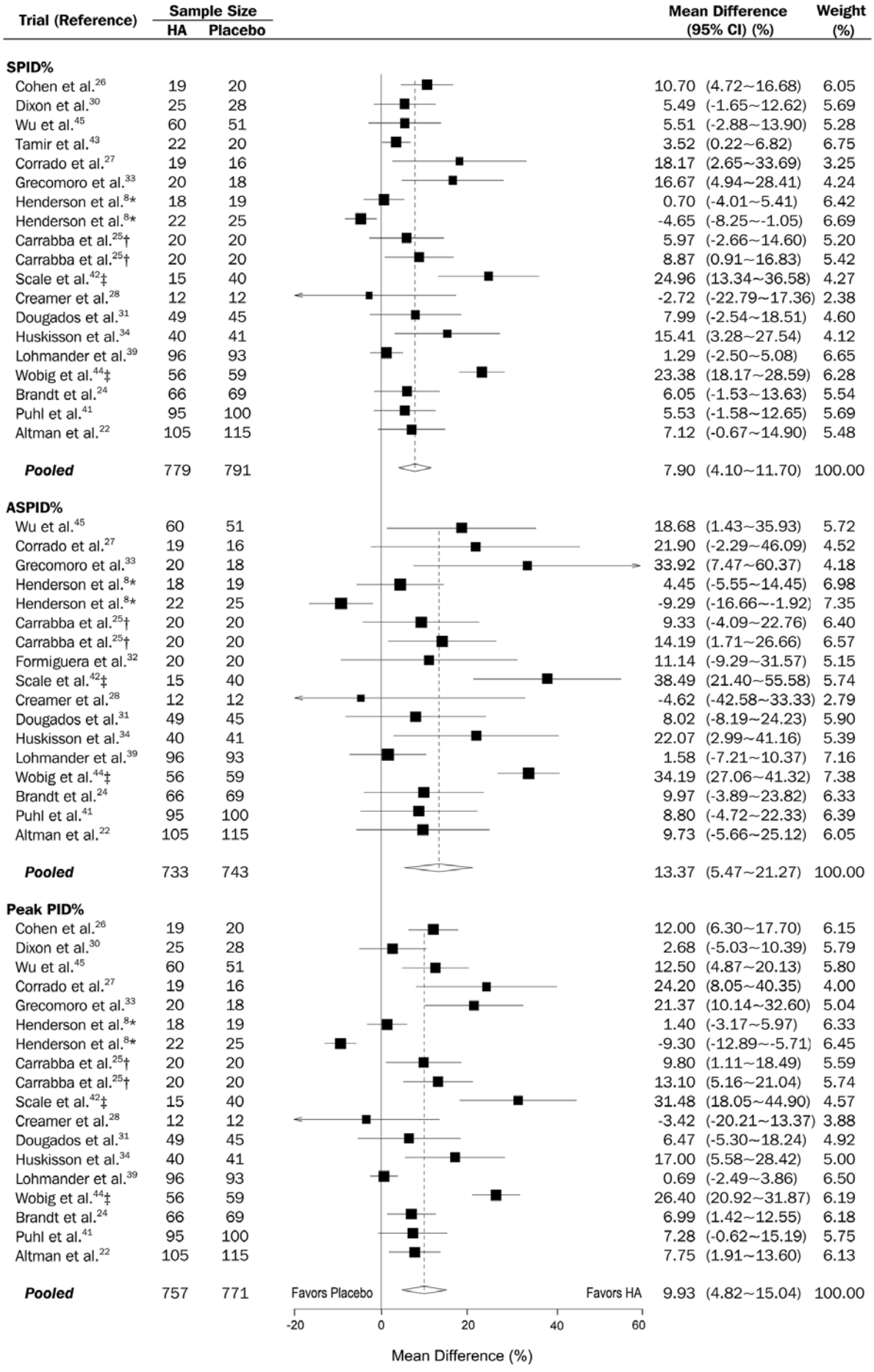

Fig. E-1
The mean differences between the hyaluronic acid and placebo groups in individual trials and the pooled mean differences under random-effects models for the efficacy scores for pain with activities. The mean differences in individual trials are shown as boxes scaled according to weighting with use of DerSimonian and Laird methods. Error bars indicate 95% confidence intervals. The pooled mean differences are shown as diamonds that span the 95% confidence interval. The data were sorted in ascending order according to the quality score of the methodology. SPID%, ASPID%, and peak PID% = efficacy scores (see text for detailed definitions); HA = hyaluronic acid; and CI = confidence interval. *This study included two trials for different severities of osteoarthritis: one for Kellgren-Lawrence grade I and II and the other for Kellgren-Lawrence grade III and IV. †This study included two trials for three-dose and five-dose schedules. ‡Trials involving cross-linked hyaluronic acid.

Table E1. The Checklist for the Assessment of the Methodological Quality

Items	Score
Reporting	
1. *Is the hypothesis/aim/objective of the study clearly described?*	1
2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*	1
3. *Are the characteristics of the patients included in the study clearly described?*	1
4. *Are the interventions of interest clearly described?*	1
5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*	2
6. *Are the main findings of the study clearly described?*	1
7. *Does the study provide estimates of the random variability in the data for the main outcomes?*	1
8. *Have all important adverse events that may be a consequence of the intervention been reported?*	1
9. *Have the characteristics of patients lost to follow-up been described?*	1
10. *Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001?*	1
External validity	
11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*	1
12. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*	1
13. *Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients receive?*	1
Internal validity - bias	
14. *Was an attempt made to blind study subjects to the intervention they have received?*	1
15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*	1
16. *If any of the results of the study were based on "data dredging", was this made clear?*	1
17. *Do the analyses adjust for different lengths of follow- up of patient?*	1
18. *Were the statistical tests used to assess the main outcomes appropriate?*	1
19. *Was compliance with the intervention reliable?*	1
20. *Were the main outcome measures used accurate (valid and reliable) ?*	1
Internal validity - confounding (selection bias)	
21. *Were the patients in different intervention groups recruited from the same population?*	1
22. *Were study subjects in different intervention groups recruited over the same period of time?*	1
23. *Were study subjects randomized to intervention groups?*	1
24. *Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*	1
25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*	1
26. *Were losses of patients to follow-up taken into account?*	1
Power	
27. *Were there power calculations?*	1
Total score	28

TABLE E2. Characteristics of the Randomized Controlled Trials Included in the Meta−Analysis*

