Characteristics of included and excluded studies

Characteristics of included studies

Cerza 2012	
Study type/Country/Treatment	Randomized, two arm, controlled trial Single Center, Italy PRP versus Hyaluronic Acid,
Participants	Mean age: 66.4, % Female: 55.8% Mean disease duration: NR Number Randomized: 120 Follow-up: 1, 3 and 6 months <u>Inclusion:</u> Age: NR Duration clinical symptoms : NR Symptomatic OA of the knee , radiological **Kellgren Lawrence** grade I-III <u>Baseline values:</u> Kellgren Lawrence grade (n(%)): I: PRP: 21(35) HA: 25(42) II: PRP: 24(40) HA: 22(37) III: PRP: 15(25) HA: 13(21) WOMAC score (mean(SD): Total: PRP: 79.6(9.5) HA: 75.4(10.7)
Intervention	<u>Intervention (n=60):</u> 4 PRP (ACP)(type NA) intra articular injections (5,5mL) Interval: weekly <u>Comparison (n=60):</u> 4 HA intra articular injections Interval: weekly
Outcomes	Primary outcome: WOMAC total score (0-96) Adverse effects
Results	WOMAC total score 1, 3 and 6 months resp. (mean(SD)): PRP:49.6(17.7), 39.1(17.8), 36.5(17.9) HA: 55.2(12.3), 57(11.7), 65.1(10.6) *P<0.001, P<0.001, P<0.001* Adverse effects: No short time side effects observed

Risk of bias (Cerza 2012)		
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were consecutively randomized..." Comment: The report states that allocation was random. Method of sequence generation process was not specified. Insufficient information about the sequence generation process to permit judgement of low risk or high risk.
Allocation concealment (selection bias)	High risk	Comment: It is not stated that allocation was concealed. Probably not done
Blinding of participants (performance bias)	Unclear risk	No reporting regarding blinding the participants. Comment: It is not stated that the participants were blind for treatment. Insufficient information about the blinding of participants to permit judgement of low risk or high risk.
Blinding of personnel (performance bias)	High risk	Quote: "The injections were performed by the unblinded physician..." Comment: Probably not done
Blinding of outcome assessment (detection bias)	Unclear risk	Just reporting that the outcome assessment was managed by the same operator. Comment: Insufficient information about blinding of the observer to permit judgement of low risk or high risk.
Incomplete outcome data (attrition bias)	Low risk	Number of allocated and analyzed participants was reported. Quote: "No patients withdrew during the study period". In each group the number of subjects analyzed were reported (n=60) and no subjects excluded from analysis.
Selective reporting (reporting bias)	Low risk	Pre-specified outcomes have been reported. Primary outcome measures (WOMAC which assess pain, stiffness and fictional limitation) have been reported.
Other bias	Unclear risk	Power analysis has been calculated. (33 patients per treat arm to provide at least 80% power to detect an anticipated effect size of 0.8 on WOMACscore).

Filardo 2012	
Study type/Country/Treatment	Randomized, two arm, controlled trial Single Center, Italy PRP versus Hyaluronic Acid
Participants	Mean age: 56.5, % Female: 37.6% Mean disease duration: 63.5 months Number Randomized: 109 Follow-up: 2, 6 and 12 months <u>Inclusion:</u> Age: NR Clinical symptoms > 4 months Monolateral symptomatic OA of the knee , radiological **Kellgren Lawrence** grade 0-III <u>Baseline values:</u> Kellgren Lawrence grade (mean): PRP: 2.2 HA: 2.1 IKDC score (mean(SD)): PRP: 50.2(15.7) HA: 47.4(14.0) Tegner score (mean(SD)): PRP: 2.9(1.4) HA: 2.6(1.2)
Intervention	<u>Intervention (n=54):</u> 3 PRP (type 2A) intra articular injections (5mL) Interval: weekly <u>Comparison (n=55):</u> 3 HA intra articular injections Interval: weekly
Outcomes	<u>Primary outcome(s):</u> IKDC score (0-100) <u>Secondary outcome(s):</u> KOOS score (0-100/category) EQ-VAS (0-100) Tegner score (0-10) Range of motion Knee circumference change Patient satisfaction Adverse effects
Results	IKDC score 2, 6 and 12 months resp. (mean(SD)): PRP: 62.8(17.6), 64.3(16.4), 64.9(16.8) HA: 61.4(16.2), 61.0(18.2), 61.7(19.0) *PRP vs. HA: NS* KOOS score 2,6 and 12 months: *PRP vs. HA: Ns* EQ-VAS: NR/NS Tegner score 12 months (mean(SD)): PRP: 3.8(1.3) HA: 3.4(1.6) *PRP vs. HA: NS* Range of motion: Not reported Knee circumference: Not reported Patient satisfaction: Not reported Adverse effects: No major complications related to the injections were observed during the treatment and follow-up. Post-injective pain reaction was significantly higher in the PRP group (*p=0.039*). However this

