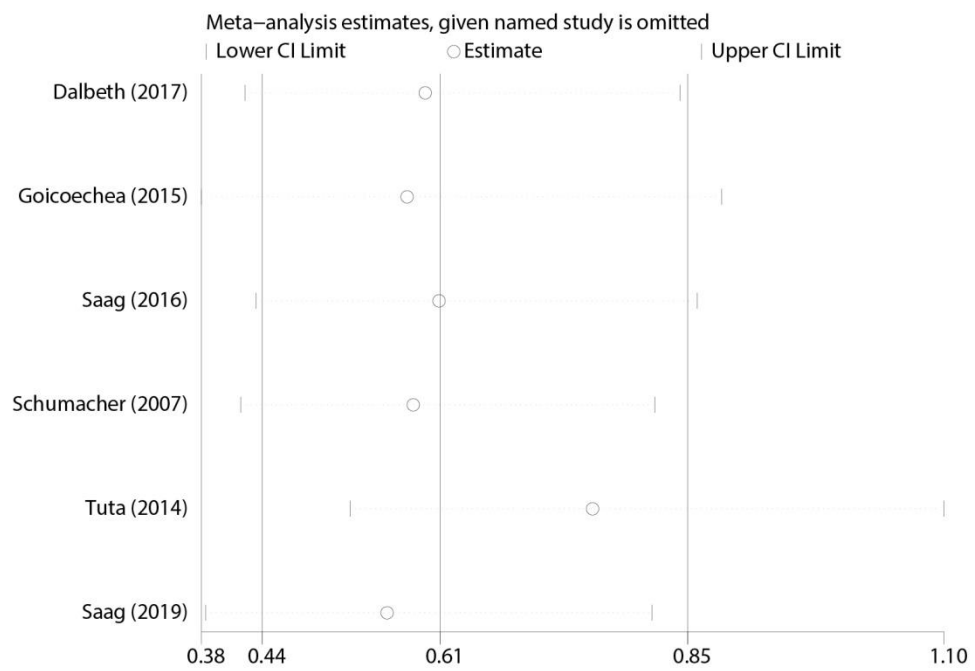
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C

