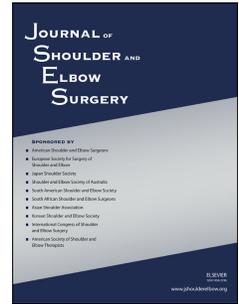


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Leukocyte-Poor Platelet-Rich Plasma Reduces Retear Risk After Arthroscopic Rotator Cuff Repair: A Meta-Analysis with Mechanistic and Economic Evaluation

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Full Title:

Leukocyte-Poor Platelet-Rich Plasma Reduces Retear Risk After Arthroscopic Rotator Cuff Repair: A Meta-Analysis with Mechanistic and Economic Evaluation

Short Running Title:

Formulation-Specific PRP Meta-Analysis

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1 **Abstract**

2 **Background:**

3 Rotator cuff repair (RCR) is one of the most common orthopedic procedures, yet 20–40% of
4 repairs fail structurally within two years, leading to pain, functional decline, and costly revision
5 surgery. Platelet-rich plasma (PRP) has been proposed to enhance tendon–bone healing, but prior
6 reviews frequently pooled heterogeneous formulations as a homogeneous intervention,
7 producing conflicting conclusions. This review aimed to clarify formulation-specific effects
8 within the PRP literature and, where benefit is observed, examine the biological rationale and
9 practical economic implications for surgical adoption.

10 **Methods:**

11 A systematic review and meta-analysis were conducted in accordance with PRISMA 2020
12 guidelines. PubMed and Embase were searched through July 2025 for comparative clinical
13 studies of intraoperative PRP augmentation during arthroscopic RCR with imaging-confirmed
14 retear outcomes. Risk of bias was assessed using ROB2 (RCTs) and ROBINS-I (nonrandomized
15 studies). Random-effects models (REML; Hartung–Knapp) pooled risk ratios (RRs) for
16 structural failure and, secondarily, mean differences in patient-reported outcomes (PROMs).
17 Prespecified subgroups included PRP formulation, tear size, and follow-up duration; sensitivity
18 analyses excluded high-risk and atypical studies. Publication bias was evaluated with Egger’s
19 regression and trim-and-fill. A pragmatic U.S. payer–perspective cost-consequence model
20 estimated revision-related economic impact using pooled absolute risk reduction (ARR), number

21 needed to treat (NNT), amortized per-case PRP setup costs, and reported reoperation rates after
22 RCR.

23 **Results:**

24 Twenty-one studies (1,279 patients) were synthesized. PRP reduced retear risk with moderate
25 heterogeneity (RR 0.74, 95% CI 0.55–0.99; $I^2 \approx 29\%$). Across formulations, LP-PRP
26 demonstrated the clearest reduction; inclusion of one critically biased trial increased
27 heterogeneity ($I^2 = 53.3\%$), whereas its exclusion yielded a precise, homogeneous estimate (RR
28 0.37, 95% CI 0.19–0.73; $I^2 = 0\%$). Benefit was most evident in medium-sized tears (RR 0.68,
29 95% CI 0.48–0.96). PROMs did not improve consistently. Publication-bias diagnostics suggested
30 small-study effects (Egger $p = 0.017$); trim-and-fill ($k_0 = 8$) yielded an exploratory adjusted RR
31 of 0.91 (95% CI 0.69–1.19). Using an ARR of 11.8% (NNT 9) for LP-PRP, economic modeling
32 projected substantial reductions in structural failures, with cost neutrality or net savings
33 achievable under low-cost preparation strategies when scaled by reported revision probabilities.

34 **Conclusion:**

35 Leukocyte-poor PRP augmentation during arthroscopic RCR is associated with reduced
36 structural retear rates, with the most consistent benefit observed in medium-sized tears and no
37 reliable improvement in PROMs. The economic value of LP-PRP is conditional rather than
38 uniform and depends on revision probability and preparation cost. When applied using low-cost
39 preparation methods, LP-PRP may achieve cost neutrality or modest savings, supporting
40 selective adoption as a structural safeguard rather than a symptomatic modifier.

