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# Optimal Surgical Treatment Method for Anterior Cruciate Ligament Rupture: Results from a Network Meta-Analysis

**Authors' Contribution:**

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

CDEF 1 **Yudi Wu**  
BCD 2 **Yajia Li**  
BC 2 **Jia Guo**  
BC 3,4 **Qiangxiang Li**  
BCD 3,5 **Jianhuang Wu**  
ABCDEF 5 **Ziqin Cao**  
ABCDEF 6 **Yulin Song**

1 Nanchang University Queen Mary School, Nanchang, Jiangxi, PR China  
2 Department of Dermatology, Xiangya Hospital, Central South University, Changsha, Hunan, PR China  
3 National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, Hunan, PR China  
4 National Clinical Research Center for Geriatric Disorders of Xiangya Hospital, Central South University (Sub-center of Ningxia), Yinchuan, Ningxia, PR China  
5 Department of Spine Surgery and Orthopaedics, Xiangya Hospital, Central South University, Changsha, Hunan, PR China  
6 Department of Orthopaedics, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, PR China

**Corresponding Authors:**

Yulin Song, e-mail: syltong@126.com, Ziqin Cao, e-mail: xyeyzqincao@csu.edu.cn

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**Conflict of interest:**

None declared

**Background:**

Previous studies have shown that primary repair (PR) and anterior cruciate ligament reconstruction (ACLR) can effectively treat ACL injuries. Our study aimed to compare different treatments of ACL tears, including autograft, allograft, hybrid graft ACLR, and PR, by assessing clinical outcomes and adverse events.

**Material/Methods:**

PubMed, Cochrane Library, Embase, and CNKI databases were searched and a frequentist-framework network meta-analysis was used.

**Results:**

Overall, PR with augmentation was superior to ACLR only for activity recovery (WMD 0.28 95%CI [0.07 to 0.49]), and there was no significant difference shown between PR without augmentation and ACLR. ACLR with irradiated allograft was a poor option for the treatment of ACL rupture, showing the weakest subjective evaluations and functional outcomes and worst safety profile. PR with or without augmentation provided fairly good postoperative efficacy results and produced less postoperative knee laxity than irradiated allograft ACLR (PR: standardized mean difference [SMD] -1.27 [-1.80 to -0.74]; ACLR: SMD -1.36 [-1.88 to -0.83]). However, PR without augmentation showed a high failure rate compared with autograft ACLR (autograft vs PR without augmentation: risk ratio 0.29 [0.10 to 0.85]).

**Conclusions:**

For surgical treatment of ACL rupture, irradiated allograft ACLR had the worst efficacy and safety and is not recommended. PR may be an ideal treatment method in terms of efficacy but it is related to a significantly higher revision risk if without augmentation. Autograft ACLR may be the preferred method currently available for most patients requiring surgical treatment of ACL rupture.

Registered in PROSPERO (CRD42021225778).

**Keywords:**

**Anterior Cruciate Ligament • Anterior Cruciate Ligament Injuries • Anterior Cruciate Ligament Reconstruction**

**Abbreviations:**

**ACL** – anterior cruciate ligament; **ACLR** – ACL reconstruction; **Autograft** – autograft reconstruction; **CHS** – cohort study; **Hybrid** – hybrid graft reconstruction; **IKDC** – International Knee Documentation Committee; **irAllograft** – allograft with irradiation reconstruction; **KOOS** – Knee Injury and Osteoarthritis Score; **nirAllograft** – allograft without irradiation reconstruction; **NOS** – Newcastle-Ottawa Scale; **nwaRepair** – primary repair without augmentation; **PR** – primary repair; **PRISMA-NMA** – Systematic Reviews and Meta-Analyses for Network Meta-analysis; **RCTs** – randomized controlled trials; **RR** – risk ratio; **SMD** – standardized mean difference; **SUCRA** – surface under the cumulative ranking; **waRepair** – primary repair with augmentation; **WMD** – weighted mean difference; **WOMAC** – Western Ontario and McMaster Universities Arthritis Index

Full-text PDF:

<https://www.medscimonit.com/abstract/index/idArt/937118>



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## Background

Anterior cruciate ligament (ACL) injury is a common knee sports injury that often occurs during high-intensity physical exercise [1]. In addition, it is estimated that 1 in every 120 people of working age have ACL injuries [2]. The ACL is the main structure limiting the tibia's anterior translation and internal rotation. In most cases, a tear or rupture is caused by excessive pivoting or anterior or valgus movement of the proximal tibia, rather than by direct contact [3].

Before the popularization of arthroscopy, the most common surgical option for treating ACL tears was open primary repair (PR). This provided good short-term outcomes but was associated with long-term problems, including high re-rupture and reoperation rates and postoperative complications [4-6]. These problems together with the development of ACL reconstruction (ACLR) led to a decline in the use of PR. However, with advances in arthroscopic technology, preoperative imaging, and surgical techniques, such as suture anchors and suture augmentation, PR is once again a viable option for ACL repair. More recent studies showed that compared with ACLR, PR had a comparable failure rate [7] and provided an earlier return of range of motion [8,9], most likely resulting from the less invasive nature of the surgery. It also has no donor site morbidity because of the lack of graft collection.

ACLR is regarded as the most accepted standard surgical therapy for active and symptomatic patients with ACL injury. There are 3 main approaches for ACLR based on graft type: autograft, allograft, and hybrid graft (combination of autograft and allograft) [10,11]. Autograft is the oldest and most common ACLR technique used because it has some unique advantages, such as the lowest rejection reaction and relatively high mechanical reliability [12]. In contrast, allograft ACLR causes no donor site morbidity but has a lower graft survival rate and a higher postoperative infection rate [3,13,14]. Hybrid graft ACLR provides a graft of suitable size, with clinical results comparable to that of autografts, and offers an alternative to autograft ACLR, especially for those patients whose tendons are damaged or undersized at harvest [15].

Despite several comparative studies, it is still unclear which is the best surgical method for ACL rupture. Previous meta-analyses have compared clinical outcomes of the different types of ACLR. The study by Li et al [16] showed the performance of the autograft and hybrid graft was similar in graft failure, graft diameter, and reoperation ratio. Meanwhile, the study by Sun et al [17] also revealed no difference in long-term outcomes and failure risk after cruciate ligament reconstruction with either autograft or synthetics; however, autografts were found to be inferior to synthetics in dealing with restoring knee joint stability and were associated with more complications. Several clinical

trials have reported functional outcome scores and revision rates after PR [18-20]. However, there are few randomized controlled trials (RCTs) or systematic reviews that have compared the efficacy and safety of the various types of ACLR and PR.

In summary, we speculated that PR could also bring ideal therapeutic effects and potentially be superior to ACLR. This network meta-analysis was aimed to compare the clinical outcomes and adverse events of autograft, allograft, hybrid graft ACLR, and PR in the surgical treatment of ACL tears. This study was not focused on professional athletes.

## Material and Methods

### Data Sources and Searches

This study was registered in the PRESPERO (registration no. CRD42021225778). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-analysis (PRISMA-NMA) guidelines [21] were strictly followed throughout this study. MeSH keywords combined with a free words retrieval strategy was adopted to search the PubMed/Medline, Cochrane Library, Embase, and CNKI databases from January 1995 to July 2022. The specific query for PubMed/Medline was as follows: ((anterior cruciate ligament injury) OR (anterior cruciate ligament injury) OR (anterior cruciate ligament rupture) OR (anterior cruciate ligament tear) OR (ACL injury) OR (ACL rupture) OR (ACL tear) AND (ACL[MeSH Terms]) OR (anterior cruciate ligament[MeSH Terms]) AND (reconstruction) OR (transplantation) OR (repair) OR (primary repair) OR (suture)). The specific query for Cochrane Library was as follows: "MeSH descriptor.[Anterior Cruciate Ligament Injuries] explode all trees" OR "MeSH descriptor.[Anterior Cruciate Ligament] explode all trees" OR "(ACL injury): ti,ab,kw OR (ACL rupture): ti,ab,kw OR (ACL tear): ti,ab,kw" OR "(anterior cruciate ligament injury): ti,ab,kw OR (anterior cruciate ligament rupture): ti,ab,kw OR (anterior cruciate ligament tear): ti,ab,kw" AND "(reconstruction): ti,ab,kw OR (transplantation): ti,ab,kw OR (repair): t,ab,kw OR (suture): ti,ab,kw OR (primary suture): ti,ab,kw". The specific query for Embase was as follows: ("anterior cruciate ligament injury": ti, ab, kw OR "anterior cruciate ligament rupture": ti, ab, kw OR "anterior cruciate ligament tear": ti, ab, kw OR "ACL injury": ti, ab, kw OR "ACL rupture": ti, ab, kw OR "ACL tear": ti, ab, kw) AND ("reconstruction": ti, ab, kw OR "transplantation": ti, ab, kw OR "repair": ti, ab, kw OR "primary repair": ti, ab, kw OR "suture": ti, ab, kw)). The specific query for CNKI was as follows [in Chinese]: ((主题: 前交叉韧带损伤 + 前交叉韧带断裂 + 前交叉韧带撕裂(精确) OR (主题: 前交叉韧带重建 + 前交叉韧带移植 + 前交叉韧带修复 + 前交叉韧带缝合(精确))). A reference lists of identified articles were further reviewed to find additional eligible studies. No language restriction was set for the publication selection.

## Study Selection

A research protocol under the PICO principle was pre-drafted as follows: (1) Population: patients underwent ACL rupture and planned surgery; (2) intervention: surgical treatment for ACL rupture; (3) comparison: different surgical methods for ACL rupture; and (4) outcomes: postoperative subjective feelings of patients, recovery of postoperative activity, functional improvement, joint laxity, and treatment failure.

Based on the PICO protocol, studies that fulfilled all of the following criteria were included: (1) Patients underwent ACLR or PR to treat ACL tears; (2) study compared 2 or more different surgery methods; (3) study used an RCT design, non-RCT design, or cohort design (CHS); and (4) the following outcomes were reported: subjective evaluation improvement, functional rehabilitation, improvement of activity, postoperative knee laxity, or the incidence of revision surgery.

The exclusion criteria were as follows: (1) The study included the revision of ACL rupture; (2) low-quality of study; (3) studies with a non-prospective design; and (4) animal or vitro basic studies, observational studies, reviews (including systematic review and meta-analyses), meeting abstracts, letters, and those with inaccessible original study data.

We would also try to contact the corresponding authors for the studies lacking complete information, and those for which no response was received were excluded. The source of data was also requested from the corresponding author for the studies presenting outcomes only in figures but not in numeric datasets, and when no response was received, 2 authors would independently try to obtain the data by the measurements shown in the figures. When there was still no access to the raw data after the above attempts, the study was excluded.

## Data Extraction and Quality Assessment

The study quality was assessed by 2 authors independently. Quality of method and bias risk for RCTs was assessed by using the Cochrane risk bias assessment tools [22]. The Newcastle-Ottawa Scale (NOS) [23] was used for the evaluation of the method quality of CHSs and non-RCTs. Three main domains – the selection of the study groups, comparability among different groups, and ascertainment of either the exposure or outcome of interest – were evaluated with a score from 0 to 9. All disputes were resolved during a discussion between the 2 authors. The following information was extracted from each included study: first author, year of publication, number of participants, average age, sex ratio, traumatic mechanism, method of surgery, average follow-up time, study design, and outcome.

## Outcome Measures

For the evaluation and comparison of the efficacy and safety of the surgical methods, the following outcome measurements were selected: postoperative subjective feelings of patients, recovery of postoperative activity, functional improvement, and safety endpoints.