	reaction was self-limiting.	
Risk of bias (Filardo 2012)		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "...according to a randomization list, provide by an independent statistician, was kept in a dedicated office". Comment: Probably done
Allocation concealment (selection bias)	Low risk	Quote: "Physician contacted statistician by a phone call just before the injective procedure". Central allocation (by telephone) Comment: Probably done
Blinding of participants (performance bias)	Low risk	Quote: "At the end of the study, the nature of the injected substance was revealed to the patients. Further: No dosage differences between groups. All of the participants underwent blood harvesting to obtain autologous PRP. Comment: Probably done
Blinding of personnel (performance bias)	High risk	Physician was not blinded. Just before the injective procedure he got informed about the treatment allocation. Comment: Probably not done
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All the clinical evaluations were performed by a medical member of staff not involved in the injective procedure" Comment: Blinding is reported and probably done.
Incomplete outcome data (attrition bias)	High risk	Number of allocated and analyzed participants was reported. 0/54 missing from PRP group, 3/55 missing from the HA group (2 due to suspected intolerance to some components of HA and 1 due to lack of efficacy).
Selective reporting (reporting bias)	Unclear risk	Primary outcomes are reported. Not all pre-specified secondary outcomes have been reported. Outcome of EQVAS, ROM, knee circumference and patients satisfaction are not reported.
Other bias	Unclear risk	Power analysis have been calculated. (96 patients per treat arm to provide at least 80% power to detect a difference of 6.7 points of the IKDC score at a 5 % level of significance and possible drop

	out of 15%).

Filardo/Kon/Ruiz 2012	
Study type/Country/Treatment	Prospective, two arm, comparative trial Multicenter, Italy PRGF (double spinning) versus PRP (single spinning)
Participants	Mean age: 52.1, % Female: 34% Mean disease duration: NR Number of participants: 144 Follow-up: 2, 6 and 12 months <u>Inclusion:</u> Age > NR Duration clinical symptoms : > 4 months Symptomatic OA of the knee, radiological **Kellgren Lawrence** grade 0-IV <u>Baseline values:</u> Kellgren Lawrence grade (N(%)): 0 (cartilage degeneration): PRP: 32(44%) PRGF: 31(43%) I-III (early OA): PRP: 24(33%) PRGF: 30(42%) VI(advanced OA): PRP: 16(22%) PRGF: 11(15%) IKDC score (mean(SD)): PRP: 42.1(13.5) PRGF: 45.0(10.1)
Intervention	<u>Intervention (n=72):</u> 3 PRP (type 2B) intra articular injections (5mL) Interval: 3 weeks <u>Comparison (n=72):</u> 3 PRP (type 4B, PRGF) intra articular injections (5mL) Interval: 3 weeks
Outcomes	<u>Primary outcome(s):</u> IKDC score (0-100) EQ VAS score (0-100) Tegner score (0-10) <u>Secondary outcome(s):</u> Patient satisfaction (%N) Adverse effects
Results	IKDC score 2, 6 and 12 months resp.(mean(SD)): PRP:60.8(16.6), 62.5(19.9), 59.9(20) PRGF: 59(16.2), 61.3(16.3), 61.6(16.2) *PRP vs. PRGF NS at all follow-up* EQ-VAS score: Not reported PRP vs. PRGF: NS Tegner score: Not reported PRP vs. PRGF: NS Patient satisfaction: PRP: 80.6% PRGF:76.4% Adverse effects: No short or long time side effects observed

	Pain (P=0.0005) and swelling (P=0.03) after injection were more frequent in the PRP group with respect to the PRGF group.

Risk of bias (Filardo/Kon/Ruiz 2012)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Hospital visit specified treatment. Comment: Probably not done
Allocation concealment (selection bias)	High risk	Quote: "...treatment allocation was due to the center the patients attended". Comment: Probably not done
Blinding of participants (performance bias)	High risk	Not reported. Comment: Probably not done
Blinding of personnel (performance bias)	High risk	Not reported. Comment: Probably not done
Blinding of outcome assessment (detection bias)	High risk	Not reported. Comment: Probably not done
Incomplete outcome data (attrition bias)	High risk	Number of participants at baseline has been reported. Number of participants at follow-up has not been reported. Exclusions and withdrawals have not been reported.
Selective reporting (reporting bias)	Unclear risk	Pre-specified primary outcomes have been reported. Secondary outcomes (EQ VAS, Tegner score) are incomplete, only significant improvent has been reported. Low risk on primary outcome reporting.
Other bias	Unclear risk	Power analyses have been calculated. (72 patients per treat arm to provide at least 80% power to detect a difference of 7.4 points of the IKDC score at a 5 % level of significance).