41

42 **Level of Evidence:** Level III, Systematic Review/Meta-analysis, Treatment Study

- 43 **Keywords:** Platelet-Rich Plasma; Rotator Cuff Repair; Tendon Healing; Meta-analysis;
- 44 Orthobiologics; Health economics

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45 Rotator cuff repair (RCR) is one of the most commonly performed orthopedic procedures, yet
46 structural failure remains a persistent challenge. Despite technical advances, 20–40% of repairs
47 exhibit radiologic retears within two years, often resulting in pain, functional decline, and costly
48 revision surgery.¹ National utilization data show that more than 300,000 RCRs are performed
49 annually in the United States, with a rising comorbidity burden among patients.^{18,47} Given these
50 clinical and economic stakes, strategies to improve tendon–bone healing have garnered
51 substantial interest.

52 Platelet-rich plasma (PRP) has emerged as a promising biologic adjunct due to its autologous
53 nature, ease of preparation, and capacity to deliver supraphysiologic concentrations of growth
54 factors to the repair site. However, PRP is not a single entity. Formulations differ widely in
55 leukocyte content, fibrin structure, and processing protocols, resulting in distinct biological
56 effects.^{12,36} This variability reflects both a lack of standardized preparation methods and the
57 absence of definitive evidence favoring one protocol over another.⁵ Leukocyte-poor PRP (LP-
58 PRP) is enriched in regenerative cytokines while minimizing pro-inflammatory mediators,
59 whereas leukocyte-rich PRP (LR-PRP) contains higher leukocyte levels that may promote
60 inflammation, fibrosis, and scar-dominated healing.^{22,28,46} These distinctions may directly
61 influence tendon–bone integration and long-term repair durability.

62 Prior systematic reviews and meta-analyses have generally treated PRP as a uniform
63 intervention, leading to conflicting conclusions.^{2,11} While some reported modest reductions in
64 re-tear rates, others found only transient or inconsistent improvements in pain and function,
65 leaving uncertainty around recommendations pertaining to clinical adoption. Notably, prior
66 publications have not integrated mechanistic rationale with formulation-specific clinical

67 outcomes or downstream economic considerations. This disconnect limits pragmatic decision-
68 making for both surgeons and payers.

69 To address this gap, we conducted a systematic review and meta-analysis examining whether
70 intraoperative PRP reduces retear risk after arthroscopic rotator cuff repair when stratified by
71 formulation. We further explored the consistency of these effects through pre-specified subgroup
72 and sensitivity analyses and estimated the potential cost implications of adoption using a
73 conservative economic model. By integrating formulation-specific analysis with clinical
74 outcomes and pragmatic economic considerations, this study aims to inform real-world surgical
75 decision-making. We hypothesized that leukocyte-poor PRP would be associated with lower
76 structural retear rates after arthroscopic rotator cuff repair compared with leukocyte-rich PRP or
77 no PRP.

78

79 **Methods**

80 This review followed the PRISMA 2020 guidelines.²⁹

81 *Search Strategy and Study Selection*

82 A systematic search of PubMed and Embase was conducted through July 2025 using
83 combinations of terms including platelet-rich plasma, PRP, rotator cuff, and repair. Eligible
84 studies were comparative clinical investigations of PRP use during arthroscopic RCR that
85 reported imaging-confirmed retear outcomes.

86 Exclusion criteria were: (1) animal studies; (2) non-PRP biologics; (3) stand-alone PRP injection
87 studies; (4) absence of a control group; (5) no imaging follow-up; and (6) incompatible retear
88 definitions. Specifically, studies were required to define retear as Sugaya grade IV or V⁴⁰, or an
89 equivalent full-thickness failure. Trials that grouped Sugaya grades III–V together without
90 stratified reporting were excluded to minimize misclassification risk.