Trial	Publication (Year)	Study Design				Characteristics of Patients			Hyaluronic Acid				Evaluated Outcome Endpoints	Outcome Instrument	QS	Industry-funded
		Blinding	Center	ITT	Escape Analgesics	Mean Age *(yr)*	OA Stage	Effusion	Type	Cross-link	MW *(KDa)*	Dose *(mg)* /Number				
Altman et al.[22]	Journal (1998)	Double	Multi	+	Aceta-minophen	63.6	KL grade II, III	No restriction	Hyalgan	−	0.73	20/5	Pain with activities Functioning	VAS	25	+
Bragantini et al.[23]	Journal (1987)	Single	Single	−	−	57.1	KL grade II, III, IV	No restriction	Hyalgan	−	0.73	20/3	Pain without activities	VAS	13	+
Brandt et al.[24]	Journal (2001)	Double	Multi	−	Aceta-minophen	66.0	KL grade II, III	No restriction	Orthovisc	−	2.90	30/3	Pain with activities Pain without activities Functioning	WOMAC	22	−
Carrabba et al.[25]†	Journal (1995)	Double	Single	−	Aceta-minophen	60.0	No restriction	Inclusion criteria	Hyalgan	−	0.73	20/3	Pain with activities Pain without activities Functioning	VAS	17	+
Carrabba et al.[25]†	Journal (1995)	Double	Single	−	Aceta-minophen	60.6	No restriction	Inclusion criteria	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities Functioning	VAS	17	+
Cohen et al.[26]	Abstract (1994)	Double	Single	−	N/A	N/A	No restriction	N/A	Hyalgan	−	0.73	20/3	Pain with activities Functioning	VAS WOMAC	12	+
Corrado et al.[27]	Journal (1995)	Single	Single	−	−	61.3	No restriction	Inclusion criteria	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities	VAS	16	−
Creamer et al.[28]	Journal (1994)	Double	Single	−	Aceta-minophen	72.2	KL grade II, III, IV	Inclusion criteria	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities	VAS	18	+
Dickson et al.[29]	Abstract (1998)	Double	Single	−	N/A	N/A	N/A	N/A	Synvisc	+	6.00	16/3	Pain with activities Pain without activities Functioning	WOMAC Lequesne	9	+
Dixon et al.[30]	Journal (1988)	Double	Multi	−	Aceta-minophen	68.5	No restriction	No restriction	Hyalgan	−	0.73	20/up to 11	Pain with activities Pain without activities Functioning	VAS	14	+
Dougados et al.[31]	Journal (1993)	Single	Multi	+	−	68.0	No restriction	Inclusion criteria	Hyalgan	−	0.73	20/4	Pain with activities Pain without activities Functioning	VAS Lequesne	19	−
Formiguera et al.[32]	Journal (1995)	Double	Single	+	−	62.0	No restriction	No restriction	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities Functioning	VAS	17	−
Grecomoro et al.[33]	Journal (1987)	Double	Single	−	−	64.9	No restriction	No restriction	Hyalgan	−	0.73	20/3	Pain with activities Pain without activities	VAS	16	−
Henderson et al.[8]‡	Journal (1994)	Double	Single	−	Aceta-minophen	61.9	KL grade I, II	No restriction	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities Functioning	VAS	16	−
Henderson et al.[8]‡	Journal (1994)	Double	Single	−	Aceta-minophen	69.4	KL grade III, IV	No restriction	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities Functioning	VAS	16	−
Huskisson et al.[34]	Journal (1999)	Double	Single	+	No restriction	65.3	KL grade II, III	No restriction	Hyalgan	−	0.73	20/5	Pain with activities Pain without activities Functioning	VAS	21	−
Lohmander et al.[39]	Journal (1996)	Double	Multi	+	No restriction	58.3	Ahlback stage I, II	No restriction	Artz	−	1.20	25/5	Pain with activities Pain without activities Functioning	VAS Lequesne	21	+
Puhl et al.[41]	Journal (1993)	Double	Multi	−	Aceta-minophen	61.4	No restriction	Exclusion criteria	Artz	−	1.20	25/5	Pain with activities Functioning	VAS Lequesne	23	+
Scale et al.[42]	Journal (1994)	Double	Single	−	−	58.5	KL grade II, III, IV	No restriction	Synvisc	+	6.00	16/3	Pain with activities Functioning	VAS Lequesne	17	+
Tamir et al.[43]	Journal (2001)	Double	Single	−	−	70.5	KL grade II, III, IV	Exclusion criteria	BioHy	−	3.00	20/5	Pain with activities Pain without activities Functioning	MODEMS	15	+
Wobig et al.[44]	Journal (1998)	Double	Multi	−	No restriction	62.0	KL grade I, II, III	Exclusion criteria	Synvisc	+	6.00	16/3	Pain with activities Functioning	VAS	21	+
Wu et al.[45]	Journal (1997)	Double	Single	−	−	69.0	No restriction	Exclusion criteria	Artz	−	1.20	25/5	Pain with activities Pain without activities Functioning	NRS	14	−

*ITT = intention-to-treat; OA = osteoarthritis; MW = molecular weight; QS = quality score of methodology; N/A = not available; KL grade = Kellgren-Lawrence grade; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; Lequesne = Lequesne Algofunctional Index; MODEMS = Musculoskeletal Outcomes Data Evaluation and Management System; NRS = numerical rating scale. Industry-funded status was determined by the authorship listing and presented information in each article. †This study included two trials for 3-dose and 5-dose schedules, respectively. ‡This study included two trials for different severity of OA: one for KL grade I, II, and the other for KL grade III, IV.