Kon 2011	
Study type/Country/Treatment	Prospective, three arm, comparative trial Multicenter, Italy PRP versus Hyaluronic Acid
Participants	Mean age: 52.9, % Female: 45.3% Mean disease duration: NR Number of participants: 150 Follow-up: 2 and 6 months <u>Inclusion:</u> Age: NR Duration clinical symptoms : > 4 months Symptomatic OA of the knee, radiological **Kellgren Lawrence** grade 0-IV <u>Baseline values:</u> Kellgren Lawrence grade (n): 0 PRP: 22 HAHW: 21 HALW: 19 I-III: PRP: 20 HAHW: 19 HALW: 22 IV PRP: 8 HAHW: 10 HALW: 9 IKDC score (mean(SD)): PRP: 41.2(10.9) HAHW: 47.3(13.9) HALW: 44.7(6.6) EQ-VAS score (mean(SD)): PRP: 53.6 (18.3) HAHW:52.2(12.5) HALW: 51.2(7.8)
Intervention	<u>Intervention (n=50):</u> 3 PRP (type 2A) intra articular injections (5mL) Interval: 2 weeks <u>Comparison 1 (n=50):</u> 3 HA intra articular injections (HW) Interval: 2 weeks <u>Comparison 2 (n=50):</u> 3 HA intra articular injections (LW) Interval: 2 weeks
Outcomes	<u>Primary outcome(s):</u> IKDC score (0-100) EQ-VAS score (0-100) <u>Secondary outcome(s):</u> Patient satisfaction (%N) Adverse effects
Results	IKDC score 2 and 6 months resp. (mean(SD)): PRP: 62.7(14.0), 64(18.7) HAHW: 54.8(15.6), 54(16) HALW: 61.7(13.1), 53.8(13.7) *P(6 mos follow up):PRP vs. HAHW 0.005* *P(6 mos follow up): PRP vs. HALW 0.003*

	EQ-VAS score 2 and 6 months resp. (mean(SD)): PRP: 73.0(13.9), 72.3(17.3) HAHW: 63(14.7), 62.4(15.2) HALW: 68.7(13.5), 61.7(14.8) *P(6 mos follow up):PRP vs. HAHW 0.002* *P*(*6 mos follow up*):*PRP vs. HALW 0.001* Patient satisfaction: PRP: 82% HAHW:66% HALW:64% *P=0.04* Adverse effects: No short or long time side effects observed

Risk of bias (Kon 2011)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Hospital visit specified treatment. Comment: Probably not done.
Allocation concealment (selection bias)	High risk	Each center performed only one treatment and so the patient treatment allocation was due to the center the patients attended. Comment: Probably not done.
Blinding of participants (performance bias)	High risk	Not reported. Comment: Probably not done
Blinding of personnel (performance bias)	High risk	Not reported. Comment: Probably not done
Blinding of outcome assessment (detection bias)	High risk	Not reported. Comment: Probably not done
Incomplete outcome data (attrition bias)	High risk	Number of participants at baseline has been reported. Number of participants at follow-up has not been reported. Exclusions and withdrawals have not been reported.
Selective reporting (reporting bias)	Low risk	Pre-specified primary and secondary outcomes have been reported.
Other bias	Unclear risk	Power analysis has been calculated. (50 patients per treat arm to provide at least 80% power to detect a difference of 10 points of the IKDC score at a 5 % level of significance).

Li 2011	
Study type/Country/Treatment	Randomized , two arm, controlled trial Single Center, China PRP versus Hyaluronic Acid
Participants	Mean age:57.9, % Female:56.7% Mean disease duration: > 4 months Number of participants: 30 Follow-up: 3, 4 and 6 months Inclusion: OA on basis of Kellgren Lawrence grade I-IV Baseline values: Kellgren Lawrence grade (n): I PRP: 6 HA: 6 II PRP: 2 HA: 3 III PRP: 4 HA: 3 IV: PRP: 3 HA: 3 IKDC score (mean(SD)): PRP: 55.4(8.8) HA: 57.5(9.4) WOMAC score (mean(SD): Total: PRP: 27.7(13.8) HA: 30.9(13.9) Lequesne index (mean(SD)): PRP: 8.0(3.7) HA: 9.3(2.9)
Intervention	Intervention (n=15): 3 PRP intra articular injections (3.5mL) Interval: 3 weeks Comparison (n=15): 3 HA intra articular injections (2 mL) Interval: 3 weeks
Outcomes	Primary outcome(s): IKDC score (0-100) WOMAC total (0-96) Lequesne index (0-24) Adverse effects
Results	IKDC score 3 and 6 months resp. (mean(SD)): PRP: 71.3(12.5), 76.4(13.5) HA: 70.1(12.5), 63.2(11.9) *P=0.78, P=0.00* WOMAC total score 3 and 6 months (mean(SD)): PRP: 13.3(9.4), 10.7(9.9)