91 *Data Extraction and Risk of Bias*

92 Study characteristics, patient demographics, PRP formulation (leukocyte-poor [LP], leukocyte-
93 rich [LR], platelet-rich fibrin matrix [PRFM], PRP gel, leukocyte PRF), tear size, follow-up
94 duration, and outcomes were extracted into a standardized spreadsheet. Risk of bias was assessed
95 using the ROB2 tool for randomized controlled trials and ROBINS-I for nonrandomized
96 studies.^{38,39}

97 *Outcomes*

98 The primary outcome was radiologic retear, defined as structural failure on postoperative
99 imaging. Where Sugaya grading was reported, retear was defined as Sugaya grade IV or V. In
100 studies reporting dichotomous outcomes, retear was defined as a full-thickness defect, consistent
101 with criteria equivalent to Sugaya grade IV. Studies defining retear as partial-thickness failure
102 (e.g., Sugaya grade III) without reporting grade-specific event counts were excluded to maintain
103 consistency in outcome definition. Secondary outcomes included patient-reported function
104 (ASES, Constant, UCLA) and pain (VAS). An exploratory economic analysis estimated the cost
105 implications of PRP adoption.

106 *Statistical Analysis*

107 Dichotomous outcomes were summarized as risk ratios (RRs) with 95% confidence intervals
108 (CIs) and pooled using a Mantel–Haenszel random-effects model with between-study variance
109 (τ^2) estimated by restricted maximum likelihood (REML). Hartung–Knapp adjustment was
110 applied for the overall model; for small-k subgroups (e.g., formulation and tear-size strata),
111 Hartung–Knapp was not applied by design. A continuity correction of 0.5 was used only when
112 any study arm contained zero events. In multi-arm trials with a shared control (e.g., Yao et al.),
113 the control group was proportionally split to avoid double-counting in subgroup analyses.
114 Heterogeneity was assessed using τ^2 , Cochran’s Q, and I^2 statistics, with prediction intervals
115 reported when available.

116 Pre-specified subgroup analyses examined:

- 117 1. PRP formulation (LP, LR, PRFM, gel, L-PRF),

118

- 119 2. Tear size (medium, large, massive), and
120
121 3. Follow-up duration, categorized as short term (≤ 6 months), midterm ($>6-12$ months), and
122 long term (>12 months).

123

124 Sensitivity analyses included: (1) exclusion of high-risk-of-bias studies; (2) randomized trials
125 only; and (3) exclusion of Auregan et al., the only study rated at critical overall risk of bias, and
126 the three-arm Yao et al. trial. Publication bias was assessed using Egger's regression and trim-
127 and-fill methods.^{13,14} Influence diagnostics included leave-one-out analyses to assess the impact
128 of individual studies on pooled estimates. Analyses were performed in R using the *meta* and
129 *metafor* packages.³²

130 *Economic Analysis*

131 A cost-consequence model was developed from a U.S. payer perspective using a perioperative,
132 episode-of-care time horizon. The model incorporated two primary cost inputs: (1) the cost of
133 revision rotator cuff repair (base case: \$5,101 per revision) and (2) the consumable cost of
134 intraoperative platelet-rich plasma (PRP) preparation (base case: \$52.27 per case).

135 Revision costs were derived from average Medicare facility reimbursement rates across
136 ambulatory surgery centers (ASC) and hospital outpatient departments using the CMS Physician
137 Fee Schedule Look-Up Tool (accessed 2025).⁹ Per-case PRP setup costs were derived from a
138 published manual PRP preparation protocol.⁸ All supplies required for PRP preparation
139 (including needles, syringes, tubes, gloves, forceps, centrifuge, and laminar flow hood) were
140 itemized and priced using contemporary U.S. vendor data (Fisher Scientific, Thomas Scientific,

141 Amazon Medical). Capital equipment was amortized over a 5-year expected lifespan, while
142 consumables were costed per use, yielding an average per-case preparation cost of \$52.27 (range
143 \$19.93–\$79.84 based on vendor pricing). This costing approach used universally available
144 consumables and amortized equipment, allowing evaluation across both hospital and ambulatory
145 surgery center settings.