TABLE E3. Subgroup Analysis of the Mean Differences for the Efficacy Scores in Pain with Activities (Non-cross-linked HA trials)*

Trial Category	SPID%		ASPID%		Peak PID%	
	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity
All trials	5.4 (2.6~8.2) [17]	<0.001	8.7 (3.1~14.4) [15]	0.005	7.4 (3.1~11.8) [16]	<0.001
Single-blind	11.2 (2.5~19.9) [2]	0.287	12.3 (-1.2~25.8) [2]	0.350	14.4 (-2.9~31.7) [2]	0.082
Double-blind	3.0 (1.5~4.5) [15]	<0.001	8.3 (2.6~14.4) [13]	0.004	6.8 (2.3~11.3) [14]	<0.001
Single-center	6.0 (1.8~10.3) [11]	<0.001	10.8 (1.9~19.7) [10]	0.001	9.4 (1.9~16.8) [10]	<0.001
Multi-center	4.0 (1.4~15.0) [6]	0.585	6.1 (0.4~11.7) [5]	0.784	3.6 (1.4~5.9) [6]	0.173
No intention-to-treat analysis	5.2 (1.9~8.6) [13]	<0.001	9.2 (1.2~17.1) [10]	0.002	7.7 (1.9~13.5) [12]	<0.001
Intention-to-treat analysis	6.2 (0.4~12.0) [4]	0.089	7.1 (0.7~13.5) [5]	0.386	6.7 (0.1~13.3) [4]	0.014
No escape analgesics	5.3 (2.5~8.1) [5]	0.107	16.2 (7.3~25.1) [5]	0.520	14.5 (9.2~19.7) [4]	0.181
Acetaminophen as escape analgesics	3.5 (-0.3~7.3) [9]	0.006	5.4 (-1.8~12.6) [8]	0.016	4.1 (-1.6~9.8) [9]	<0.001
No restriction on escape analgesics	7.1 (-6.5~20.7) [2]	0.029	10.0 (-9.8~29.8) [2]	0.056	7.9 (-8.0~23.8) [2]	0.007
Mean age of patients ≤ 65 years	5.7 (2.1~9.3) [8]	0.052	11.4 (5.6~17.2) [8]	<0.001	8.6 (3.8~13.5) [8]	<0.001
Mean age of patients > 65 years	4.0 (-0.4~8.4) [8]	0.002	7.6 (-4.8~20.1) [6]	<0.001	4.6 (-3.8~13.0) [7]	<0.001
Without the most advanced OA stage	2.8 (0.4~5.4) [5]	0.116	6.2 (0.9~11.7) [5]	0.364	5.1 (0.9~9.4) [5]	0.013
With the most advanced OA stage	-0.1 (-7.9~6.4) [3]	0.004	-9.1 (-16.3~-1.9) [2]	0.813	-9.0 (-12.6~-5.5) [2]	0.502
No restriction on OA stage	8.3 (5.5~11.0) [9]	0.644	13.2 (7.4~18.9) [8]	0.730	11.0 (7.4~14.6) [9]	0.137
Effusion as inclusion criteria	8.0 (3.3~12.8) [5]	0.558	11.4 (4.0~18.8) [5]	0.762	10.6 (5.9~15.4) [5]	0.179
Effusion as exclusion criteria	4.1 (1.2~6.9) [3]	0.826	12.6 (1.9~23.2) [2]	0.377	10.0 (4.5~15.5) [2]	0.352
No restriction on effusion	5.1 (0.9~9.5) [9]	<0.001	7.2 (-10.6~15.4) [8]	0.002	5.8 (0.2~11.3) [9]	<0.001
Trial duration ≤ 12 weeks	4.7 (-1.3~10.7) [7]	<0.001	5.3 (-4.9~15.5) [6]	0.005	6.2 (-2.3~14.8) [7]	<0.001
Trial duration > 12 weeks	4.5 (2.6~6.4) [10]	0.239	9.4 (4.5~14.3) [9]	0.324	8.1 (3.9~12.3) [9]	0.001
Sample size ≤ 100	6.1 (2.1~10.1) [12]	<0.001	9.6 (10.5~18.1) [10]	0.001	8.1 (1.3~14.9) [11]	<0.001
Sample size > 100	3.6 (0.9~6.3) [5]	0.542	7.2 (1.5~12.9) [5]	0.465	6.4 (2.0~10.8) [5]	0.016
Non-industry-funded	6.5 (0.8 ~12.2) [8]	<0.001	10.9 (1.6~20.2) [9]	0.001	8.9 (0.8~17.0) [8]	<0.001
Industry-funded	4.5 (2.7~6.4) [9]	0.296	7.1 (1.7~12.4) [6]	0.639	6.7 (2.6~10.8) [8]	0.005