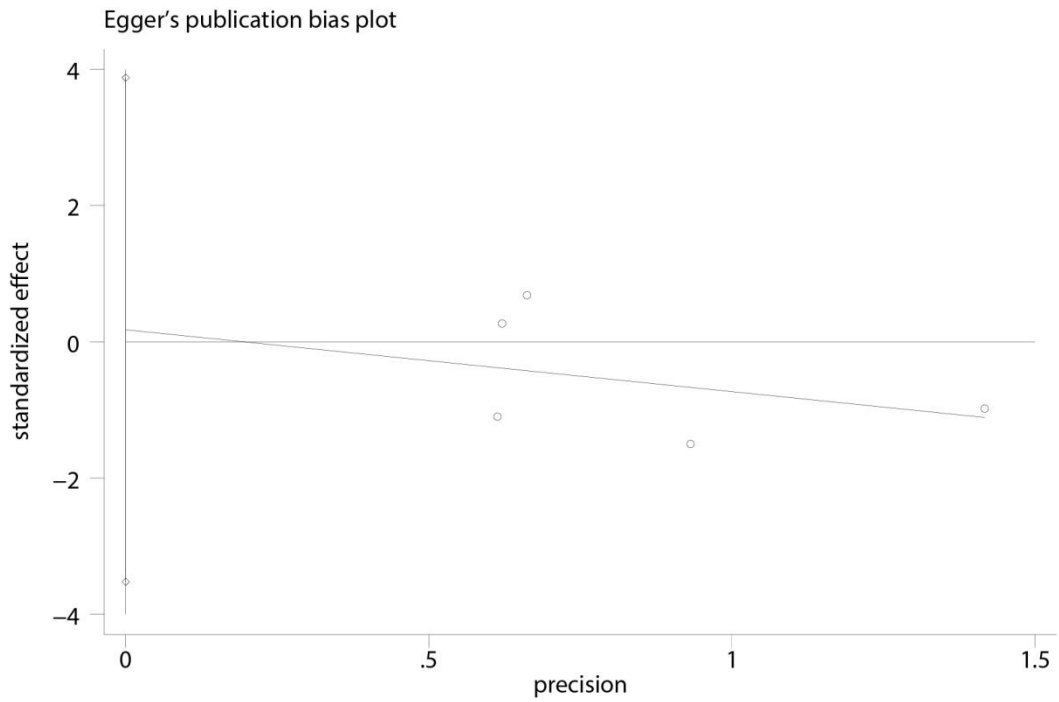


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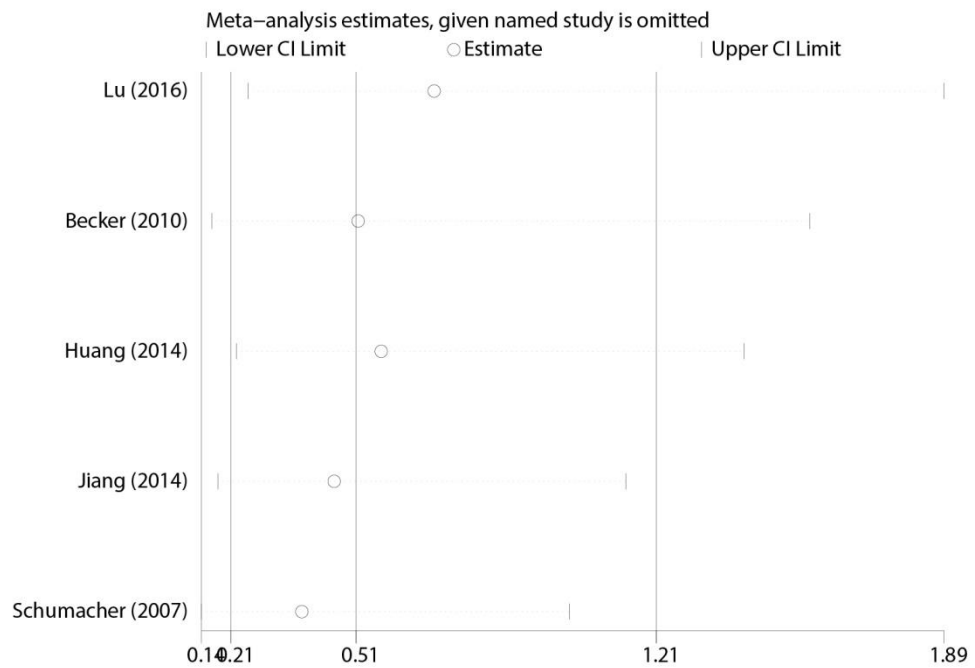


**Supplementary Figure 4:** Egger publication bias plot (A) and sensitivity analysis result (B) of comparison between febuxostat and allopurinol in MACE with low CV risk. Egger publication bias plot (C) and sensitivity analysis result (D) of comparison between febuxostat and allopurinol in CVE with low CV risk. CV: Cardiovascular; CVE: Cardiovascular events; MACE: Major adverse cardiovascular events.