146 Retear risks for leukocyte-poor PRP (LP-PRP) and leukocyte-rich PRP (LR-PRP) were derived
147 from pooled meta-analytic estimates. Absolute risk reduction (ARR) and number needed to treat
148 (NNT) were calculated, and national projections were generated by applying pooled estimates to
149 approximately 300,000 annual rotator cuff repairs in the United States.^{18,47} As not all structural
150 failures proceed to revision surgery, revision-cost avoidance estimates were conservatively
151 scaled using a base-case revision probability of 6%, consistent with prospective series
152 summarized in a contemporary narrative review and with large administrative cohorts reporting
153 low rates of subsequent ipsilateral shoulder surgery after arthroscopic rotator cuff repair.
154 ^{16,24,27}Exploratory sensitivity analyses evaluated higher revision probabilities (up to 12%) to
155 reflect variability across clinical settings and follow-up durations. Indirect costs, quality-adjusted
156 life-years, and non-revision healthcare utilization were excluded from the primary model to
157 avoid introducing additional assumptions and maintain a conservative analytic framework.

158

159 **Results**

160 *Study Characteristics*

161 Twenty-one studies involving 1,279 patients (660 receiving PRP, 619 control) were included,
162 comprising 14 randomized controlled trials and 7 comparative nonrandomized studies^{3,4,6,7,10,19–}
163 ^{21,23,25,26,30,33–35,37,42,43,48–50} (Fig. 1, PRISMA flow diagram). All trials reported imaging-confirmed
164 retears defined as Sugaya grade IV–V or an equivalent full-thickness failure. Most studies
165 involved medium-to-large tears repaired arthroscopically. Risk of bias was generally low to
166 moderate among RCTs and moderate to serious among nonrandomized studies. Auregan et al.
167 (2019) was the only study rated at critical overall risk of bias.

168 *Primary Outcome — Retear Rate*

169 Across all formulations, intraoperative PRP reduced structural retear risk compared with control
170 (RR 0.74, 95% CI 0.55–0.99) with moderate heterogeneity ($I^2 \approx 29\%$) (Fig. 2).

171 When stratified by formulation (Fig 3), LP-PRP showed the strongest directional benefit (RR
172 0.53, 95% CI 0.21–1.31) but with $I^2 = 53.3\%$ driven primarily by *Auregan et al.* Excluding
173 Auregan produced a homogeneous, precise effect (RR 0.37, 95% CI 0.19–0.73; $I^2 = 0\%$) (Suppl.
174 Fig. 1). LR-PRP trended protective but remained nonsignificant (RR 0.76, 95% CI 0.52–1.12; I^2
175 = 0%). Other constructs (e.g., PRFM, gel) showed no consistent advantage (Suppl. Fig. 1)

176 *Sensitivity Analyses*

177 Sensitivity analyses confirmed the direction and stability of the overall effect. Restricting to
178 randomized controlled trials strengthened the signal (RR 0.64, 95% CI 0.42–0.97; $I^2 = 0.4\%$),
179 while excluding high-risk-of-bias studies yielded a similar trend (RR 0.74, 95% CI 0.49–1.12; I^2

180 = 0.4%). Removal of the three-arm Yao et al. (2024) trial produced comparable results (RR 0.75,
181 95% CI 0.57–0.99; $I^2 = 0.3\%$).

182 *Auregan et al.* (2019) was the only study at critical overall risk of bias. With Auregan included,
183 the LP-PRP subgroup I^2 was 53.3%. Excluding Auregan reduced I^2 to 0% and narrowed the CI
184 around a stable, stronger effect (RR 0.37, 95% CI 0.19–0.73). Using the observed control event
185 rate of 18.7%, this corresponds to ARR 11.8% and NNT 9 to prevent one re-tear.

186 *Tear Size and Follow-Up Duration*

187 The clearest and most consistent benefit was observed in medium-sized tears (RR 0.68, 95% CI
188 0.48–0.96; $I^2 = 0.1\%$; Fig. 4), which represented the largest subgroup across 16 studies (n=895;
189 466 PRP, 429 control). Protective effects were also seen in large tears (RR 0.80, 95% CI 0.41–
190 1.57; Fig. 4) although with wider confidence intervals given the smaller sample size across 5
191 studies (n=323; 163 PRP, 160 control). No measurable benefit was found in massive tears, which
192 were assessed in a single study (n=61; 31 PRP, 30 control). Benefit was observed across short-,
193 mid-, and long-term follow-up periods, with no significant time-by-treatment interaction (Suppl.
194 Fig. 2).