*HA = hyaluronic acid; SPID%, ASPID%, peak PID% = efficacy scores, see text for detailed definitions; n = number of trials; CI = confidence interval; OA = osteoarthritis. Industry-funded status was determined by the authorship listing and presented information in each article. †P values of the test for between-study heterogeneity were calculated by χ^2 test for Q statistics.

TABLE E4. Subgroup Analysis of the Mean Differences for the Efficacy Scores in Pain without Activities (Non-cross-linked HA trials)*

Trial Category	SPID%		ASPID%		Peak PID%	
	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity
All trials	6.0 (0.7~11.2) [10]	<0.001	11.0 (-3.7~25.7) [9]	<0.001	7.0 (-1.8~15.7) [9]	<0.001
Single-blind	11.9 (-1.6~25.4) [3]	0.028	33.0 (-11.4~77.4) [3]	0.046	13.2 (1.42~25.0) [3]	0.027
Double-blind	4.3 (-1.6~10.2) [7]	<0.001	4.5 (-9.3~18.3) [6]	0.007	4.0 (-6.6~14.6) [6]	<0.001
Single-center	5.2 (-0.7~11.0) [8]	<0.001	11.9 (-4.2~28.0) [8]	<0.001	6.4 (-3.8~16.6) [7]	<0.001
Multi-center	9.2 (-0.5~18.9) [2]	0.081	4.8 (-28.0~37.6) [1]		9.4 (-0.1~18..9) [2]	0.062
No intention-to-treat analysis	6.3 (0.6~11.9) [9]	<0.001	12.4 (-5.3~30.2) [7]	<0.001	7.4 (-2.2~17.0) [8]	<0.001
Intention-to-treat analysis	3.4 (-6.4~13.2) [1]		7.5 (-15.7~30.7) [2]	0.822	4.0 (-4.7~12.6) [1]	
No escape analgesics	8.6 (3.1~14.1) [5]	0.102	22.6 (6.3~38.9) [5]	0.110	11.0 (2.5~19.5) [4]	0.045
Acetaminophen as escape analgesics	3.4 (-4.3~11.2) [5]	<0.001	2.4 (-14.6~19.3) [4]	0.002	3.6 (-8.3~15.6) [5]	<0.001
Mean age of patients ≤ 65 years	8.7 (0.2~17.2) [4]	0.012	27.3 (8.3~46.3) [4]	<0.001	11.3 (3.2~19.4) [4]	<0.001
Mean age of patients > 65 years	4.4 (-4.2~13) [5]	<0.001	0.1 (-23.6~23.7) [3]	<0.001	2.0 (-14.2~18.2) [4]	<0.001
Without the most advanced OA stage	2.1 (-2.0~6.1) [1]		9.1 (-7.1~25.3) [1]		4.1 (0.0~8.2) [1]	
With the most advanced OA stage	7.3 (-6.6~21.2) [3]	<0.001	21.6 (-62~105.2) [2]	<0.001	4.7 (-34.9~44.4) [2]	<0.001
No restriction on OA stage	8.0 (4.7~11.3) [6]	0.318	11.3 (1.3~21.3) [6]	0.950	9.6 (6.4~12.9) [6]	0.404
Effusion as inclusion criteria	5.1 (0.6~9.5) [4]	0.948	10.9 (-0.2~22.0) [4]	0.957	7.8 (3.4~12.2) [4]	0.633
Effusion as exclusion criteria	7.5 (4.6~10.5) [2]	0.667	15.7 (-16.7~48.1) [1]		5.9 (-3.6~15.4) [1]	
No restriction on effusion	7.2 (-4.0~18.3) [4]	<0.001	13.1 (-16.6~42.8) [4]	<0.001	6.3 (-9.2~21.8) [4]	<0.001
Trial duration ≤ 12 weeks	4.8 (-2.5~12.1) [6]	<0.001	12.3 (-7.4~31.9) [6]	<0.001	6.5 (-4.9~18.0) [6]	<0.001
Trial duration > 12 weeks	8.4 (5.9~11.0) [4]	0.200	10.3 (-8.6~29.1) [3]	0.899	9.9 (5.8~14.1) [3]	0.115
Non-industry-funded	1.1 (-5.3~7.4) [5]	0.001	2.2 (-13.9~18.2) [6]	0.037	1.9 (-9.3~13.1) [5]	<0.001
Industry-funded	9.8 (4.9~14.6) [5]	0.027	24.3 (-0.1~49.3) [3]	0.017	12.3 (8.4~16.1) [4]	0.103