For measuring postoperative function status, no restriction was placed on the types of questionnaires used in functional evaluation. The Lequesne Index was the first choice, followed by other functional measurement scales, including the Knee Injury and Osteoarthritis Score (KOOS) and the Western Ontario and McMaster Universities Arthritis Index (WOMAC). The standardized mean difference (SMD) was used to incorporate these different scales into the same network.

By using the Subjective International Knee Documentation Committee (IKDC) score, postoperative subjective feelings were assessed. The recovery of postoperative activity was assessed with the Tenger score. The weighted mean difference (WMD) with 95% confidence intervals (CIs) was calculated for the IKDC and Tenger scores.

The safety endpoints were joint laxity and treatment failure. The degree of laxity was the relaxation difference comparing the operated knee with the non-operated knee measured by the KT-1000 or KT-2000 scale. The SMD with a 95%CI was calculated for the laxity scores. Failure was defined as all patients who had a re-tear or recurrent laxity, regardless of whether or not they underwent revision surgery. The risk ratio (RR) and 95%CI were used for the measurement of the relative failure rate.

## Statistical Analysis

Frequentist method network meta-analysis was conducted in Stata/MP (version 14.0, Stata Corp, College Station, TX, USA) with a random-effects model. The proportional variance-covariance matrix data were pooled by multivariate meta-regression with the random effect; restricted maximum-likelihood was applied in the evaluation of model fit [24].

By using global inconsistency tests and node-split tests, the inconsistencies were evaluated, and the consistency model was used under the condition of no existing significant inconsistency, or else the sensitivity analysis would be applied for the inconsistency source identification. Funnel plots and Egger's tests were used to assess potential publication bias for each endpoint, and by using the trim and filling method, endpoints with underlying asymmetric funnel plots were estimated for whether significant publication bias existed or not [25]. We also ranked the relative efficacy and safety of different surgical methods through the surface under the cumulative

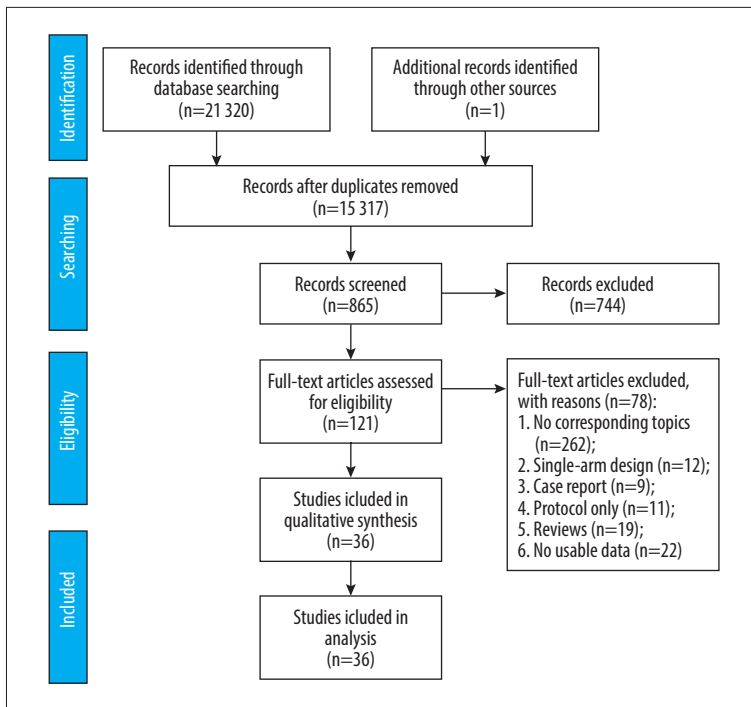


Figure 1. PRISMA Flow Diagram.

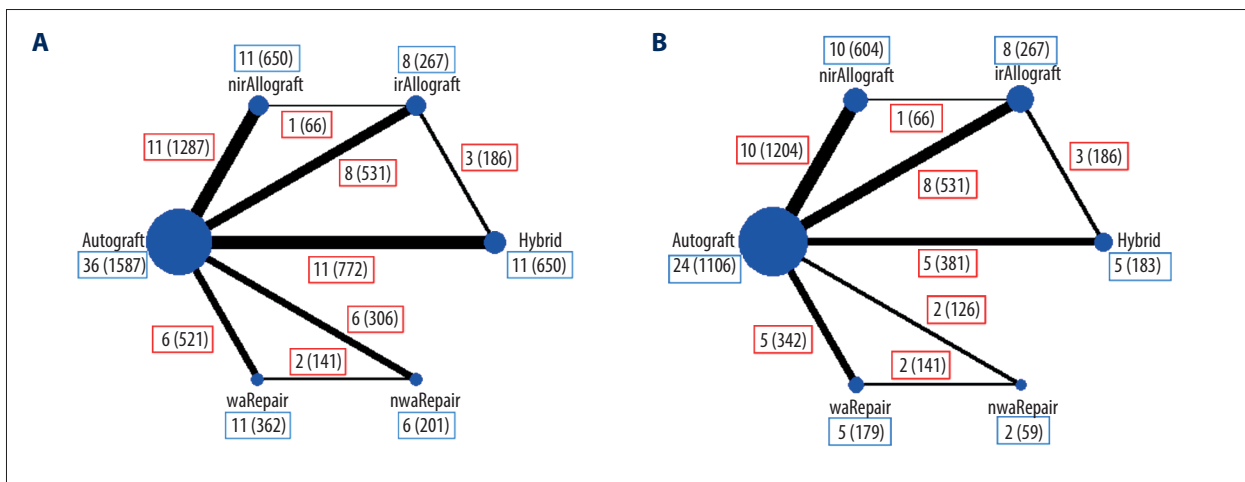


Figure 2. Structure of network formed by interventions. The lines between treatment nodes indicate the direct comparisons made with evidences, the size of nodes indicate the number of participants involved in each treatment. Numbers (n/n) with a blue frame near the line indicate ‘number of trials/number of participants’ of the related treatment group, numbers (n/n) with a red frame near the line indicate ‘number of trials/number of participants’ of the related comparisons. (A) Main network meta-analysis. (B) Subgroup analysis. (Made with Stata/MP, version 14.0, manufacturer Stata Corp.).

ranking (SUCRA) values [26], and cluster-ranking plots for the optimal choice.

A direct pairwise meta-analysis was conducted to compare the relative efficacy of PR (with or without augmentation) with autograft using RevMan (Review Manager, Version 5.3, Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The heterogeneity across studies was tested by the Q and I<sup>2</sup> statistics. The fixed-effects model was

preferred, but if there was significant heterogeneity ( $P < 0.05$  or  $I^2 > 50\%$ ), the random-effects model was applied.

Although CHSs and non-RCTs can provide important data, study designs introduce unmanageable confounding factors and potential bias. Because of this, a subgroup analysis that included only RCTs was performed to reconfirm the results obtained by the main network meta-analysis. A network plot was used to graphically summarize the evidence incorporated into this

**Table 1.** Baseline characteristics of included studies.

Author	No.	Year	Number of patients	Mean age	Male/Female	Traumatic mechanism
Gagliardi AG et al [31]	1	2019	179	15.48	87/92	Low-energy trauma 164 High-energy trauma 0
Meunier A et al [39]	2	2007	100	21.44	68/32	NR
Hoogeslag RAG et al [19]	3	2019	48	21.50	138/20	NR
Achtnich A et al [27]	4	2016	40	31.80	NR	NR
Bottoni CR et al [29]	5	2015	97	29.05	84/13	Low-energy trauma 98 High-energy trauma 2
Sporshiem AN et al [44]	6	2019	150	29.00	36/28	NR
Sun K et al [46]	7	2009	99	30.55	70/29	Low-energy trauma 88 High-energy trauma 10
Murray MM et al [41]	8	2020	100	17.00	44/56	NR
Schliemann B et al [43]	9	2017	60	28.65	23/37	NR
Wang HD et al [52]	10	2017	57	32.70	19/38	NR
Murray MM et al [40]	11	2016	20	24.35	6/14	Low-energy trauma 19 High-energy trauma 1
Edgar CM et al [30]	12	2008	83	29.22	46/37	NR
Li J et al [37]	13	2016	80	31.37	50/30	NR
Kösters C et al [34]	14	2020	85	28.16	56/29	NR
Sun K et al [60]	15	2009	156	32.26	124/32	Low-energy trauma 154 High-energy trauma 2
Sun K et al [47]	16	2009	65	24.89	17/48	Low-energy trauma 61 High-energy trauma 4
Sun K et al [48]	17	2011	67	30.60	15/52	Low-energy trauma 61 High-energy trauma 4
Sun K et al [58]	18	2011	186	30.42	149/37	Low-energy trauma 61 High-energy trauma 8
Jia YH et al [33]	19	2015	106	29.50	54/52	NR
Tian S et al [50]	20	2016	121	30.21	96/25	Low-energy trauma 113 High-energy trauma 8
Tian S et al [49]	21	2016	83	28.89	66/17	Low-energy trauma 77 High-energy trauma 6
Yoo SH et al [54]	22	2015	132	27.09	120/12	NR
Tian S et al [51]	23	2010	69	31.25	56/13	Low-energy trauma 60 High-energy trauma 9
Bi HY et al [28]	24	2013	86	32.00	60/26	NR
Sun K et al [45]	25	2004	53	32.34	44/9	NR
Gorschewsky O et al [32]	26	2002	201	32.97	150/51	NR
Li J et al [38]	27	2015	95	30.62	50/45	Low-energy trauma 87 High-energy trauma 8
Murray MM et al [18]	28	2019	20	24.35	6/14	Low-energy trauma 19 High-energy trauma 1



Table 1 continued. Baseline characteristics of included studies.

Author	No.	Year	Number of patients	Mean age	Male/Female	Traumatic mechanism
Darnley JE et al [56]	29	2016	54	20.90	34/20	NR
Zheng X et al [55]	30	2019	97	30.77	69/28	NR
Kraeutler MJ et al [35]	31	2017	148	33.78	NR	NR
Pennock AT et al [42]	32	2016	40	15.65	15/25	NR
Leo BM et al [36]	33	2016	95	27.20	60/35	NR
Xu H et al [59]	34	2018	76	35.66	52/24	Low-energy trauma 67 High-energy trauma 9
Burrus MT et al [57]	35	2015	58	26.90	20/38	NR
Xu H et al [53]	36	2017	68	33.90	43/25	NR

Author	Surgery method	Mean follow-up (months)	Study design	Control intervention I	Control intervention II	Control intervention III
Gagliardi AG et al [31]	Arthroscopy	36.0	Cohort study	Autograft	Repair with augmentation	/
Meunier A et al [39]	Arthroscopy	180.0	Randomized clinical trial	Repair with augmentation	Repair without augmentation	Autograft
Hoogeslag RAG et al [19]	Arthroscopy	24.0	Randomized clinical trial	Repair with augmentation	Autograft	/
Achtnich A et al [27]	Arthroscopy	28.0	Non-randomized clinical trial	Repair without augmentation	Autograft	/
Bottoni CR et al [29]	Arthroscopy	120.0	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Sporshem AN et al [44]	Arthroscopy	360.0	Randomized clinical trial	Repair without augmentation	Repair with augmentation	Autograft
Sun K et al [46]	Arthroscopy	31.0	Randomized clinical trial	Autograft	Non-irradiated allograft	Irradiated allograft
Murray MM et al [41]	Arthroscopy	24.0	Randomized clinical trial	Repair without augmentation	Autograft	/
Schliemann B et al [43]	Arthroscopy	12.0	Randomized clinical trial	Repair with augmentation	Autograft	/
Wang HD et al [52]	Arthroscopy	36.0	Cohort study	Hybrid	Autograft	/
Murray MM et al [40]	Arthroscopy	3.0	Cohort study	Repair without augmentation	Autograft	/
Edgar CM et al [30]	Arthroscopy	50.0	Cohort study	Autograft	Non-irradiated allograft	/
Li J et al [37]	Arthroscopy	67.2	Randomized clinical trial	Autograft	Irradiated allograft	Hybrid
Kösters C et al [34]	Arthroscopy	24.0	Randomized clinical trial	Repair with augmentation	Autograft	/
Sun K et al [60]	Arthroscopy	67.2	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Sun K et al [47]	Arthroscopy	31.0	Randomized clinical trial	Autograft	Irradiated allograft	/