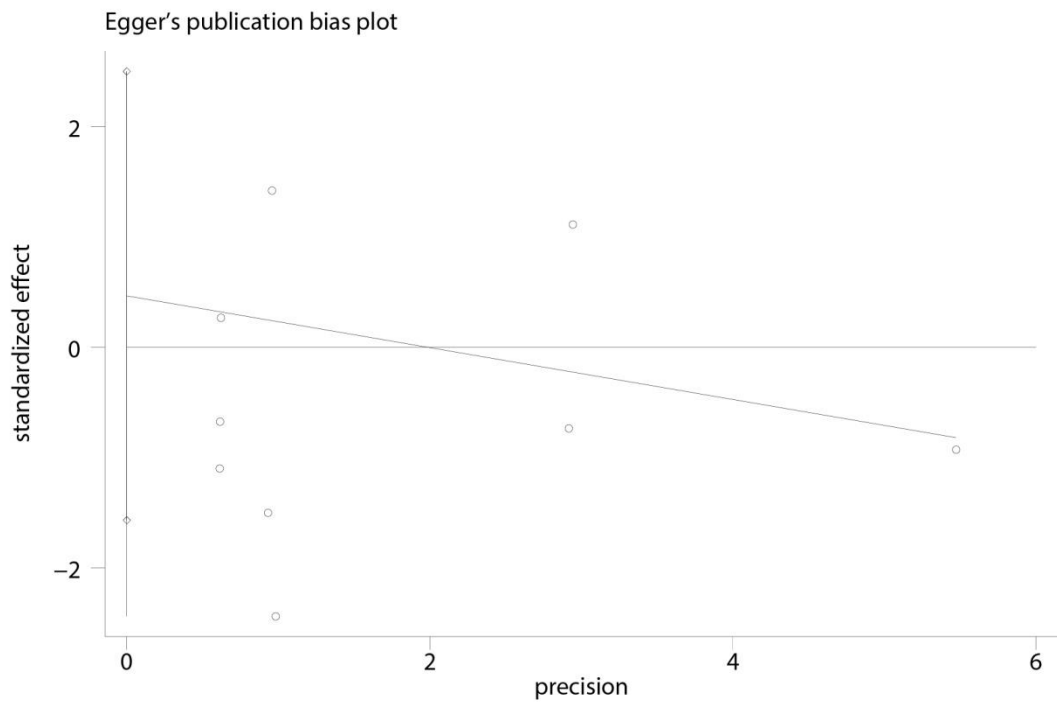
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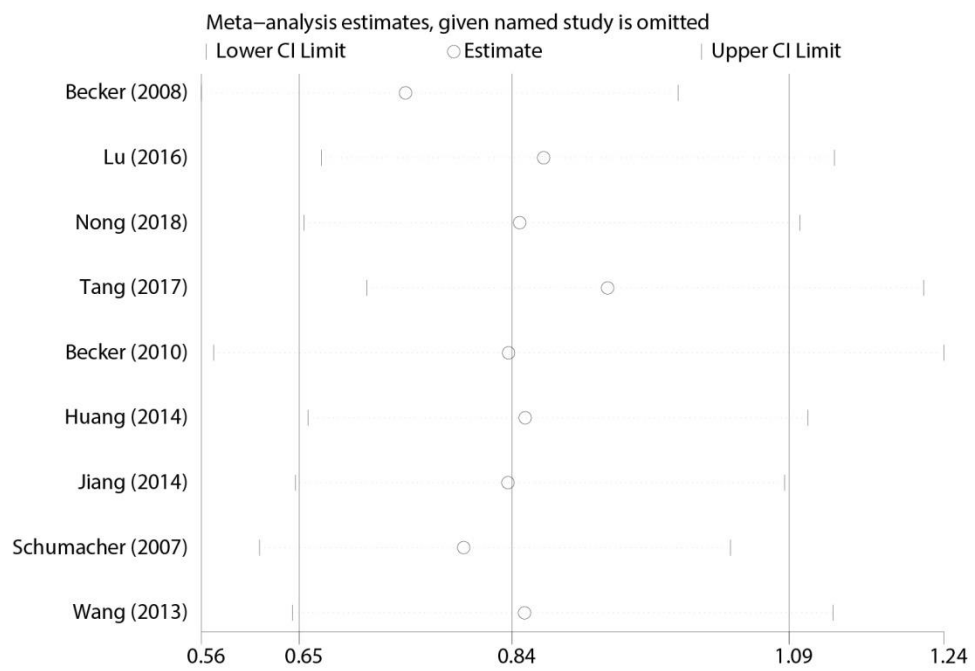
B