	HA: 13.8(4.7), 20.6(8.3) *P=0.85, P=0.01* Lequesne index 3 and 6 months resp. (mean(SD)): PRP: 4.8(2.4), 3.1(1.0) HA: 4.7(2.0), 6.6(2.1) *P=0.87, P=0.00* Adverse effects (N/Duration(h)(SD)) PRP:12/36.2(25.1) HA:12/34.5(28.4) *P=0.86*

Risk of bias (Li 2011)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No translation available
Allocation concealment (selection bias)	Unclear risk	No translation available
Blinding of participants (performance bias)	Unclear risk	No translation available
Blinding of personnel (performance bias)	Unclear risk	No translation available
Blinding of outcome assessment (detection bias)	Unclear risk	No translation available
Incomplete outcome data (attrition bias)	Unclear risk	No translation available
Selective reporting (reporting bias)	Unclear risk	No translation available
Other bias	Unclear risk	No translation available

Patel 2013	
Study type/Country/Treatment	Randomized, three arm, controlled trial Single Center, India PRP versus Placebo (Saline)
Participants	Mean age: 52.8, % Female: 70.7% Mean disease duration: NR Number Randomized: 78 (156 knees) Follow-up: 6 weeks, 3 and 6 months <u>Inclusion:</u> Age: NR Duration clinical symptoms: NR OA of the knee according ACR criteria, radiological **Ahlbäck** grade I or II <u>Baseline values:</u> Ahlbäck grade (n): I: PRP: 37 2PRP:36 Saline:25 II: PRP 11 2PRP:10 Saline:18 WOMAC score (mean (SD)): Pain: PRP: 10.17(3.82) 2PRP: 10.62(3.73) Saline: 9.04(3.73) Stiffness: PRP: 3.06(2.08) 2PRP:3.5(2.09) Saline:2.70(2.02) Physical function: PRP: 36.12(13.08) 2PRP: 39.10(11.34) Saline: 38.80(12.44) Total: PRP: 49.56(17.83) 2PRP: 53.20(16.18) Saline: 45.54(17.29) VAS pain (mean(SD)): PRP: 4.56(0.61) 2PRP: 4.64(0.56) Saline: 4.57(0.62)
Intervention	<u>Intervention (n=27/52 knees):</u> Single PRP (type 4B) intra articular injection (8mL) <u>Comparison 1 (n=25/50 knees):</u> 2 PRP (type 4B) intra articular injections (8mL) Interval: 3 weeks

	Comparison 2 (n=23/46 knees): Single saline intra articular injection (8mL)
Outcomes	Primary outcome(s): WOMAC Subscale pain (0-20) Secondary outcome(s): WOMAC Subscale stiffness (0-8) WOMAC subscale physical function (0-68) WOMAC total (0-96) VAS pain score (0-10) Patient satisfaction (%N) (satisfied, partly satisfied, not satisfied) Adverse effects
Results	WOMAC subscale and total score 6 weeks, 3 and 6 months resp. (mean): Pain: PRP: 4.26, 3.74, 5.00 2PRP: 4.38, 4.88, 6.18 Saline: 9.48, 10.35, 10.87 *PRP vs. 2PRP: NS* *PRP vs. Saline: P<0.001* *2PRP vs. Saline: P< 0.001* Stiffness: PRP: 2.12, 1.76, 2.10 2PRP: 2.28, 2.00, 1.88 Saline: 2.76, 2.91, 2.76 *PRP vs. 2PRP: NS* *PRP vs. Saline: P<0.001* *2PRP vs. Saline: P< 0.001* Physical function: PRP: 18.98, 16.98, 20.08 2PRP: 18.30, 18.82, 22.40 Saline: 34.54, 37.43, 39.46 *PRP vs. 2PRP: NS* *PRP vs. Saline: P<0.001* *2PRP vs. Saline: P< 0.001* Total: PRP: 25.36, 22.48, 27.18 2PRP: 24.96, 25.70, 30.48 Saline: 46.78, 50.70, 53.09 *PRP vs. 2PRP: NS* *PRP vs. Saline: P<0.001* *2PRP vs. Saline: P< 0.001* VAS pain score 6 months (mean(SD)): PRP: 2.16(1.5) 2PRP: 2.54(1.7) Saline: 4.61(0.7) *PRP vs. 2PRP: P=0.410* *PRP vs. Saline: P<0.001* *2PRP vs. Saline: <0.001* Patient satisfaction 6 months: PRP :67.3% 2PRP:64.0% Saline: 4.3% Adverse effects (%): Related to infiltration PRP: 22.2% 2PRP: 44% Saline: 0% Significant difference between PRP groups and Saline

