Table S1. PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1,2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3,4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3,4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6,7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6,7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6,7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6,7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6,7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6,7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6,7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6,7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6,7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6,7

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6,7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6,7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9,10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9,10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9,10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9,10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9,10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	12

Table S2. Search strategies and detailed records.

Relevant text of ADAMTS5 rs226794	Relevant text of Osteoarthritis
1. A Disintegrin And Metalloproteinase With Thrombospondin Motifs 5 Protein	**21.** osteoarthritis
2. ADAMTS11 Protein	**22.** osteoarthritides
3. Aggrecanase-2	**23.** osteoarthrosis
4. Aggrecanase 2	**24.** osteoarthroses
5. ADAMTS-5 Protein	**25.** arthritis, degenerative
6. adams 5 Protein	**26.** arthritides, degenerative
7. ADAMTS5 Protease'	**27.** degenerative arthritides
8. polymorphisms, genetic	**28.** degenerative arthritis
9. genetic polymorphisms	**29.** arthrosis
10. genetic polymorphism	**30.** arthroses
11. polymorphism	**31.** osteoarthrosis deformans
12. polymorphisms	**32.** 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
13. nucleotide polymorphism, single	**Combined (Final Strategy)**
14. nucleotide polymorphisms, single	**33.** 20 and 32
15. polymorphisms, single nucleotide	
16. single nucleotide polymorphisms	
17. snps	
18. single nucleotide polymorphism	
19. rs226794	
20. (1 or 2 or 3 or 4 or 5 or 6 or 7) and (8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18) or (19)	

MeSH Browser：http：//www.nlm.nih.gov/mesh/MBrowser.html

PubMed：http：//www.ncbi.nlm.nih.gov/pubmed

Cochrane Library：http：//www.thecochranelibrary.com

Embase：https：//www.embase.com

Table S3. Basic description of articles included in the meta-analysis

First author (Year)	Country	Ethnicity	Disease	Sample size Case/Control	OR (95%CI)	HWE	MAF
Rodriguez, 2008	Spain	Caucasian	Knee OA	277/294	1.41(0.95-2.09)	0.216	11.6%
Canbek, 2016	Turkey	Caucasian	Knee OA	95/80	0.91(0.49-1.68)	0.282	13.1%
Gu, 2013	China	Asian	Knee OA	420/312	1.14(0.91-1.43)	0.461	29.2%
Chen, 2015	China	Asian	Knee OA	166/204	1.13(0.84-1.51)	0.809	46.1%
Chou, 2019	China	Asian	Knee OA	154/208	0.63(0.27-1.48)	0.980	21.7%
This study, 2021	Taiwan	Asian	Knee OA	606/564	0.93(0.79-1.10)	0.983	48.6%

Table S4. Quality evaluation of articles on ADAMTS5

	Selection				Comparability		Exposure		
item/Study	Adequate definition of cases	Representativeness of the cases	Selection of Controls	Definition of Controls	Control for age and gender:	Control for additional factor	Exposure assessment	Same method of ascertainment for all subjects	Non-response rate
Rodriguez,2008	a	a	a	a	b	a	a	a	b
Canbek, 2016	a	a	a	a	b	a	a	a	b
Gu, 2013	a	a	a	a	b	a	a	a	b
Chen, 2015	a	a	a	a	b	a	a	a	b
Chou, 2019	a	a	b	a	a	a	a	a	b

Adequate definition of cases : a: yes, with independent validation. b: yes, eg record linkage or based on self reports. c: no description.

Representativeness of the cases : a: consecutive or obviously representative series of cases; b: potential for selection biases or not stated

Selection of Controls : a: community controls. b: hospital controls. c: no description.

Definition of Controls : a: no history of disease. b: no description of source.

Control for age and BMI : a: Yes. b: No.

Control for additional factor : a: Yes. b: No.

Exposure assessment : a: secure record (eg surgical records) b: structured interview where blind to case/control status. c: interview not blinded to case/control status. d: written self report or medical record only. e: no description.

Same method of ascertainment for all subjects : a: Yes. b: No.

Non-response rate : a: same rate for both groups. b: non respondents described. c: rate different and no designation.