**Table 1 continued.** Baseline characteristics of included studies.

Author	Surgery method	Mean follow-up (months)	Study design	Control intervention I	Control intervention II	Control intervention III
Sun K et al [48]	Arthroscopy	42.2	Randomized clinical trial	Autograft	Irradiated allograft	/
Sun K et al [58]	Arthroscopy	93.0	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Jia YH et al [33]	Arthroscopy	81.0	Randomized clinical trial	Non-irradiated allograft	Autograft	/
Tian S et al [50]	Arthroscopy	55.2	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Tian S et al [49]	Arthroscopy	82.8	Randomized clinical trial	Autograft	Irradiated allograft	/
Yoo SH et al [54]	Arthroscopy	33.6	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Tian S et al [51]	Arthroscopy	38.5	Randomized clinical trial	Autograft	Irradiated allograft	/
Bi HY et al [28]	Arthroscopy	38.5	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Sun K et al [45]	Arthroscopy	19.0	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Gorschewsky O et al [32]	Arthroscopy	24.0	Randomized clinical trial	Autograft	Non-irradiated allograft	/
Li J et al [38]	Arthroscopy	71.2	Randomized clinical trial	Autograft	Irradiated allograft	Hybrid
Murray MM et al [18]	Arthroscopy	24.0	Cohort study	Repair without augmentation	Autograft	/
Darnley JE et al [56]	Arthroscopy	24.0	Cohort study	Autograft	Hybrid	/
Zheng X et al [55]	Arthroscopy	20.1	Randomized clinical trial	Autograft	Hybrid	Irradiated allograft
Kraeutler MJ et al [35]	Arthroscopy	50.1	Randomized clinical trial	Autograft	Hybrid	/
Pennock AT et al [42]	Arthroscopy	24.0	Non-randomized clinical trial	Hybrid	Autograft	/
Leo BM et al [36]	Arthroscopy	24.0	Non-randomized clinical trial	Autograft	Hybrid	/
Xu H et al [59]	Arthroscopy	27.0	Cohort study	Autograft	Hybrid	/
Burrus MT et al [57]	Arthroscopy	46.2	Non-randomized clinical trial	Hybrid	Autograft	/
Xu H et al [53]	Arthroscopy	24.0	Non-randomized clinical trial	Autograft	Hybrid	/

**Table 2.** Methodological quality and risk of bias evaluation of randomized controlled studies.

Author	No.	1. Sequence generation	2. Allocation concealment	3. Blinding	4. Incomplete outcome data	5. Selective outcome reporting	6. Other source of bias
Meunier A et al [39]	2	H	U	U	L	L	L
Hoogeslag RAG et al [19]	3	L	U	U	L	L	L
Bottoni CR et al [29]	5	L	H	L	L	L	L
Sporsheim AN et al [44]	6	L	H	L	L	L	L
Sun K et al [46]	7	L	H	U	L	L	L
Murray MM et al [41]	8	L	H	U	L	L	L
Schliemann B et al [43]	9	L	U	L	L	L	L
Li J et al [37]	13	L	U	U	L	L	L
Kösters C et al [34]	14	L	L	U	L	L	L
Sun K et al [60]	15	L	U	U	L	L	L
Sun K et al [47]	16	L	U	U	L	L	L
Sun K et al [48]	17	L	U	H	L	L	L
Sun K et al [58]	18	L	U	H	L	L	L
Jia YH et al [33]	19	L	L	H	L	L	L
Tian S et al [50]	20	L	H	H	L	L	L
Tian S et al [49]	21	L	H	H	L	L	L
Yoo SH et al [54]	22	L	L	L	L	L	U
Tian S et al [51]	23	L	U	U	L	L	U
Bi HY et al [28]	24	L	H	H	L	L	L
Sun K et al [45]	25	L	H	H	L	L	L
Gorschewsky O et al [32]	26	L	L	U	L	L	L
Li J et al [38]	27	L	U	U	L	L	L
Zheng X et al [55]	30	L	H	H	L	L	L
Kraeutler MJ et al [35]	31	L	H	H	L	L	L

L – low risk of bias; U – unclear risk of bias; H – high risk of bias.

network meta-analysis, in which the lines between treatment nodes indicated the direct comparisons made within the evidence and the size of nodes indicated the number of population involving in each treatment.

When the 95%CI did not cover 1 for RR or 0 for SMD and WMD, it was considered significant for differences between treatments.  $P < 0.05$  was considered statistically significant.

## Results

### Literature Selection

Thirty-six studies [27-62] were identified through systematic screening (Figure 1). Six different surgical methods were identified and analyzed: autograft (Autograft), allograft with irradiation (irAllograft), allograft without irradiation (nirAllograft), hybrid graft (Hybrid), PR with augmentation (waRepair), and PR without augmentation (nwaRepair). The irAllograft group was chosen as the standard control group



**Table 3.** Methodological quality and risk of bias evaluation of non-randomized control and cohort design studies.

Author	No.	Selection			Comparability		Outcome		
		Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Gagliardi AG et al [31]	1	1	1	1	0	2	1	1	1
Achnich A et al [27]	4	1	1	1	1	1	1	1	1
Wang HD et al [52]	10	1	1	1	1	2	1	1	1
Murray MM et al [40]	11	1	1	1	1	2	1	0	0
Edgar CM et al [30]	12	1	1	1	1	2	1	1	1
Murray MM et al [18]	28	1	1	1	1	2	1	1	1
Darnley JE et al [56]	29	1	1	1	1	1	1	1	1
Pennock AT et al [42]	32	1	1	1	1	1	0	1	1
Leo BM et al [36]	33	1	1	1	1	2	0	1	1
Xu H et al [59]	34	1	1	1	1	2	1	1	1
Burrus MT et al [57]	35	1	1	1	1	2	0	1	1
Xu H et al [53]	36	1	1	1	1	1	1	1	1

because in the pre-analysis it had the worst performance for efficacy and safety.

### Study Characteristics

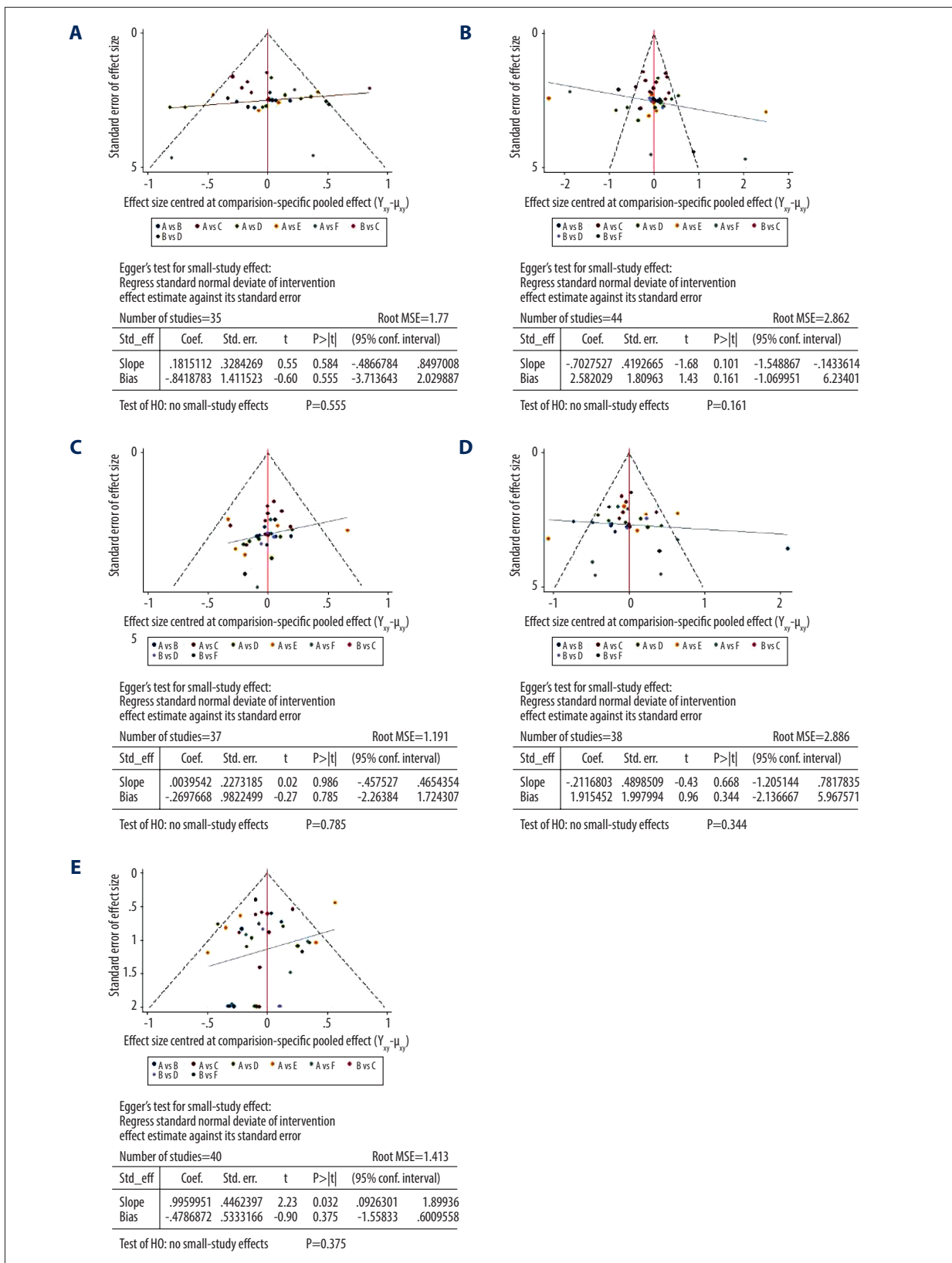
The network plot for main and subgroup results is presented in **Figure 2**. The main network included 24 RCTs, 5 non-RCTs, and 7 CHs, and a total of 3231 patients. A gap of evidence was found between the Hybrid and nwaRepair groups in the main and subgroup networks. A total of 1587, 267, 650, 362, 201, 164 patients were included in the Autograft, irAllograft, nirAllograft, Hybrid, waRepair, and nwaRepair groups, respectively, for the main network, and 1106, 267, 183, 179, and 59 patients were included in the Autograft, irAllograft, nirAllograft, Hybrid, waRepair, and nwaRepair groups for the subgroup network. The average age was 28.12±5.04 (years, mean±SD), and the proportion of male patients was 64% (range 30-87%) (**Table 1**).

The quality and bias-risk assessments of all studies are presented in **Tables 2 and 3**. Two main sources of bias were found. Considering the specificity of the surgical intervention in this study, blinding participants and surgeons was almost impossible; meanwhile, it was also difficult to conceal the allocations. It caused a relatively high and inevitable risk of performance bias. The funnel plots and Egger's tests did not indicate publication bias in any network (**Figure 3**). Cluster-rank plots are presented in **Figure 4**. The league plots, which showed the relative effects between different groups, are presented in **Tables 4-8**.