Risk of bias (Patel 2013)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The participants were randomly divided by computer-derived random charts into 3 groups". Comment: Probably done
Allocation concealment (selection bias)	Unclear risk	Not reported. Comment: Insufficient information to permit judgement of "low risk" or "high risk"
Blinding of participants (performance bias)	Unclear risk	Quote: "...double blinded" - "...participants were blinded" Comment: Different dosage used in comparison group 2 makes it difficult to blind these patients. Insufficient information about blinding of participants.
Blinding of personnel (performance bias)	High risk	Not reported. Reporting "double blinded" means participants and observers. Comment: Probably not done
Blinding of outcome assessment (detection bias)	Low risk	Quote: "...by a blinded observer" Comment: Blinding is reported and probably done.
Incomplete outcome data (attrition bias)	High risk	Number of allocated and analyzed participants has been reported. Reasons for missing data are reported. 1/27 was excluded from Intervention group as he underwent TKR elsewhere. 3/26 from comparison 2 group (placebo) did not received allocated intervention, refused for treatment.
Selective reporting (reporting bias)	Unclear risk	Pre-specified primary and secondary outcomes have been reported in the pre-specified way. Since no measure of dispersion (i.e. standard deviation, standard error) for primary outcome was reported, this outcome was not included in the RevMan analysis.

Other bias	Unclear risk	Power analysis has been calculated. (21 patients per treat arm to provide at least 80% power to detect a difference of 1.5 points in the VAS pain score at a 5 %level of significance).

Say 2013	
Study type/Country/Treatment	Prospective, two arm, comparative trial Single Center, Turkey PRP versus Hyaluronic Acid
Participants	Mean age: 55.7, % Female: 87.8% Mean disease duration: NR Number of participants: 90 Follow-up: 3 and 6 months <u>Inclusion:</u> Age: NR Duration clinical symptoms : > 3 months Symptomatic OA of the knee, radiological **Kellgren Lawrence** grade I-III <u>Baseline values:</u> Kellgren Lawrence grade (N): I PRP: 1 HA: 1 II PRP: 17 HA: 15 III PRP: 27 HA: 29 KOOS score (mean(SD)): PRP: 46(16.2) HA:43.8(8.6) VAS pain score (mean(SD)): PRP: 7.3(1.6) HA: 7(1.3)
Intervention	<u>Intervention (n=45):</u> Single PRP (type 4B) intra articular injection (2.5mL) <u>Comparison (n=45):</u> 3 HA intra articular injections (LW) Interval: 3 weeks
Outcomes	<u>Primary outcome(s):</u> KOOS total score (0-100) VAS pain score (0-10) <u>Secondary outcome(s):</u> Patient satisfaction Adverse effects
Results	KOOS total score 3 and 6 months resp. (mean(SD)): PRP: 76.9(7.5), 84.4(6.2) HA: 68.6(3.7), 73.2(4.6) *P=0.02, P=0.001*

	VAS pain score 3 and 6 months resp. (mean(SD)): PRP:2.3(1.6), 1.7(1.4) HA: 4.1(1.3), 3(1) *P=0.001, P=0.001* Patient satisfaction: Not Reported Adverse effects: Not reported

Risk of bias (Say 2013)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "...patients were separated into two groups of ..." Comment: Probably not done.
Allocation concealment (selection bias)	High risk	Allocation concealment probably not done
Blinding of participants (performance bias)	High risk	Different dosage used in both treatment groups. Comment: Probably not done
Blinding of personnel (performance bias)	High risk	Not reported. Comment: Blinding of personnel is probably not done
Blinding of outcome assessment (detection bias)	High risk	Not reported. Comment: Blinding of outcome assessment is probably not done
Incomplete outcome data (attrition bias)	Unclear risk	Number of participants at baseline and follow up has been reported. Exclusions and withdrawals have not been reported.
Selective reporting (reporting bias)	Unclear risk	Pre-specified primary outcomes have been reported, secondary outcome have not been reported.
Other bias	High risk	No power analysis has been reported.