C

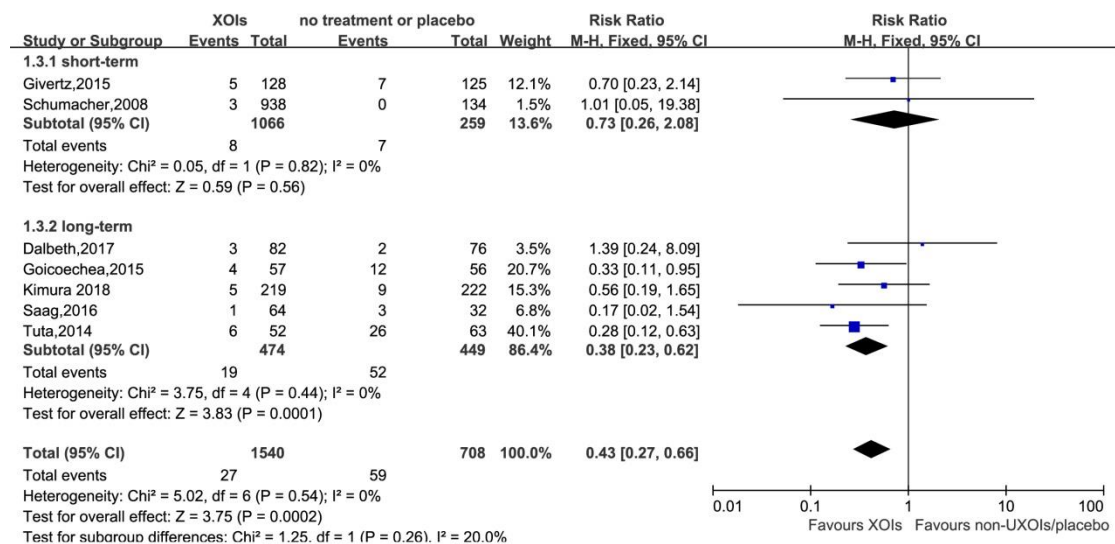


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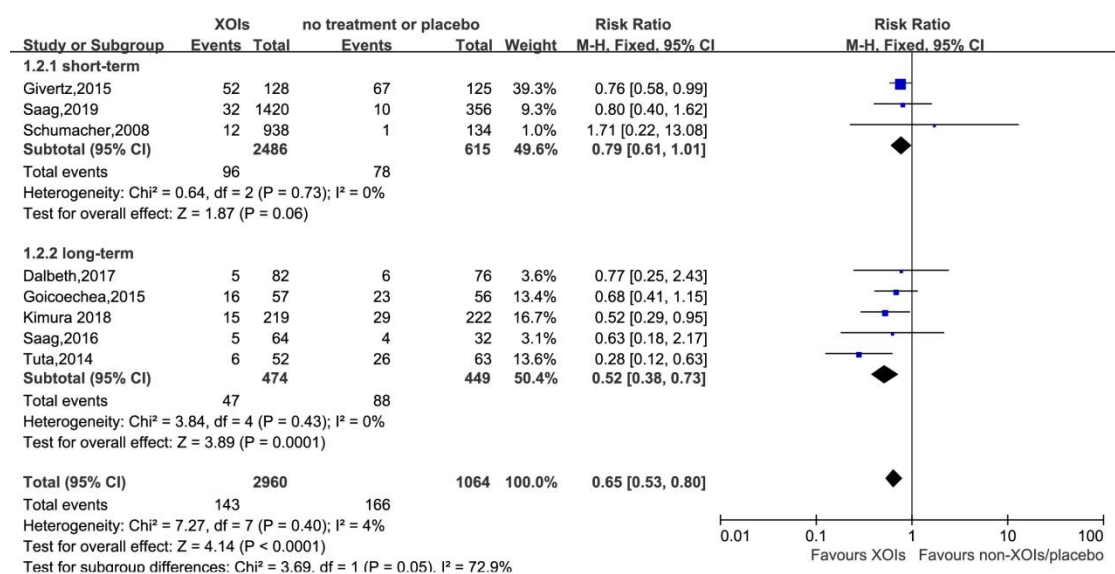


**Supplementary Figure 5:** Subgroup meta-analysis based on short-term (<12 m) and long-term (≥12 m) of MACE (A) and CVE (B) in comparison between XOIs and placebo. Subgroup meta-analysis based on short-term (<12 m) and long-term (≥12 m) of MACE (C) and CVE (D) in comparison between allopurinol and febuxostat. XOIs: Xanthine oxidase inhibitors; MACE: major adverse cardiovascular events, CVE: cardiovascular events.