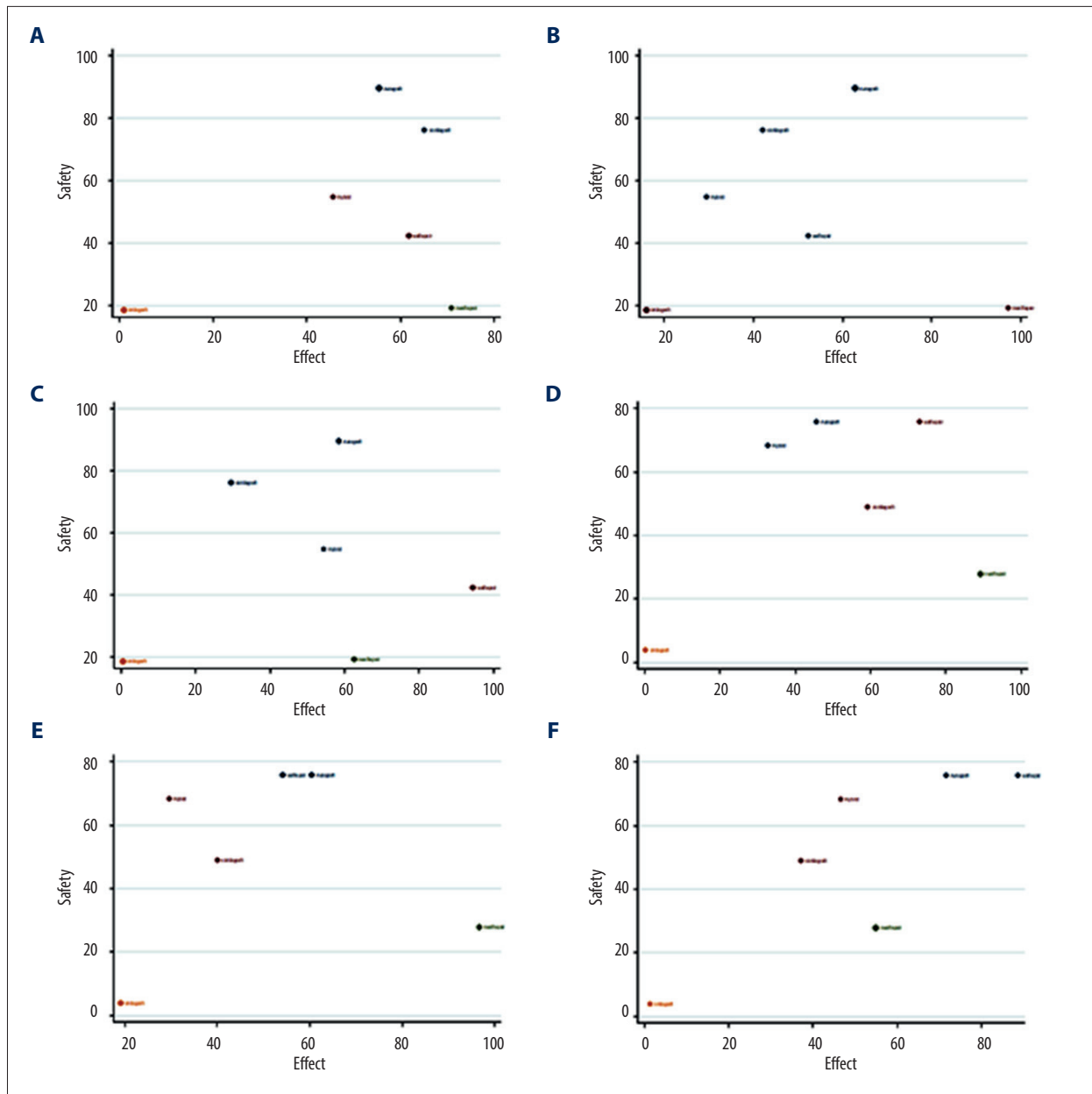
### Network Meta-Analysis

#### Subjective Evaluation Improvement

There were 28 trials with 2403 patients included in the final analysis. No inconsistency was detected and the consistency model was used.



**Figure 3.** Publication bias and Egger's test for main networks. (A) Subjective improvement. (B) Functional improvement. (C) Activity recovery. (D) Postoperative laxity. (E) Failure rate.



**Figure 4.** Cluster-rank plots. (A) The cluster-rank plot of subjective improvement and failure rate from main network analyses. (B) The cluster-rank plot of functional improvement and failure rate from main network analyses. (C) The cluster-rank plot of activity recovery and failure rate from main network analyses. (D) The cluster-rank plot of subjective improvement and failure rate from subgroup analyses. (E) The cluster-rank plot of functional improvement and failure rate from subgroup analyses. (F) The cluster-rank plot of activity recovery and failure rate from subgroup analyses. (The cluster-rank value is the product of the abscissa and ordinate of each treatment.)

The SUCRA results showed that the nwaRepair group had the highest postoperative subjective evaluation improvement (SUCRA=70.9%), followed by nirAllograft (SUCRA=65.2%) and waRepair (SUCRA=61.8%), while the lowest was irAllograft (SUCRA=1.0%). Paradoxically, all groups except nwaRepair (WMD 4.77, 95% CI [-0.23 to 9.78]), were significantly superior to irAllograft. The interpretation of the results should be done cautiously.

#### Functional Improvement

A total of 32 trials with 2976 patients were included in this network. No significant inconsistency was detected and the consistency model was used.

**Table 4.** The league plots of subjective improvement. Main network analysis (red) and subgroup analysis (blue). (From the top left to the bottom right, higher comparator vs lower comparator, WMD with 95% CI).

nwRepair	-2.53 (-9.40, 4.34)	-3.58 (-9.92, 2.76)	-4.10 (-10.17, 1.97)	-4.72 (-11.06, 1.62)	-7.93 (-14.26, -1.59)
0.76 (-4.76, 6.28)	waRepair	-1.05 (-4.70, 2.60)	-1.57 (-4.78, 1.64)	-2.19 (-5.89, 1.51)	-5.40 (-9.08, -1.72)
0.69 (-4.30, 5.68)	-0.08 (-3.55, 3.40)	nirAllograft	-0.52 (-2.34, 1.31)	-1.14 (-3.70, 1.42)	-4.35 (-6.82, -1.87)
1.01 (-3.63, 5.66)	0.25 (-2.75, 3.26)	0.33 (-1.52, 2.18)	Autograft	-0.62 (-2.47, 1.23)	-3.83 (-5.64, -2.01)
1.33 (-3.55, 6.20)	0.56 (-2.75, 3.88)	0.64 (-1.68, 2.96)	0.31 (-1.20, 1.82)	Hybrid	-3.21 (-5.38, -1.04)
4.77 (-0.23, 9.78)	4.01 (0.49, 7.53)	4.09 (1.56, 6.62)	3.76 (1.88, 5.64)	3.45 (1.34, 5.56)	irAllograft

**Table 5.** The league plots of functional improvement. Main network analysis (red) and subgroup analysis (blue). (From the top left to the bottom right, higher comparator vs lower comparator, SMD with 95% CI).

nwaRepair	-0.95 (-2.05, 0.16)	-0.95 (-2.05, 0.15)	-1.12 (-2.33, 0.09)	-1.25 (-2.54, 0.05)	-1.35 (-2.58, -0.11)
0.76 (-0.09, 1.60)	Autograft	-0.01 (-0.74, 0.72)	-0.18 (-0.67, 0.32)	-0.30 (-0.98, 0.38)	-0.40 (-0.95, 0.15)
0.80 (-0.09, 1.69)	0.05 (-0.54, 0.63)	waRepair	-0.17 (-1.05, 0.71)	-0.29 (-1.29, 0.71)	-0.40 (-1.31, 0.52)
0.90 (-0.04, 1.84)	0.14 (-0.28, 0.56)	0.10 (-0.62, 0.82)	nirAllograft	-0.13 (-0.96, 0.71)	-0.23 (-0.94, 0.49)
1.01 (0.06, 1.96)	0.25 (-0.19, 0.70)	0.21 (-0.53, 0.94)	0.11 (-0.50, 0.72)	Hybrid	-0.10 (-0.85, 0.65)
1.14 (0.17, 2.12)	0.39 (-0.09, 0.87)	0.34 (-0.42, 1.10)	0.25 (-0.37, 0.87)	0.14 (-0.45, 0.72)	irAllograft

**Table 6.** The league plots of activity recovery. Main network analysis (red) and subgroup analysis (blue). (From the top left to the bottom right, higher comparator vs lower comparator, WMD with 95% CI).

waRepair	-0.20 (-0.75, 0.34)	-0.22 (-0.54, 0.11)	-0.30 (-0.73, 0.12)	-0.38 (-0.76, -0.01)	-0.77 (-1.18, -0.36)
0.23 (-0.31, 0.78)	nwaRepair	-0.02 (-0.58, 0.55)	-0.10 (-0.74, 0.53)	-0.18 (-0.78, 0.41)	-0.57 (-1.19, 0.05)
0.30 (0.01, 0.60)	0.07 (-0.49, 0.63)	Autograft	-0.09 (-0.36, 0.19)	-0.17 (-0.34, 0.01)	-0.55 (-0.80, -0.31)
0.31 (-0.06, 0.69)	0.08 (-0.53, 0.68)	0.01 (-0.22, 0.23)	Hybrid	-0.08 (-0.40, 0.25)	-0.47 (-0.80, -0.13)
0.45 (0.10, 0.79)	0.21 (-0.37, 0.80)	0.14 (-0.02, 0.31)	0.13 (-0.15, 0.41)	nirAllograft	-0.39 (-0.68, -0.09)
0.84 (0.46, 1.23)	0.61 (0.00, 1.22)	0.54 (0.30, 0.78)	0.53 (0.23, 0.84)	0.40 (0.11, 0.69)	irAllograft

**Table 7.** The league plots of postoperative laxity. Main network analysis (red) and subgroup analysis (blue). (From the top left to the bottom right, higher comparator vs lower comparator, SMD with 95% CI).

Autograft	-0.29 (-1.61, 1.04)	0.03 (-0.90, 0.96)	0.31 (-0.31, 0.93)	0.81 (0.07, 1.55)	2.32 (1.74, 2.89)
-0.05 (-0.46, 0.36)	nwaRepair	0.32 (-1.12, 1.75)	0.60 (-0.86, 2.07)	1.10 (-0.42, 2.61)	2.60 (1.15, 4.06)
-0.14 (-0.55, 0.27)	-0.09 (-0.60, 0.43)	waRepair	0.29 (-0.84, 1.41)	0.78 (-0.41, 1.97)	2.29 (1.18, 3.40)
-0.22 (-0.56, 0.12)	-0.17 (-0.70, 0.36)	-0.08 (-0.61, 0.45)	nirAllograft	0.49 (-0.46, 1.45)	2.00 (1.18, 2.82)
-0.33 (-0.70, 0.04)	-0.28 (-0.83, 0.28)	-0.19 (-0.75, 0.36)	-0.11 (-0.61, 0.39)	Hybrid	1.51 (0.73, 2.28)
-1.41 (-1.74, -1.08)	-1.36 (-1.88, -0.83)	-1.27 (-1.80, -0.74)	-1.19 (-1.64, -0.73)	-1.08 (-1.51, -0.65)	irAllograft

**Table 8.** The league plots of failure rate. Main network analysis (red) and subgroup analysis (blue). (From the top left to the bottom right, higher comparator vs lower comparator, RR with 95% CI).