Spaková 2012	
Study type/Country/Treatment	Prospective, two arm, comparative trial Single Center, Slovakia PRP versus Hyaluronic Acid
Participants	Mean age: 53,0 % Female: 46.7% Mean disease duration: NR Number of participants: 120 Follow-up: 3 and 6 months Inclusion: Age: NR Duration clinical symptoms : > 12 months Symptomatic OA of the knee , radiological **Kellgren Lawrence** grade I-III Baseline values: Kellgren Lawrence grade (n): I PRP: 2 HA: 2 II PRP: 39 HA: 37 III PRP: 19 HA: 21 WOMAC score (mean(SD): PRP: 38.76(16.5) HA: 43.21(13.7) NRS pain score (mean(SD)): PRP: 5.27(1.87) HA: 6.02(1.77)
Intervention	Intervention (n=60): 3 PRP (type 1B) intra articular injections Interval: weekly Comparison (n=60): 3 HA intra articular injections Interval: weekly
Outcomes	Primary outcome(s): WOMAC total score (0-96) NRS pain score (0-10) Secondary outcome: Adverse effects
Results	WOMAC total score 3 and 6 months resp.(mean(SD)): PRP: 14.35(14.18), 18.85(14.09) HA: 26.17(17.47), 30.90(16.57)

		P<0.01, P<0.01 NRS pain score 3 and 6 months resp. (mean(SD)): PRP:2.06(2.02), 2.69(1.86) HA: 3.98(2.27), 4.3(2.07) *P<0.01, P<0.01* Adverse effects: No short or long time side effects observed

Risk of bias (Spaková 2012)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients were randomly divided into two groups. The first group of 60 patients..." Comment: Probably not done
Allocation concealment (selection bias)	High risk	No allocation concealment has been reported. Comment: Probably not done
Blinding of participants (performance bias)	High risk	No blinding of participants has been reported. Comment: Probably not done
Blinding of personnel (performance bias)	High risk	No blinding of personnel has been reported. Comment: Probably not done
Blinding of outcome assessment (detection bias)	High risk	No blinding of outcome assessment has been reported. Comment: Probably not done
Incomplete outcome data (attrition bias)	High risk	Number of participants at baseline and follow up has been reported only at 3 months of follow up. Exclusions and withdrawals have not been reported.
Selective reporting (reporting bias)	Low risk	All pre-specified primary and secondary outcomes have been reported.
Other bias	High risk	No power analysis has been reported.

Sánchez 2012	
Study type/Country/Treatment	Randomized, two arm, controlled trial Multicenter, Spain PRGF-Endoret versus Hyaluronic Acid
Participants	Mean age: 59.7, % Female: 51.7% Mean disease duration: NR Number Randomized: 176 Follow-up: 1, 2 and 6 months <u>Inclusion:</u> Age: between 40 and 72 y Duration clinical symptoms : NR OA of the knee according ACR criteria, radiological **Ahlbäck** grade I- III <u>Baseline values:</u> Ahlbäck grade (n(%) I PRGF: 45(51) HA: 42(49) II PRGF: 32(36) HA: 32(38) III PRGF: 12(13) HA: 11(13) WOMAC score, normalized (mean, SD) Pain: PRGF: 40.4(16) HA: 38.4(5.6) Stiffness: PRGF: 41.8(17.3) HA: 38.5(18.3) Physical function: PRGF: 39.6(16.3) HA: 38.8(17.4) Global: PRGF: 121.8(44.4) HA: 115.6 (45.1) Lequesne index (mean(SD)): PRGF: 9.5(3.0) HA: 9.1(3.2)
Intervention	<u>Intervention (n=89):</u> 3 PRP (type 4B, PRGF) intra articular injections Interval: weekly <u>Comparison (n=87):</u> 3 HA intra articular injections

	Interval: weekly
Outcomes	Primary outcome(s): % of patients having a 50% decrease in the summed WOMAC pain subscale score Secondary outcome(s): Normalized WOMAC total score (0-300) Normalized WOMAC pain score (0-100) Normalized WOMAC stiffness score (0-100) Normalized WOMAC physical function score Lequesne index (0-24) Adverse effects
Results	50% decrease WOMAC pain score 6 months (N(%)): PRGF: 34(38.2) HA: 21(24.1) *P=0.044* Normalized WOMAC total score 6 months (mean(SD)): PRGF:74.0(42.7) HA:78.3(48.1) *P=0.561* Normalized WOMAC Pain score 6 months (mean(SD)): PRGF:24.1(15.5) HA:26.9(15.8) *P=0.265* PRGF:25.2(15.4) HA:25.5(17.9) *P=0.901* PRGF:24.8(15.9) HA:25.9(17.2) *P=0.682* Lequesne index 6 months (mean(SD): PRGF: 5.2(3.4) HA: 5.4(3.3) *P=0.714* Adverse effects: No significant difference (*P=0.811*) between groups and most are not related to the type of treatment.