195 *Patient-Reported Outcomes*

196 No clinically meaningful improvements were observed in patient-reported outcomes. Pooled
197 analyses of ASES, Constant, and UCLA scores revealed no significant between-group
198 differences, and although VAS pain showed a statistically detectable reduction favoring PRP
199 (MD = -0.1, $p = 0.028$), the magnitude was well below the minimal clinically important
200 difference (MCID), indicating no true clinical benefit (Fig. 5A–D).⁴¹

201 *Small-Study Effects and Publication Bias*

202 Egger's regression indicated funnel plot asymmetry ($p = 0.017$), consistent with small-study
203 effects. Trim-and-fill imputed $k_0 = 8$ studies; the bias-adjusted estimate attenuated to RR 0.91
204 (95% CI 0.69–1.19), interpreted cautiously as a sensitivity analysis rather than a corrected effect
205 size (Suppl. Fig. 3–4).

206 *Economic Implications*

207 Using pooled LP-PRP estimates (Fig. 6), application across approximately 300,000 annual U.S.
208 rotator cuff repairs was projected to prevent an estimated 35,343 structural retears. When scaled
209 using the base-case revision probability of 6%, this corresponded to approximately 2,120
210 avoided revision procedures annually; under exploratory sensitivity scenarios extending revision
211 probability to 12%, up to 4,241 avoided revisions were projected.

212 Under these assumptions, the modeled break-even total PRP cost per case ranged from
213 approximately \$36 at a 6% revision probability to approximately \$72 under the exploratory 12%
214 scenario. At the base-case PRP consumable cost (\$52.27 per case), the implied break-even
215 revision probability was approximately 9%. When applied nationally, the modeled net cost
216 impact ranged from an estimated \$4.9 million deficit under conservative assumptions to an
217 estimated \$6.0 million surplus under higher revision-rate scenarios. These projections reflect
218 short-term, episode-of-care economic effects only; long-term societal costs and quality-of-life
219 outcomes were not incorporated into the base model.

220

221 **Discussion**

222 This meta-analysis demonstrates that intraoperative platelet-rich plasma (PRP) reduces structural
223 failure after arthroscopic rotator cuff repair, with the most consistent and durable effect observed
224 in leukocyte-poor PRP (LP-PRP). In contrast to prior reviews that pooled heterogeneous PRP
225 formulations and yielded conflicting conclusions, our stratified approach shows that the clinical
226 signal depends on formulation. Including the single study at critical overall risk of bias (Auregan
227 et al.) inflated heterogeneity in the LP-PRP subgroup ($I^2 = 53.3\%$), whereas excluding it
228 eliminated heterogeneity ($I^2 = 0\%$) and clarified a precise effect (RR 0.37, 95% CI 0.19–0.73),
229 supporting a formulation-specific effect under lower-bias conditions. LP-PRP demonstrated the
230 most consistent formulation-specific signal, with LR-PRP trending protective but nonsignificant;
231 PRFM and gels showed no consistent advantage. The pattern supports LP-PRP as the leading
232 candidate for structural protection, pending confirmation in larger, formulation-specific trials
233 (Fig. 3). The consistent protective effect observed with LP-PRP suggests that its relevance
234 extends beyond healing biology: preventing revision surgery not only reduces healthcare costs
235 but also spares patients the pain, rehabilitation burden, and prolonged loss of quality of life
236 associated with repeat operations. Taken together, these findings highlight LP-PRP as both a
237 clinically and economically meaningful adjunct, whereas other formulations have not
238 demonstrated the same level of reliability.