Autograft	1.37 (0.74, 2.52)	1.06 (0.41, 2.72)	0.96 (0.43, 2.14)	1.94 (0.79, 4.78)	3.52 (1.83, 6.76)
0.85 (0.38, 1.91)	nirAllograft	0.77 (0.25, 2.35)	0.70 (0.26, 1.91)	1.42 (0.47, 4.30)	2.58 (1.17, 5.69)
0.60 (0.26, 1.39)	0.70 (0.22, 2.24)	Hybrid	0.91 (0.26, 3.15)	1.84 (0.51, 6.68)	3.33 (1.16, 9.53)
0.47 (0.19, 1.19)	0.56 (0.16, 1.89)	0.79 (0.22, 2.79)	waRepair	2.02 (0.86, 4.71)	3.66 (1.32, 10.13)
0.29 (0.10, 0.85)	0.35 (0.09, 1.32)	0.49 (0.13, 1.92)	0.62 (0.20, 1.98)	nwaRepair	1.81 (0.58, 5.70)
0.30 (0.13, 0.73)	0.36 (0.12, 1.07)	0.51 (0.17, 1.55)	0.64 (0.18, 2.27)	1.03 (0.26, 4.07)	irAllograft

**Table 9.** Detailed results of main network analysis.

Treatment	SMD (95% CI) for subjective improvement	SURCA for subjective improvement, %	SMD (95%CI) for Functional improvement	SURCA for functional improvement, %	SMD (95% CI) for activity improvement
irAllograft	Reference	1.0	Reference	16.0	Reference
Autograft	3.76 (1.88, 5.64)	55.0	0.39 (-0.09, 0.87)	62.9	0.54 (0.30, 0.78)
nirAllograft	4.09 (1.56, 6.62)	65.2	0.25 (-0.37, 0.87)	42.1	0.40 (0.11, 0.69)
Hybrid	3.45 (1.34, 5.56)	45.7	0.14 (-0.45, 0.72)	29.5	0.53 (0.23, 0.84)
waRepair	4.01 (0.49, 7.53)	61.8	0.34 (-0.42, 1.10)	52.3	0.84 (0.46, 1.23)
nwaRepair	4.77 (-0.23, 9.78)	70.9	1.14 (0.17, 2.12)	97.2	0.61 (0.00, 1.22)
Treatment	SURCA for activity improvement, %	SMD (95% CI) for laxity	SURCA for laxity, %	RR (95% CI) for failure	SURCA for failure, %
irAllograft	0.5	Reference	0.0	Reference	18.4
Autograft	58.5	-1.41 (-1.74, -1.08)	84.0	0.30 (0.13, 0.73)	89.5
nirAllograft	29.5	-1.19 (-1.64, -0.73)	47.8	0.36 (0.12, 1.07)	76.0
Hybrid	54.5	-1.08 (-1.51, -0.65)	35.9	0.51 (0.17, 1.55)	54.7
waRepair	94.5	-1.27 (-1.80, -0.74)	60.2	0.64 (0.18, 2.27)	42.4
nwaRepair	62.5	-1.36 (-1.88, -0.83)	72.1	1.03 (0.26, 4.07)	19.1

The nwaRepair group had the highest probability of having the best postoperative functional improvement (SMD 1.14, 95%CI [0.17 to 2.12] SUCRA=97.2%), followed by Autograft (SMD 0.39, 95%CI [-0.09 to 0.87], SUCRA=62.9%) and waRepair (SMD 0.34, 95%CI [-0.42 to 1.10], SUCRA=52.3%), with nirAllograft being the lowest (SUCRA=16.0%). Based on the SMD, only nwaRepair was significantly better than nirAllograft.

#### Activity Recovery

A total of 25 trials with 2330 patients were included in this network. No significant inconsistency was detected, and the consistency model was used. All groups were significantly better than

the nirAllograft group for postoperative activity status. Based on the SUCRA ranking, the best groups for activity recovery were waRepair (WMD 0.84, 95%CI [0.46 to 1.23], SUCRA=94.5%), nwaRepair (WMD 0.61, 95%CI [0.00 to 1.22], SUCRA=62.5%), and Autograft (WMD 0.54, 95%CI [0.30 to 0.78], SUCRA=58.5%).

#### Safety Outcomes

A total of 26 trials (2241 patients) reporting the degree of postoperative knee laxity and 28 trials (2727 patients) reporting the failure rate were assessed in these 2 networks, respectively. No significant inconsistencies were detected, and the consistency model was used for both networks.

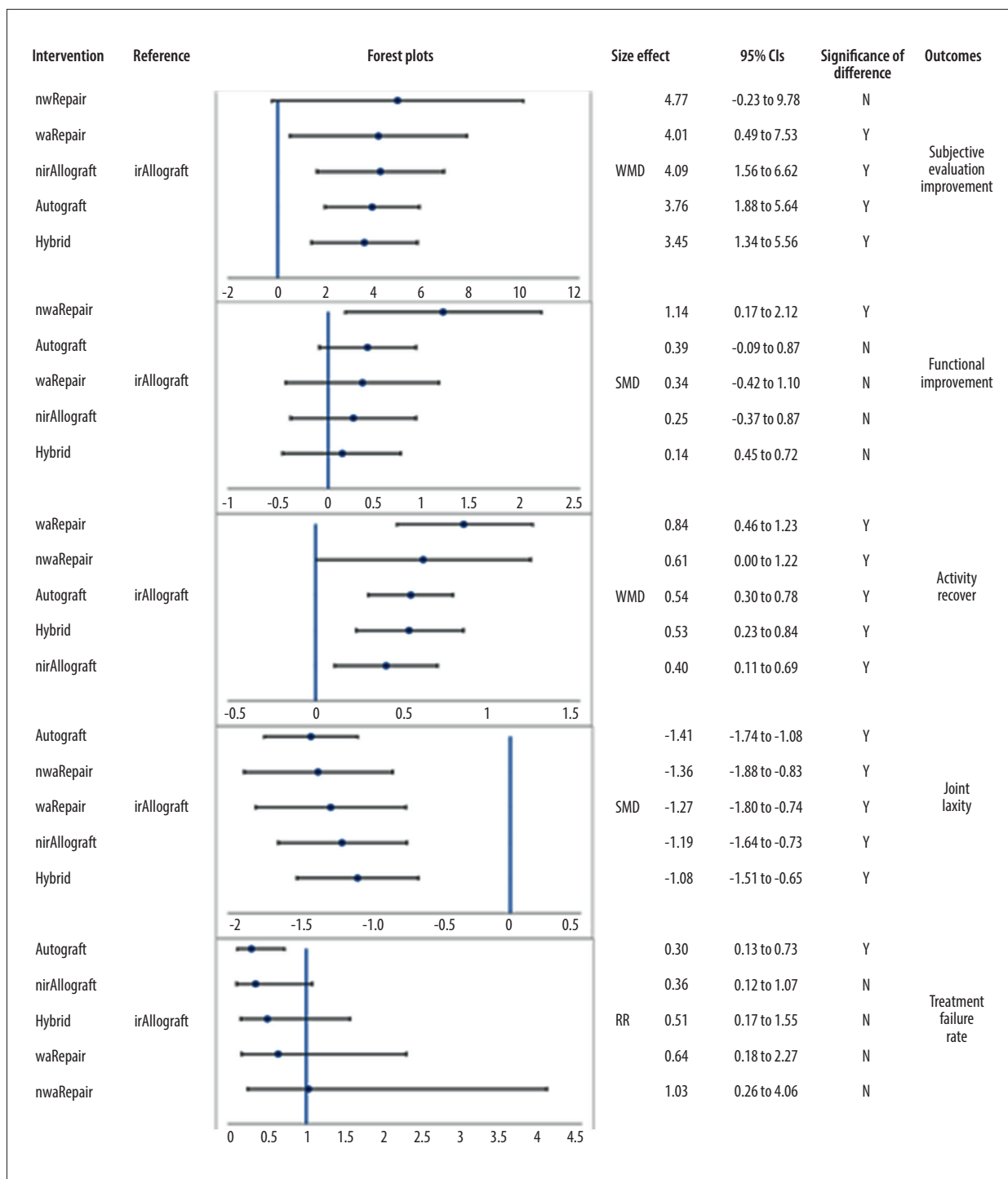


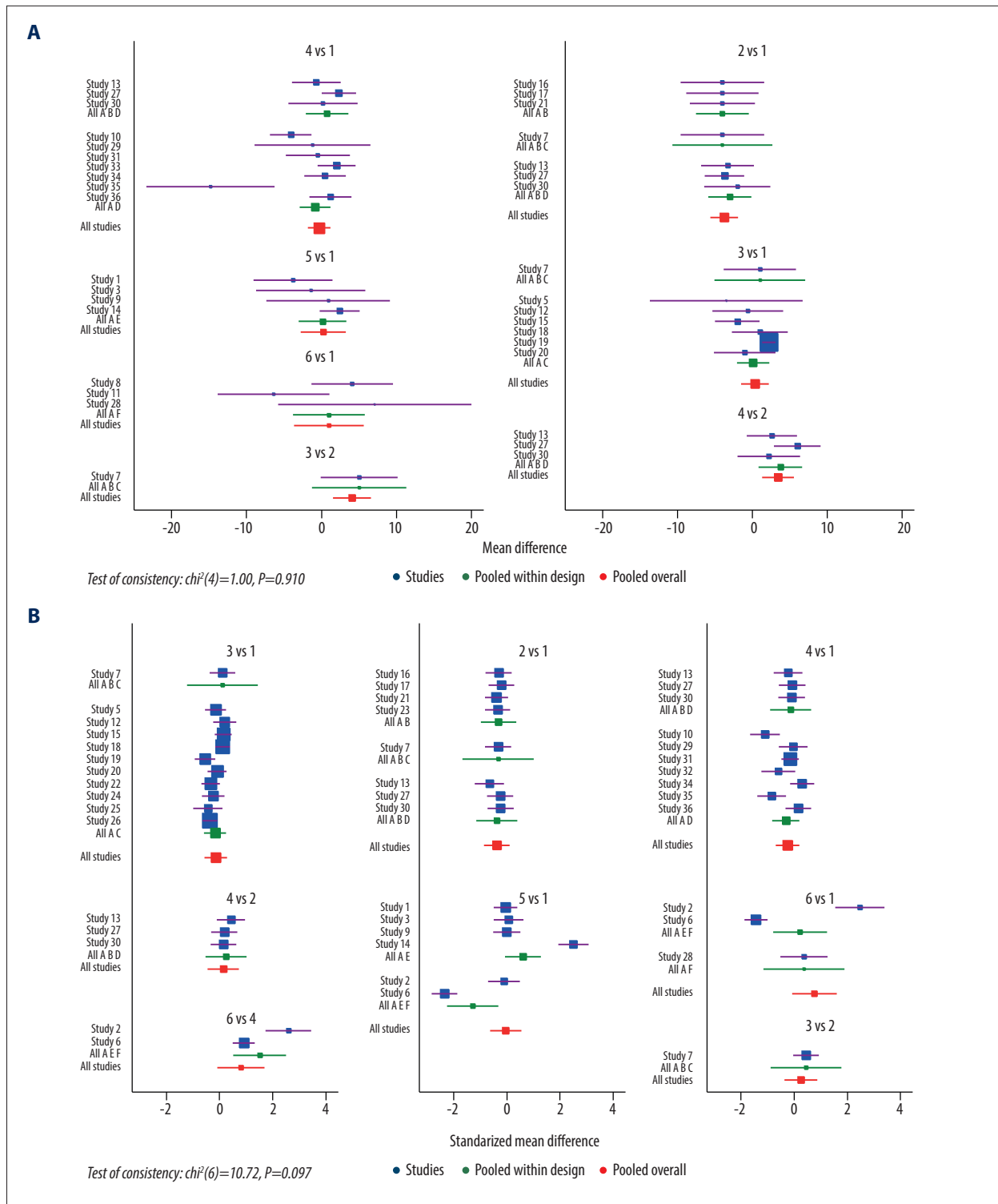
Figure 5. Forest plots of network comparisons of main network meta-analysis (made with Microsoft Excel, version 2019MSO).