Risk of bias (Sánchez 2012)		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "... the treatment assigned by randomization was delivered. A stratified randomization (1 stratum per center) was carried out". Randomization was carried out by using specific computer software. Comment: Probably done
Allocation concealment (selection bias)	Low risk	Quote: " ...keeping that relation in a sealed envelope". „This envelope was not opened until the moment before applying the treatment". Comment: Probably done

Blinding of participants (performance bias)	Low risk	No difference between the intervention and comparison group regarding dosage. The application area was hidden from view and blood was drawn for all patients. Comment: probably done
Blinding of personnel (performance bias)	High risk	Not reported. Reporting "double blinded" means participants and observers. Comment: Probably not done
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Response was assessed by researchers not involved in the application of treatment. The data report forms did not make any references to the treatment applied". Comment: Probably done
Incomplete outcome data (attrition bias)	Low risk	Analysis: Intention to treat. Number of patients randomized and analyzed was reported. The exclusion and withdrawal percentages did not differ significantly between groups
Selective reporting (reporting bias)	Low risk	All pre-specified primary and secondary outcomes have been reported in the pre-specified way.
Other bias	Low risk	Power analysis has been calculated. (110 patients per treat arm to provide at least 90% power to detect differences in the proportions of patients achieving 50% pain improvement with PRGF vs HA at a 5 % level of significance).

Vaquerizo 2013	
Study type/Country/Treatment	Randomized, two arm, controlled trial Multicenter, Spain PRGF-Endoret versus Durolane Hyaluronic Acid
Participants	Mean age: 63.6, % Female: 60.4 Mean disease duration: NR Number Randomized: 96 Follow-up: 24 and 48 weeks <u>Inclusion:</u> Age: > 50 y Clinical symptoms: > 6 months OA of the knee according ACR criteria, radiological **Kellgren Lawrence** grade II to IV <u>Baseline values:</u> Kellgren Lawrence grade n(%): II PRGF: 14(29.2) HA: 18 (37.5) III PRGF: 26(54.2) HA: 21(43.8) IV PRGF: 8(16.7) HA: 9(18.8) WOMAC score (mean (SD)): Pain PRGF: 9.6(2.5) HA: 10.2(3.5) Stiffness: PRGF: 3.7(1.7) HA: 4.0(2.0) Physical function: PRGF: 32.6(9.9) HA: 36.7(13.7) Total: PRGF: 45.9(12.7) HA: 50.8(18.4) Lequesne Index: (mean(SD)) PRGF: 12.8(3.8) HA: 13.1(3.8)
Intervention	<u>Intervention (n=48):</u>

	3 PRP (type 4B, PRGF) intra articular injection (8mL) Interval: 2 weeks <u>Comparison (n=48)</u> Single HA (Durolane) intra-articular injection
Outcomes	<u>Primary outcome(s):</u> % of patients having a 30% decrease and 50% decrease in the summed WOMAC subscale scores –pain, stiffness and physical function and Lequesne index <u>Secondary outcome(s):</u> WOMAC subscales pain (0-20), stiffness (0-8), physical function (0-68) and total score (0-96) Lequesne scale (0-24) Adverse effects
Results	30% decrease WOMAC score 24 and 48 weeks resp. (N(%)): Pain: PRGF: 40(83), 28(58.3) HA: 7(17), 5(11.9) *P<0.001, P<0.001* Stiffness: PRGF: 24(52), 24(52.2) HA: 11(27), 5(12.2) *P<0.02, P<0.001* Physical function: PRGF:29(60), 26(54.2) HA: 7(17), 7(16.7) *P<0.001, P<0.001* 50% decrease WOMAC score (N(%)) Pain: PRGF: 26(54), 15(31) HA: 5(11), 1(2) *P<0.001, P<0.001* Stiffness: PRGF: 16(35), 16(33 HA: 7(16), 2(5) *P=0.035, P=0.001* Physical function: PRGF: 19(40), 15(31) HA: 5(11), 0(0) *P=0.001, P=0.001* 30% decrease Lequesne (N(%)): PRGF: 35(73), 23(47.9) HA: 7(17), 1(2.4) *P<0.001, P<0.001* 50% decrease Lequesne (N(%)): PRGF: 14(29), 9(19) HA: 2(4), 1(2) *P=0.002, P=0.017* WOMAC total score 24 and 48 weeks resp. (mean(SD)): PRGF: 27.2(15.1), 30.8(15.5) HA: 50.4(23.2), 54.2(19.2) *P*<0.001, *P*<0.001 Lequesne index 24 and 48 weeks resp. (mean(SD)): PRGF: 5.2(3.4), 8.9(3.7) HA: 5.4(3.3), 14.4 (3.8) *P=<0.001, P=0.001*