239 *Biological Rationale for LP-PRP*

240 The biologic plausibility of LP-PRP is well-supported by preclinical evidence. Tendon-to-bone
241 healing relies on a coordinated interplay between growth factors and immune cell phenotypes.
242 LP-PRP delivers supraphysiologic concentrations of TGF- β , VEGF, EGF, and PDGF, which

243 promote fibroblast activity, collagen deposition, and angiogenesis.^{44,45} Crucially, unlike
244 leukocyte-rich formulations, LP-PRP dampens pro-inflammatory cytokines such as IL-1 β , IL-6
245 and TNF- α , fostering a regenerative rather than inflammatory environment at the tendon–bone
246 interface.^{45,46}

247 Animal models reinforce this mechanism: LP-PRP sustains M2 macrophage predominance and
248 reduces inflammatory signaling, whereas LR-PRP increases cytokine-driven fibrosis.^{28,31}
249 Macrophage polarization studies similarly show that M1 phenotypes impede matrix regeneration,
250 while M2 macrophages support angiogenesis and collagen alignment²². Excessive TGF- β 1,
251 meanwhile, risks promoting scar-dominated healing with mechanically inferior collagen I/III
252 ratios.¹ By shifting the immune response toward M2 predominance, LP-PRP appears to support
253 organized tendon–bone integration rather than fibrotic scar. Collectively, these findings explain
254 why LP-PRP, but not LR-PRP, reliably reduces structural retears: by steering healing toward
255 organized enthesis regeneration rather than fibrotic encapsulation. (Fig. 3).

256 *Clinical Implications*

257 Clinically, LP-PRP was associated with a meaningful reduction in retear risk, corresponding to
258 an absolute risk reduction (ARR) of 11.8% and a number needed to treat (NNT) of 9 to prevent
259 one retear, based on a control event rate of 18.7%. The most pronounced effect was seen in
260 medium-sized tears (Fig. 4), where repair durability remains a challenge. Large tears showed
261 similar directional trends with wider confidence intervals, and massive tears demonstrated no
262 measurable benefit.

263 Although patient-reported outcomes (ASES, Constant, UCLA, VAS) were not significantly
264 improved (Fig. 5), this aligns with prior studies.^{2,11,15,48} PROMs typically improve following any

265 successful repair but tend to decline over time when retears occur. Prospective cohort studies
266 confirm that structural failure predicts subsequent deterioration in pain and function scores¹⁷.
267 Our findings suggest LP-PRP acts primarily as a structural safeguard—reducing failure risk
268 without accelerating short-term symptomatic recovery. This interpretation is consistent with both
269 the biologic mechanism and long-term clinical trajectory of re-tear-associated decline.

270 *Economic Relevance*

271 Revision rotator cuff repair is resource-intensive, costly, and disruptive to patient recovery,
272 making even modest reductions in re-tear risk clinically and economically meaningful. Using a
273 conservative, episode-of-care cost-consequence framework grounded in Medicare
274 reimbursement data, the present analysis demonstrates that the economic impact of leukocyte-
275 poor PRP augmentation is highly sensitive to the proportion of structural failures that proceed to
276 revision surgery. When revision probabilities ranging from 6% to 12% were incorporated, LP-
277 PRP was associated with modeled outcomes spanning from modest net cost deficits to modest
278 net cost savings at the national level, with near cost-neutrality at intermediate values.

279 These findings underscore that the economic value of LP-PRP is conditional rather than uniform.
280 Importantly, the break-even total PRP cost per case fell within a relatively narrow range under
281 plausible revision probabilities, suggesting that low-cost preparation strategies may achieve cost
282 neutrality. Because commercial-kit-based systems often have higher per-case costs than manual
283 preparation, the break-even thresholds reported here can be interpreted as cost ceilings above
284 which LP-PRP is unlikely to be cost-neutral under the modeled revision probabilities. In settings
285 where PRP-related costs are not routinely reimbursed, financial responsibility may be transferred
286 to patients, shifting the economic evaluation from a payer-centered framework toward shared

287 physician–patient decision-making. Under these circumstances, even when structural benefit is
288 observed, the value of PRP augmentation may depend on individual patient preferences,
289 financial capacity, and treatment priorities. Accordingly, the present economic results should be
290 interpreted as illustrative of potential payer-side impact under defined assumptions, rather than
291 as evidence of universal cost savings, and as highlighting the importance of cost-reduction
292 strategies in facilitating real-world adoption.