*Only the attributes influencing the estimates of HA efficacy were listed. HA = hyaluronic acid; SPID%, ASPID%, peak PID% = efficacy scores, see text for detailed definitions; n = number of trials; CI = confidence interval; OA = osteoarthritis. Industry-funded status was determined by the authorship listing and presented information in each article. †P values of the test for between-study heterogeneity were calculated by χ^2 test for Q statistics.

TABLE E5. Subgroup Analysis of the Mean Differences for the Efficacy Scores in Functioning (Non-cross-linked HA trials)*

Trial Category	SFID%		ASFID%		Peak FID%	
	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity	Pooled Mean Difference (95% CI) *(%)* [n]	P Value† for Heterogeneity
All trials	5.3 (2.1~8.5) [8]	0.033	11.7 (6.3~16.2) [7]	0.229	8.2 (3.8~12.6) [8]	0.001
No intention-to-treat analysis	5.4 (1.3~9.6) [6]	0.013	12.0 (3.5~20.6) [6]	0.088	9.0 (3.2~14.7) [6]	<0.001
Intention-to-treat analysis	5.8 (0.6~10.9) [2]	0.868	10.6 (0.7~20.5) [2]	0.885	6.6 (1.0~12.2) [2]	0.918
No escape analgesics	10.5 (1.9~19.0) [2]	0.076	20.2 (10.8~29.6) [2]	0.110	16.4 (-2.8~35.6) [2]	0.002
Acetaminophen as escape analgesics	2.4 (0.3~4.5) [5]	0.577	7.3 (0.8~13.8) [4]	0.880	4.3 (2.1~6.6) [5]	0.279
No restriction on escape analgesics	5.3 (-2.5~13.1) [1]		9.9 (-3.8~23.6) [1]		6.3 (-1.8~14.3) [1]	
Without the most advanced OA stage	5.0 (-1.3~11.4) [2]	0.927	9.3 (-2.0~20.7) [2]	0.892	5.8 (-0.3~11.8) [2]	0.859
No restriction on OA stage	5.6 (1.6~9.5) [6]	0.010	12.3 (4.3~20.3) [5]	0.092	9.2 (3.5~14.8) [6]	<0.001
Effusion as inclusion criteria	6.3 (1.8~10.9) [3]	0.974	10.5 (2.4~18.7) [3]	0.973	8.4 (3.5~13.4) [3]	0.859
Effusion as exclusion criteria	8.5 (-3.1~20.2) [2]	0.003	15.4 (-6.4~37.1) [2]	0.005	16.0 (-3.6~35.5) [2]	<0.001
No restriction on effusion	1.7 (-0.9~4.3) [3]	0.525	9.4 (-2.0~20.7) [2]	0.892	3.0 (0.3~5.6) [3]	0.598
Trial duration ≤ 12 weeks	6.5 (0.4~12.6) [2]	0.829	10.2 (0.2~20.1) [2]	0.848	9.5 (3.1~16.0) [2]	0.855
Trial duration > 12 weeks	3.5 (1.5~5.5) [6]	0.014	12.2 (3.7~20.7) [5]	0.090	8.0 (2.7~13.3) [6]	0.001
Non-industry-funded	8.4 (4.6~12.3) [4]	0.178	15.8 (8.5~23.1) [4]	0.200	10.9 (1.8~20.0) [4]	0.004
Industry-funded	2.2 (0.1~4.5) [4]	0.437	7.2 (0.4~14.1) [3]	0.719	4.3 (2.0~6.6) [4]	0.168