A

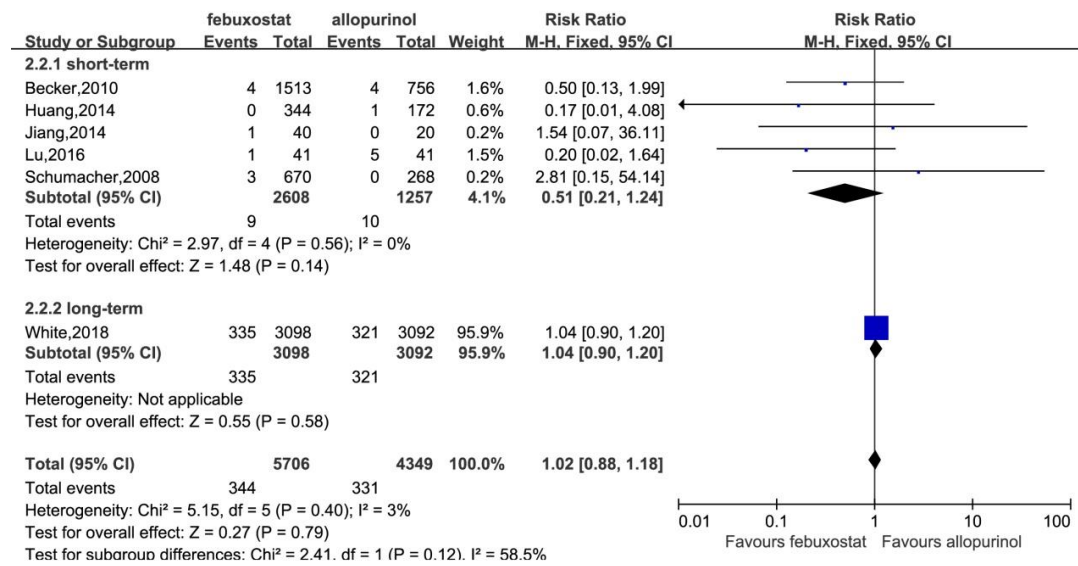


B

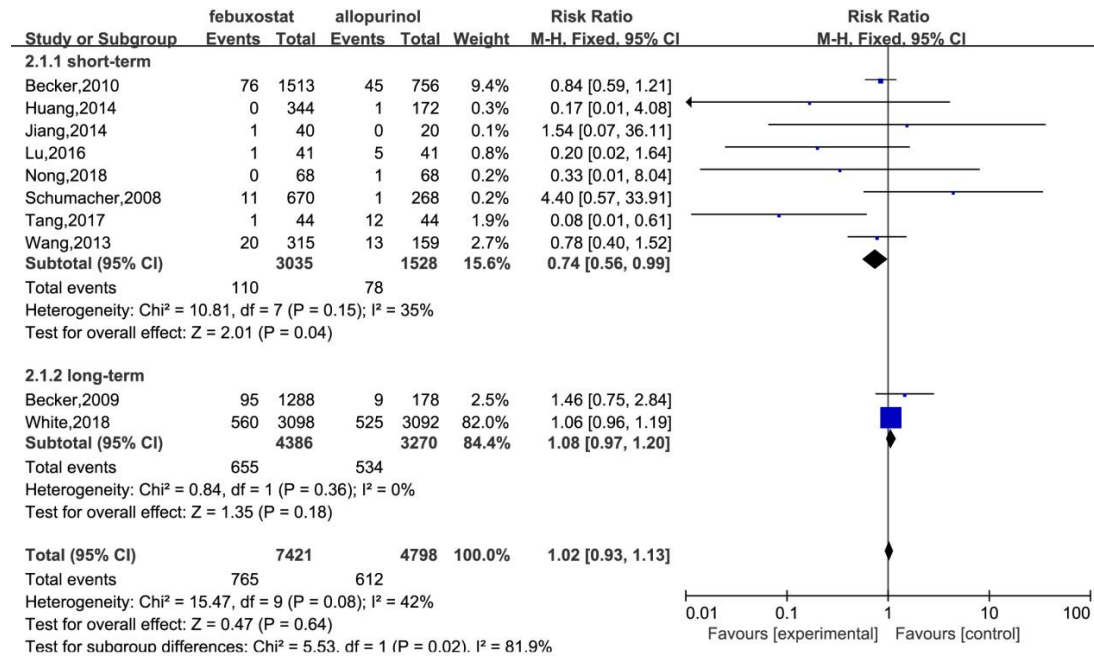




C



D



**Supplementary Table 1:** Methodological quality assessment of prospective cohort studies treating hyperuricemia and gout with uric-lowering therapies.

Authors	Year	Selection				Comparability	Outcome Assessment			Score
		1	2	3	4	5	6	7	8	
Ekundayo	2010	*	*	*	*	**		*		7
Fang	2000	*	*	*	*	*	*	*		7
Franse	2000		*	*	*			*		4
Kanbay	2012		*	*	*		*			4
Sciacqua	2015		*	*	*	**	*	*		7
Turak	2014	*	*	*	*		*			5
Zalawadiya	2015	*	*	*	*		*	*		6