All groups had significantly less joint laxity than the irAllograft group. The Autograft group had the lowest degree of laxity (SMD -1.41, 95%CI [-1.74 to -1.08], SUCRA=84.0%), followed by the nwaRepair group (SMD -1.36, 95%CI [-1.88 to -0.83], SUCRA=72.1%) and waRepair group (SMD -1.27, 95%CI [-1.80 to -0.74], SUCRA=60.2%). There was no significant difference

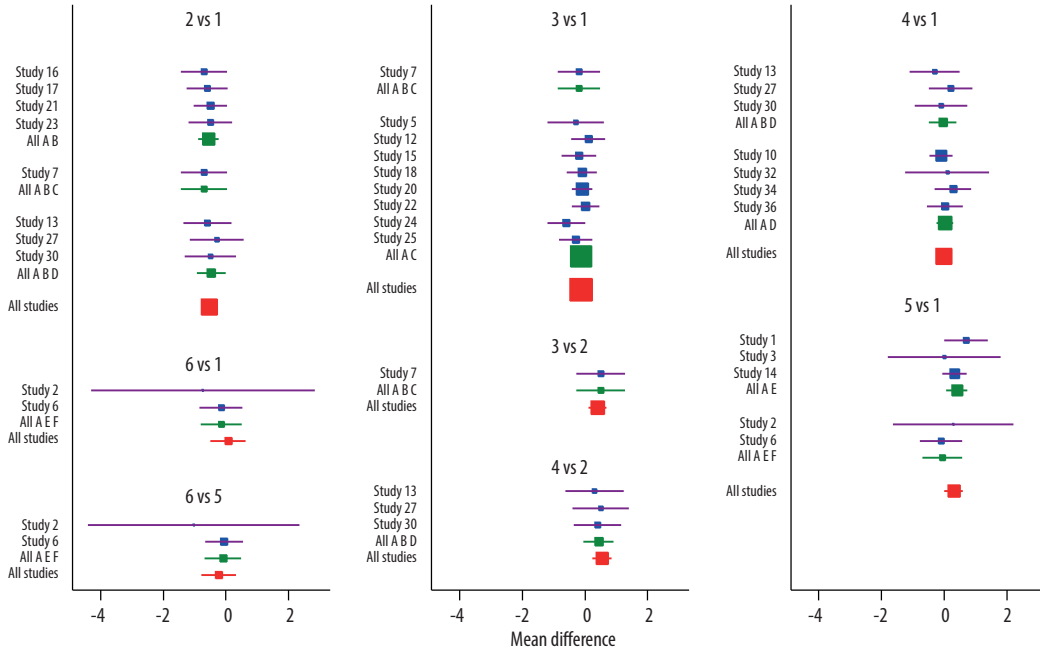
among the Autograft, nwaRepair, repair, nirAllograft, and Hybrid groups.

The Autograft group also had the lowest rate of failure (RR 0.30, 95%CI [0.13 to 0.73], SUCRA=89.5%), followed by nirAllograft (RR 0.36, 95%CI [0.12 to 1.07], SUCRA=76.0%) and





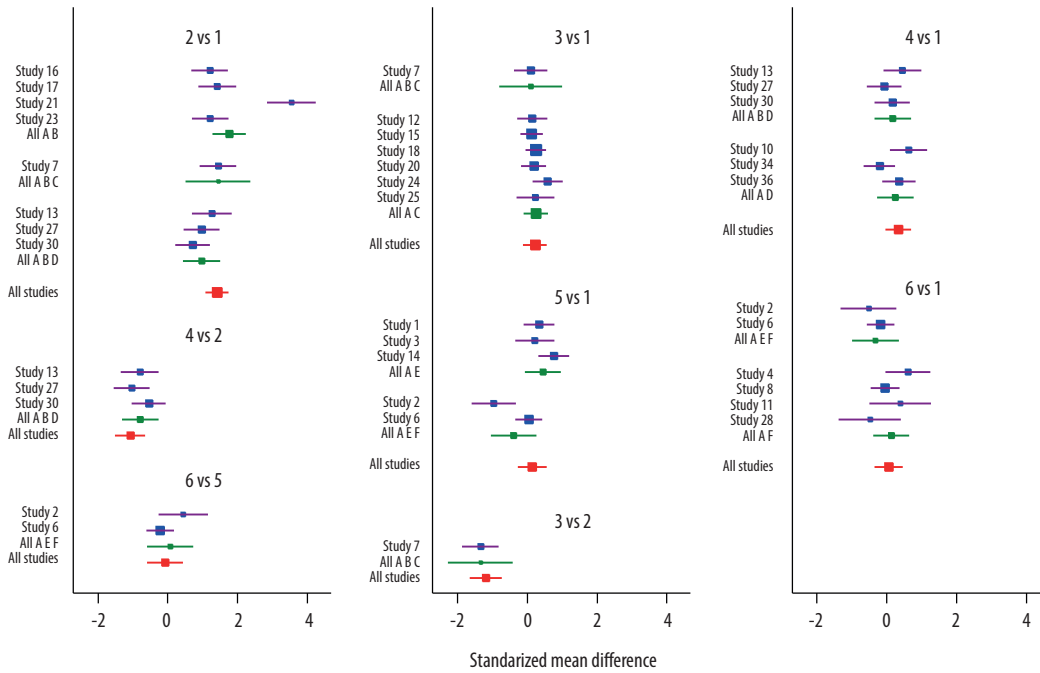
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Test of consistency:  $\chi^2(5)=1.99, P=0.850$

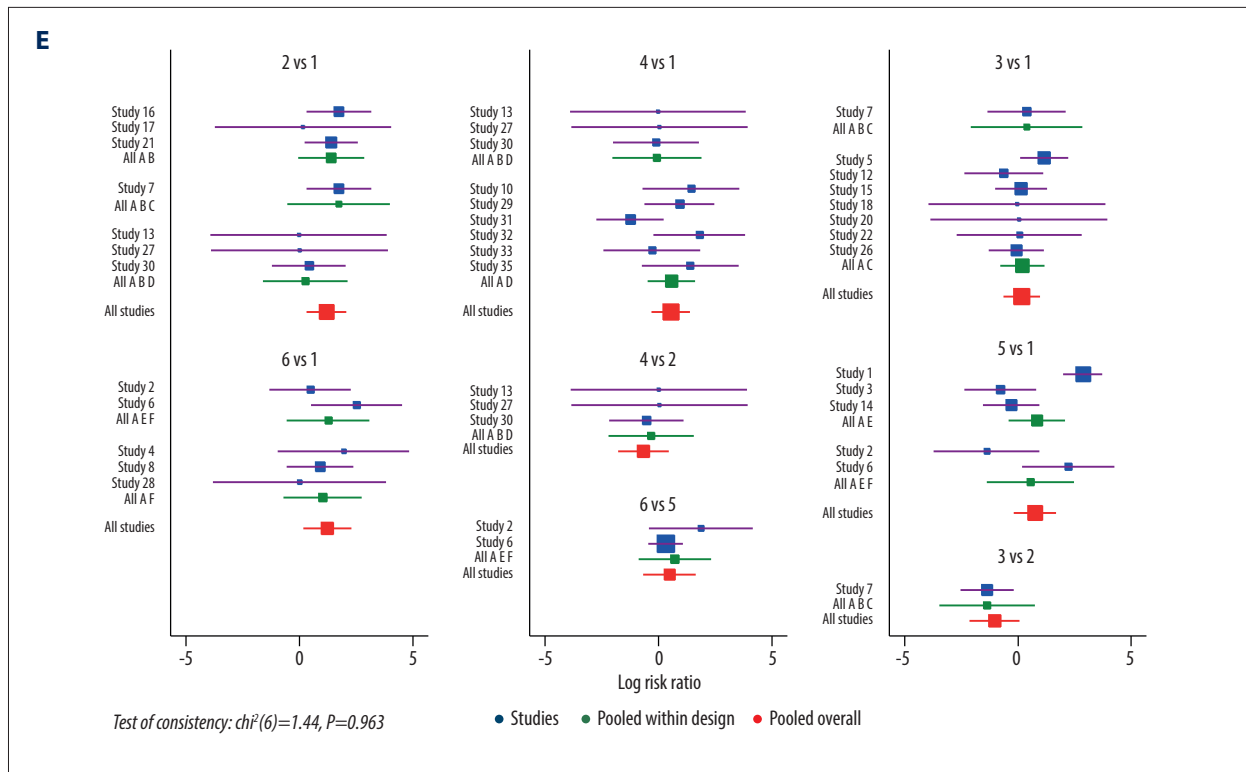
● Studies ● Pooled within design ● Pooled overall

D



Test of consistency:  $\chi^2(6)=9.04, P=0.172$

● Studies ● Pooled within design ● Pooled overall



**Figure 6.** Forest plots incorporated direct comparisons and indirect comparisons of main network meta-analysis. (A) Subjective improvement. (B) Functional improvement. (C) Activity recovery. (D) Postoperative laxity. (E) Failure rate. (A or 1: Autograft; B or 2: Allograft with irradiation; C or 3: Allograft without irradiation; D or 4: Hybrid graft; E or 5: Repair with augmentation; F or 6: Repair without augmentation).

Hybrid graft (RR 0.51, 95%CI [0.17 to 1.55], SUCRA=54.7%). No significant difference was shown between nwaRepair and irAllograft (RR 1.03, 95%CI [0.26 to 4.07], SUCRA=19.1%). It is worth noting that nwaRepair had significantly higher failure rates than Autograft (RR 3.40, 95%CI [1.18 to 9.82]). Detailed SUCRA values of the main network analyses are presented in **Table 9**, and the forest plots are presented in **Figures 5 and 6**.

### Subgroup Analysis of RCTs

All 24 RCTs (2541 patients) were included in this subgroup analysis. No inconsistencies were reported, and the consistency model was used for all outcomes. The only difference from the full analysis was in activity recovery. In the RCTs subgroup analysis, no significant difference was shown between nwaRepair and irAllograft (WMD 0.57, 95%CI [-0.05 to 1.19]) in activity recovery (**Table 10**). Forest plots for results of subgroup analysis are shown in **Figures 7 and 8**.

### Direct Pairwise Meta-Analysis

Direct pairwise comparisons of the postoperative efficacy and safety of PR and ACLR showed significant heterogeneity in all outcomes. Therefore, based on a pre-analysis, the direct

comparisons were separated into 2: waRepair vs ACLR, and nwaRepair vs ACLR (**Tables 11, 12**). Sensitivity analysis was used to minimize heterogeneity.

Direct comparison of waRepair with ACLR showed significant heterogeneity in activity improvement ( $I^2=67.5\%$ ) and consequently, a random-effects model was used for this outcome, while a fixed-effects model was used for other outcomes. The only significant difference between waRepair and ACLR was in activity improvement outcome (WMD 0.28 95%CI [0.07 to 0.49]). Considering the heterogeneity, this result should be viewed with caution.

Direct comparison of nwaRepair with ACLR showed significant heterogeneity in subjective evaluation improvement ( $I^2=58.80\%$ ) and functional improvement ( $I^2=92.30\%$ ), and a random-effects model was used for these 2 outcomes. No significant differences were found between nwaPR and ACLR.