*Only the attributes influencing the estimates of HA efficacy were listed. HA = hyaluronic acid; SFID%, ASFID%, peak FID% = efficacy scores, see text for detailed definitions; n = number of trials; CI = confidence interval; OA = osteoarthritis. Industry-funded status was determined by the authorship listing and presented information in each article. †P values of the test for between-study heterogeneity were calculated by χ^2 test for Q statistics.

Table E6. Meta-regression Analysis of the Mean Differences for the Efficacy Scores in Different Outcome Endpoints (Non-cross-linked HA trials)*

Regression Covariate	Estimated Regression Coefficient / Residual Heterogeneity Variance τ^2†								
	Pain with Activities			Pain without Activities			Functioning		
	SPID%	ASPID%	Peak PID%	SPID%	ASPID%	Peak PID%	SFID%	ASFID%	Peak FID%
No covariate	- / 0.0019	- / 0.0060	- / 0.0060	- / 0.0056	- / 0.0315	- / 0.0159	- / 0.0010	- / 0.0017	- / 0.0025
Publication year	-0.0016 / 0.0022	0.0003 / 0.0065	0.0002 / 0.0064	-0.0096 / 0.0076	-0.0551 / 0.0286	-0.0169 / 0.0146	0.0068‡/ 0.0002	0.0085 / 0.0019	0.0058 / 0.0021
Quality score of methodology	0.0000 / 0.0021	-0.0004 / 0.0067	-0.0015 / 0.0068	-0.0272 / 0.0043	-0.0725 / 0.0334	-0.0252 / 0.0161	-0.0033 / 0.0018	-0.0193‡/ 0.0000	-0.0071 / 0.0041
Molecular weight of HA	-0.0084 / 0.0023	0.0034 / 0.0067	-0.0055 / 0.0065	0.0079 / 0.0069	0.1055 / 0.0343	-0.0259 / 0.0170	0.0070 / 0.0012	-0.0042 / 0.0027	-0.0002 / 0.0030
Mean age of patients	-0.0021 / 0.0020	-0.0036 / 0.0066	-0.0053 / 0.0068	-0.0082 / 0.0077	-0.0370‡/ 0.0091	-0.0151 / 0.0150	0.0037 / 0.0020	0.0181‡/ 0.0000	-0.0047 / 0.0045
Trial duration	0.0010 / 0.0014	0.0022 / 0.0040	0.0004 / 0.0053	0.0013 / 0.0038	-0.0001 / 0.0343	0.0008 / 0.0145	-0.0006 / 0.0013	0.0013 / 0.0023	-0.0011 / 0.0027
Sample size	-0.0000 / 0.0022	-0.0001 / 0.0071	-0.0001 / 0.0071	-0.0007 / 0.0061	-0.0028 / 0.0336	-0.0011 / 0.0180	-0.0002 / 0.0017	-0.0007‡/ 0.0002	-0.0003 / 0.0039

*HA = hyaluronic acid; SPID%, ASPID%, peak PID%, SFID%, ASFID%, peak FID% = efficacy scores, see text for detailed definitions. †Residual heterogeneity variance τ^2 represents residual between-study variance τ^2 after accounting for the heterogeneity resulting from the difference in each covariate. τ^2 in the "no covariate" row are identical to the moment estimators of between-study variance τ^2 obtained from random-effects models of DerSimonian and Laird methods[20]. ‡Estimated regression coefficient is significantly different from zero (p value < 0.05).