		Adverse effects: PRGF: 14.6% HA: 18.8% PRGF vs. HA: *P=.610* Withdrawals: PRGF: 0 HA: 1

Risk of bias (Vaquerizo 2013)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A simple randomization was carried out" Comment: Probably done. The use of specific software for randomization as a random component in the sequence generation process was described.
Allocation concealment (selection bias)	Low risk	Quote: "..keeping that relation in a sealed envelope" Comment: Probably done. The envelope was not opened until the moment before the treatment was applied.
Blinding of participants (performance bias)	High risk	Different dosage used in both treatment groups makes it impossible to blind the patients. Comment: Probably not done
Blinding of personnel (performance bias)	High risk	Different dosage, preparation of PRGF at each treatment visit and insufficient information about blinding personnel makes blinding of personnel dubious. Comment: Probably not done
Blinding of outcome assessment (detection bias)	Low risk	Quote: „The response was assessed by researchers not involved in the application of treatment. In the data report forms, there was no reference to the treatment that had been applied. The evaluation of the patients´ status and disease progression was performed by physicians in a blinded way".

		Comment: Probably done
Incomplete outcome data (attrition bias)	High risk	Number of allocated and analyzed participants was reported. 6 months follow up: No missing data in both groups. 12 months follow up: No missing in intervention group and 6/48 missing from comparison group Comment: Differ across groups at longer term outcome (> 6 months)
Selective reporting (reporting bias)	Low risk	All pre-specified primary and secondary outcomes have been reported in the pre-specified way.
Other bias	Unclear risk	Power analysis has been calculated. (48 patients per group to provide at least 80% power to detect differences in the WOMAC pain scale superior to 1.2 for PGRF vs HA at a 5 %level of significance taking into account 10% losses). Per protocol analysis

Characteristics of excluded studies

Study	Reason for exclusion
Yang 2008	Intervention of interest: Autologous conditioned serum (Orthokine)
Baltzer 2009	Intervention of interest: Autologous conditioned serum (Orthokine)
Klatt 2011	Point/counterpoint discussion: Total knee arthroplasty versus PRP
ClinicalTrail.gov identifier NCT00728611	Study has been completed. Unfortunately, no additional information was available.

Characteristics of ongoing studies

Laver 2011	
Study name	Platelet Rich Plasma (PRP) as a Treatment for Knee Osteoarthritis - A Randomized-Double-Blind Trail
Methods	Randomized, two arm, controlled trial
Participants	Patients with knee osteoarthritis, age between 40 and 75 years old. Inclusion: diagnosed osteoarthritis of the knee more than 1 year, no knee deformation. Exclusion: mental or physical disabilities, pregnancy, deformities of the knee.
Intervention	Biological: Platelet rich plasma (PRGF) Drug: Hyaluronic acid (HA)
Outcomes	Primary outcome: Improvement in pain, function, quality of life and activity level in OA of the knee

	1-2 years
Starting date	September 2011
Contact information	Lior Laver tel: +972-50-8464466 laver17@gmail.com
Notes	Study not yet open for participant recruitment
ClinicalTrails.gov identifier	NCT01270412

Nayana 2011	
Study name	A prospective, Randomized, Double-blinded, Clinical Trail, Comparing Platelet-rich Plasma Intra articular Knee Injections Versus Corticosteroid Intra-articular Knee injections for Knee Osteoarthritis
Methods	Randomized, two arm, controlled trial
Participants	Patients with knee osteoarthritis, age between 40 and 80 years old. Inclusion: degenerative OA of the knee confirmed radiologically, degenerative osteoarthritis of the knee replacement candidate, walking ability in patients with or without external support and baseline in pain VAS greater than 60 Exclusion: neoplastic disease, immunosuppressive states, received IA injections of steroids, anesthetic and/or HA in the last 3 months, patients who have undergone arthroscopic surgery on the last 3 months, patients with involvement of bone metabolism except osteoporosis, fibromyalgia, liver disease, deficit coagulation, thrombocytopenia, anticoagulant treatment
Intervention	Biological: platelet-rich plasma Drug: Corticosteroid
Outcomes	Primary outcome: Visual analogue pain scale (VAS) one moment after treatment. Secondary outcome: Visual analogue pain scale (VAS) one, three and six months after treatment, adverse events, scale of the SF 36 quality of life one, three and six months after treatment.
Starting date	July 2011
Contact information	Nayana Joshi tel: 0034934893481 njoshijubert@gmail.com
Notes	Study is ongoing, but not recruiting participants
ClinicalTrails.gov identifier	NCT01381081