### Discussion

This is the first network meta based on high-quality studies to compare the functional recovery and adverse effects of PR

**Table 10.** Detailed results of subgroup analysis.

Treatment	SMD (95% CI) for subjective improvement	SURCA for subjective improvement, %	SMD (95%CI) for functional improvement	SURCA for functional improvement, %	SMD (95% CI) for activity improvement
irAllograft	Reference	0.3	Reference	19.1	Reference
Autograft	3.83 (2.01, 5.64)	45.6	0.40 (-0.15, 0.95)	60.5	0.55 (0.31, 0.80)
nirAllograft	4.35 (1.87, 6.82)	59.3	0.23 (-0.49, 0.94)	40.0	0.39 (0.09, 0.68)
Hybrid	3.21 (1.04, 5.38)	32.7	0.10 (-0.65, 0.85)	29.6	0.47 (0.13, 0.80)
waRepair	5.40 (1.72, 9.08)	73.0	0.40 (-0.52, 1.31)	54.2	0.77 (0.36, 1.18)
nwaRepair	7.93 (1.59, 14.26)	89.1	1.35 (0.11, 2.58)	96.7	0.57 (-0.05, 1.19)

Treatment	SURCA for activity improvement, %	SMD (95% CI) for laxity	SURCA for laxity, %	RR (95% CI) for failure	SURCA for failure, %
irAllograft	0.9	Reference	0.0	Reference	3.8
Autograft	65.6	-2.32 (-2.89, -1.74)	76.8	0.28 (0.15, 0.55)	75.6
nirAllograft	32.8	-2.00 (-2.82, -1.18)	47.2	0.39 (0.18, 0.86)	48.8
Hybrid	47.9	-1.51 (-2.28, -0.73)	29.9	0.30 (0.10, 0.86)	68.2
waRepair	91.1	-2.29 (-3.40, -1.18)	66.5	0.27 (0.10, 0.76)	75.7
nwaRepair	61.7	-2.60 (-4.06, -1.15)	79.5	0.55 (0.18, 1.73)	27.8

with ACLR in the surgical treatment of ACL rupture. The important observations from this analysis are: (1) waRepair and nwaRepair ranked the best for postoperative efficacy in activity recovery and subjective and functional improvement, while ACLR with irAllograft was a poor option for the surgical treatment of ACL rupture, with the weakest efficacy and the worst safety profile; (2) ACLR with allograft without irradiation produced a similar improvement in subjective evaluation improvement when compared with PR, but less functional improvement and activity recovery; (3) PR produced less postoperative knee laxity than irradiated allograft ACLR but had a higher failure rate than ACLR with Autograft, if without an augmentation. This suggests that PR may have other potentially serious complications that could necessitate revision surgery; (4) ACLR with autograft and hybrid graft yielded good results for efficacy and safety, and both were good choices for surgery; and (5) ACLR with autograft was the safest and most stable surgery method according to the results of postoperative knee laxity and revision rate and the cluster-rank analysis.

In a study by Sun et al [46], autograft and non-irradiated allograft ACLR had comparable outcomes for postoperative symptoms, functional improvement, and activity level, and both had a lower incidence of graft failure than irradiated allograft ACLR. Separately, Curran et al [61] studied the effects of irradiated allograft ACLR and showed that the low dose of irradiation could

weaken the strength and stiffness of the allograft, result in altered graft function, and affect the clinical outcomes of ACLR. Our findings are consistent with these results. In addition, the network meta-analysis by Yang et al [62] compared the long-term outcomes of different grafts in ACLR and recommended double-bundle hamstring autograft as the best choice for its good prognosis. Another study [63] compared different tendon grafts for ACLR and also revealed that autografts (especially quadriceps tendon autografts) rather than artificial ligaments were suitable for primary ACLR because artificial ligaments could increase the risk of knee laxity. Compared with the previous studies, the present study pointed out that PR could be an ideal surgical method in terms of efficacy but is related to a significantly higher revision risk, and autograft ACLR may be the optimal strategy for surgical treatment of ACLR.

In this analysis, the PR technique showed similar and even better clinical outcomes than autograft and hybrid graft ACLR. This most likely resulted from the lack of harvesting of the graft tissue and avoiding donor site complications, leading to better activity recovery and subjective and functional improvements. However, it should be noted that while PR was shown to produce less knee laxity, it was found to lead to a relatively high graft failure rate compared with that of autograft and non-irradiated allograft. One explanation for this is that after PR surgery the scar formed for healing of the ruptured ACL

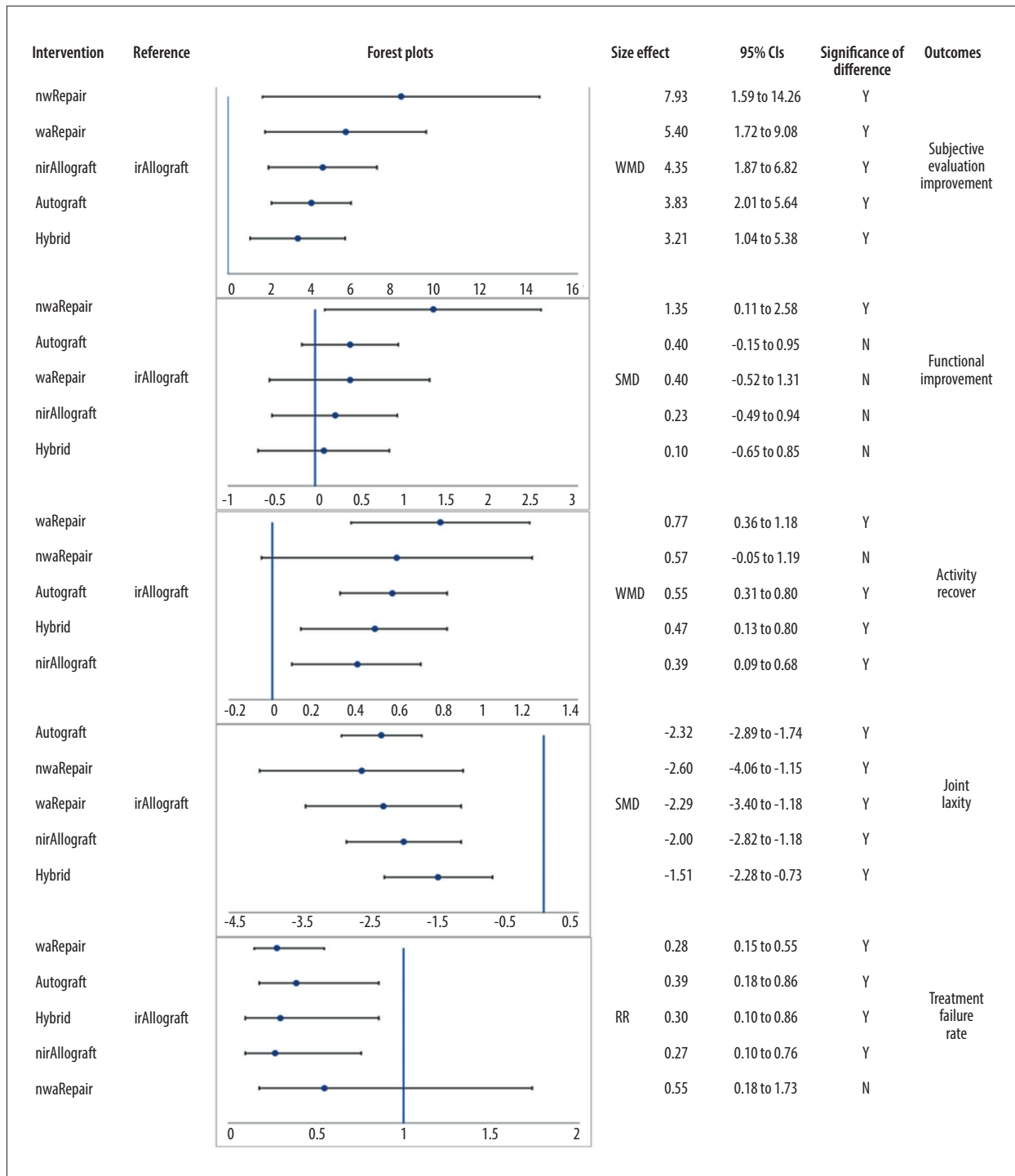
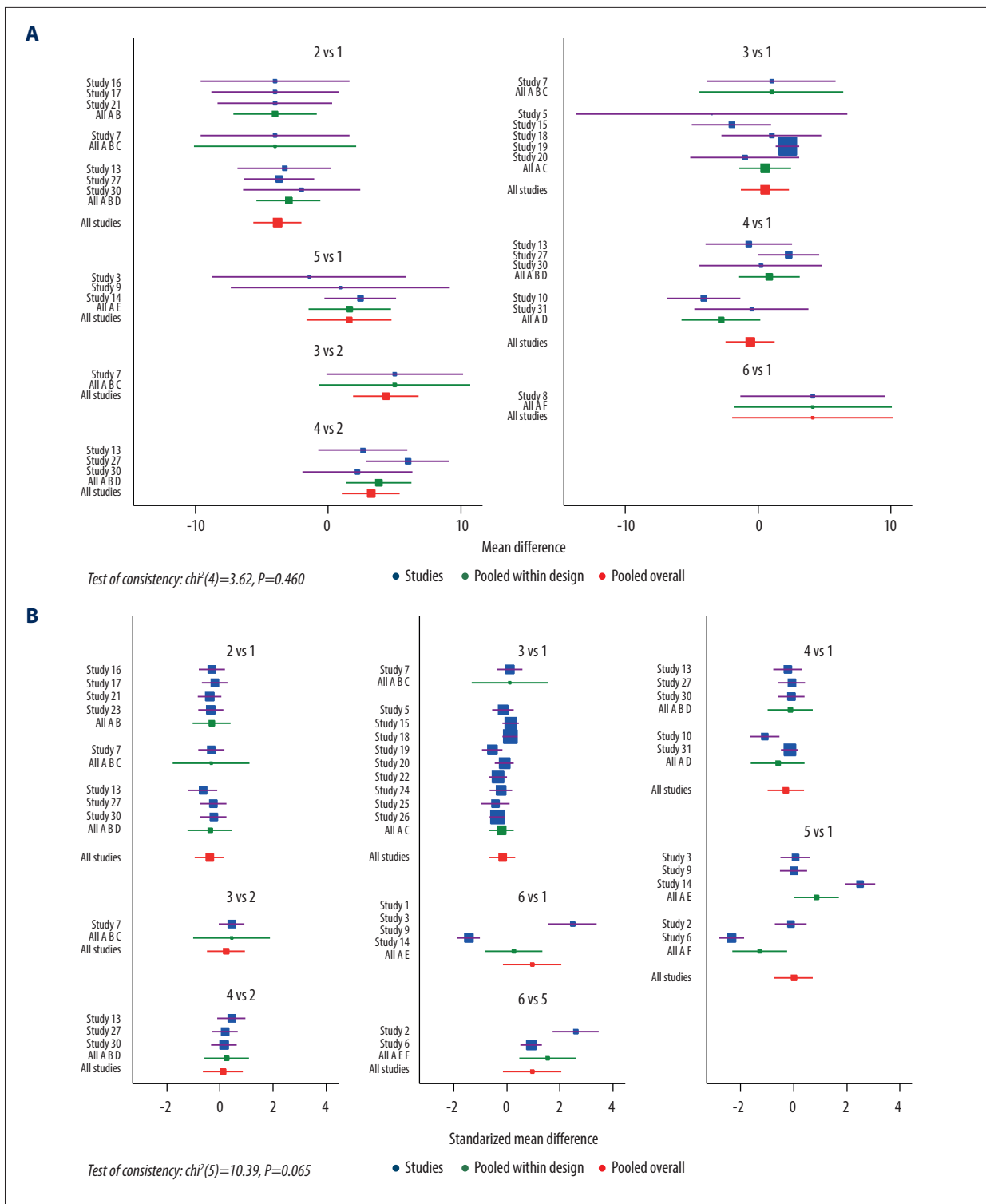


Figure 7. Forest plots of network comparisons of subgroup network meta-analysis (made with Microsoft Excel, version 2019MSO).

leads to a contracture of ACL or/and limited knee movement (Hoogeslag et al [19]).

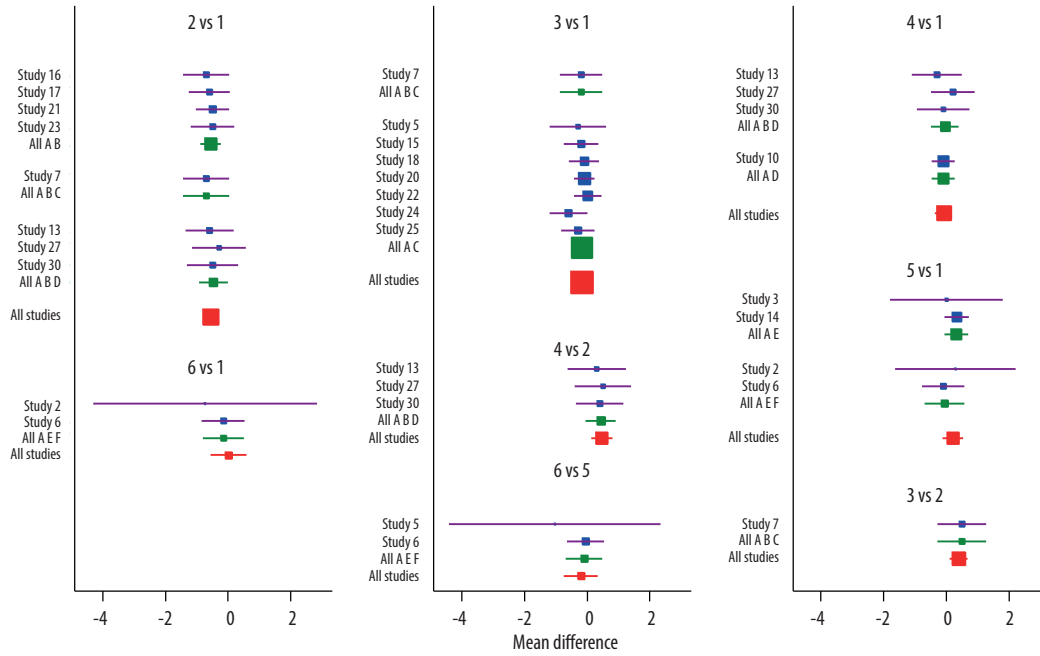
There were still several limitations in this study. First, some factors can affect outcomes but cannot be adjusted or removed by statistical methods, such as the skill of the surgeons and

the quality of the postoperative rehabilitation. Second, an RCT is more sensitive to complications, with a high incidence and a short period, while observational studies can more effectively assess the complications with a low incidence and a long period. Given the important role of observational studies, such as cohort studies, in exploring the long-term efficacy and safety

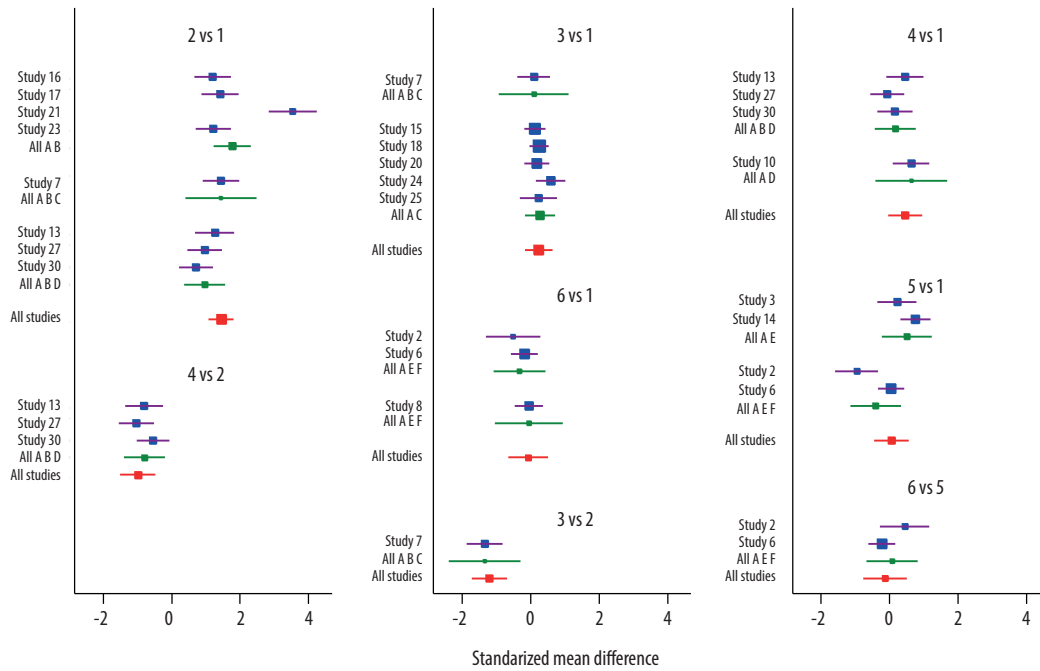


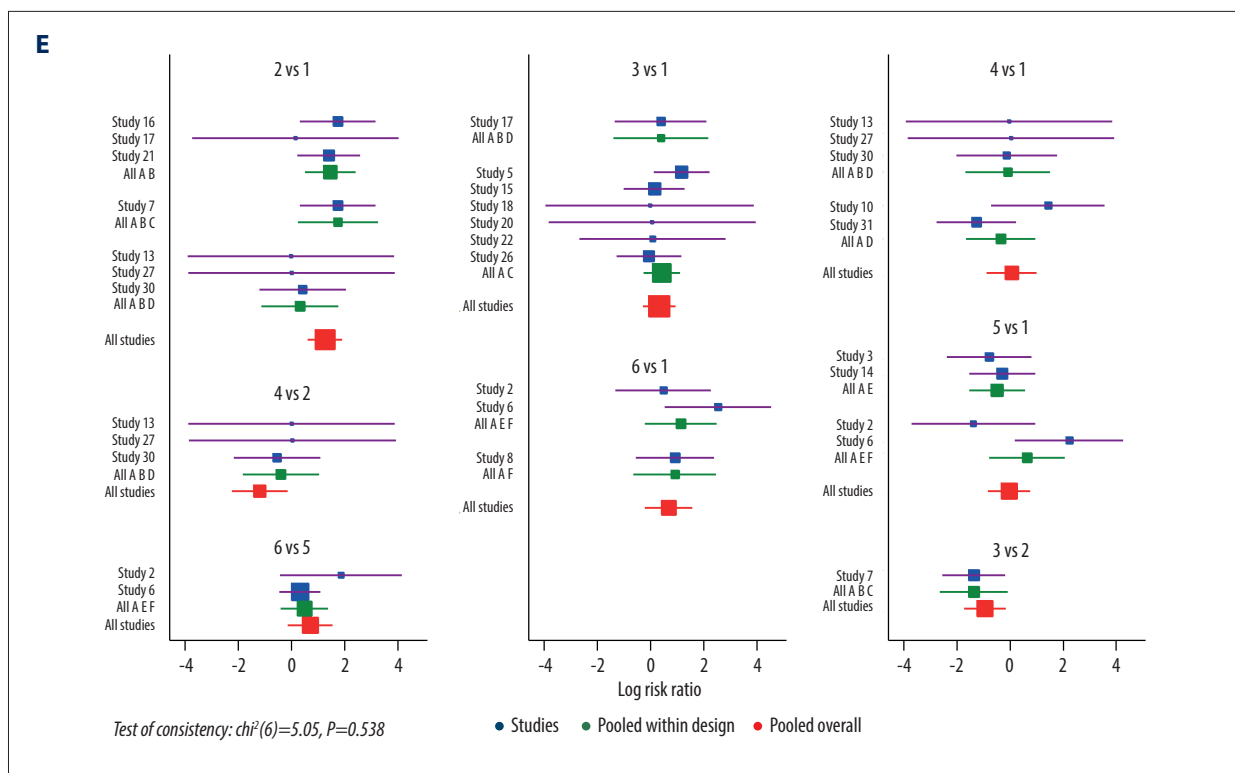


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**Figure 8.** Forest plots incorporated direct comparisons and indirect comparisons of subgroup analysis. (A) Subjective improvement. (B) Functional improvement. (C) Activity recovery. (D) Postoperative laxity. (E) Failure rate. (A or 1: Autograft; B or 2: Allograft with irradiation; C or 3: Allograft without irradiation; D or 4: Hybrid graft; E or 5: Repair with augmentation; F or 6: Repair without augmentation.).

**Table 11.** The detailed results of direct pair-wise meta-analyses between primary repair (PR) with augmentation and anterior cruciate ligament reconstruction (ACLR).

Comparison (PR with augmentation vs ACLR)	No. of trials	No. of patients	Heterogeneity, I <sup>2</sup>	Effect index	Effect size
Subjective improvement	3	193	4.50%	WMD (95% CI)	0.157 (-0.127 to 0.440)
Functional improvement	4	335	0.00%	SMD (95% CI)	-0.042 (-0.302 to 0.218)
Activity improvement	5	461	67.50%	SMD (95% CI)	0.278 (0.068 to 0.488)
Laxity	5	461	0.00%	WMD (95% CI)	0.18 (-0.081 to 0.442)
Failure	3	200	0.00%	RR (95% CI)	0.535 (0.221 to 1.296)

of ACL rupture surgery and although CHSs and non-RCTs potentially have confounding factors that can bias the results, we still included them in the analysis and used a subgroup analysis to examine the impact of observational studies on the results. The subgroup analysis on the RCTs showed only 1 difference from the main network analysis, suggesting that any

biases from CHSs and non-RCTs were unlikely to be a factor in this analysis. Third, studies with no events in both treatment arms were inevitably included in the failure rate network. Omitting studies with rare events was recommended by the Cochrane Handbook, but this is still controversial as it can alter the biased evaluations and the accuracy of the combined

**Table 12.** The detailed results of direct pair-wise meta-analyses between primary repair (PR) without augmentation and anterior cruciate ligament reconstruction (ACLR).

Comparison (PR without augmentation vs ACLR)	No. of trials	No. of patients	Heterogeneity, I <sup>2</sup>	Effect index	Effect size
Subjective improvement	3	140	58.80%	WMD (95% CI)	0.074 (-0.574 to 0.722)
Functional improvement	3	146	92.30%	SMD (95% CI)	0.195 (-0.437 to 0.827)
Activity improvement	2	126	0.00%	WMD (95% CI)	-0.109 (-0.461 to 0.242)
Laxity	6	306	36.50%	SMD (95% CI)	-0.03 (-0.341 to 0.280)
Failure	4	243	43.10%	RR (95% CI)	1.638 (0.658 to 4.078)

estimation. Therefore, we included such trials and used a 0.5 zero-cell correction. However, the results of the failure rates should be interpreted with caution. Fourth, while funnel plots and Egger's tests showed no significant publication bias or small study effects, only a limited number of trials were included, and therefore more high-quality trials are warranted.

## Conclusions

For surgical treatment of ACLR, irradiated allograft ACLR had the worst efficacy and safety and is not recommended. PR may be an ideal treatment method in terms of efficacy but it is related to a significantly higher revision risk if done without augmentation. Autograft ACLR may be the optimal method currently available for most patients requiring surgical treatment of ACL rupture.

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## Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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