293 *Strengths and Limitations*

294 This review has several notable strengths. Chief among these is its formulation-specific
295 approach, which distinguishes leukocyte-poor from leukocyte-rich PRP rather than pooling
296 heterogeneous biologic preparations as a single intervention. Structural failure was objectively
297 defined using postoperative imaging, with outcomes harmonized to full-thickness retear
298 equivalent to Sugaya grade IV. All analyses were conducted using standardized risk-of-bias
299 assessment tools and pre-specified subgroup and sensitivity frameworks. The analytic workflow
300 and figures were generated using fully reproducible code, enhancing transparency and
301 reproducibility. Findings remained consistent after exclusion of the single critically biased trial,
302 supporting the robustness of the observed structural effect. In addition, the pragmatic economic
303 model incorporated real-world cost inputs and readily implementable manual preparation
304 methods, allowing evaluation across both hospital and ambulatory surgical center settings.

305 Several limitations warrant consideration. PRP preparation protocols and reporting methods
306 varied across included studies, and despite outcome harmonization, definitions of retear were not
307 fully standardized across trials. Subgroup analyses were limited by relatively small sample sizes,
308 and a number of nonrandomized studies carried moderate to serious risk of bias. Publication bias

309 cannot be excluded; funnel-plot asymmetry suggested possible small-study effects, and bias-
310 adjusted estimates should be interpreted as exploratory. Moreover, most trials lacked objective
311 strength testing within age-adjusted Constant scores, limiting conclusions regarding functional
312 recovery. Finally, the economic analysis captured short-term, episode-of-care healthcare
313 expenditures only and did not incorporate indirect costs, long-term societal impact, or quality-of-
314 life outcomes.

315 **Conclusion**

316 Intraoperative leukocyte-poor platelet-rich plasma (LP-PRP) appears to reduce retear risk after
317 arthroscopic rotator cuff repair, with consistent benefits across study designs that strengthen
318 when high-risk trials are excluded. Excluding the single critically-biased study reduced
319 heterogeneity from 53.3% to 0%, clarifying a precise, formulation-specific effect. By linking
320 biologic plausibility with structural protection and demonstrating favorable cost projections
321 under conservative assumptions, this meta-analysis offers a formulation-specific framework to
322 inform clinical adoption. LP-PRP represents a feasible, low-cost adjunct that improves repair
323 durability without altering short-term recovery or patient-reported outcomes—making it both a
324 biologically rational and economically practical strategy in modern shoulder surgery. Taken
325 together, these results position LP-PRP as a formulation-specific adjunct worthy of consideration
326 in optimizing RCR outcomes at scale.

327

328

329

330 **Acknowledgments**

331 ChatGPT (OpenAI, San Francisco, CA; GPT-5) was used under author supervision to assist with
332 R code organization, syntax corrections, and minor language refinement. All statistical analyses,
333 results, and interpretations were independently verified by the authors, who take full
334 responsibility for the accuracy and integrity of the work.

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514 **Figure Legends**

515

516 Figure 1. PRISMA flow diagram of study selection

517 Caption: PRISMA 2020 diagram showing study identification, screening, eligibility, and

518 inclusion. Of 396 records, 336 were screened after duplicates; 35 full texts were assessed, and 21

519 studies were included (one with two PRP arms analyzed separately). Reasons for exclusion at

520 full text: overlapping population (n=1), incompatible outcomes (n=7), no postoperative imaging

521 (n=1), irrelevant intervention (n=1), and intervention timing outside the prespecified window

522 (n=3).

523 *PRP, platelet-rich plasma.*

524

525 Figure 2. Overall retear after arthroscopic rotator cuff repair: PRP vs control

526 Forest plot of imaging-confirmed retears comparing PRP with control. Effects are risk ratios

527 (RR, log scale) pooled with a random-effects model (REML; Hartung–Knapp). Squares show

528 study estimates (size \propto weight), horizontal lines indicate 95% CIs, and the diamond is the pooled

529 effect. PRP reduced retear risk (RR 0.74, 95% CI 0.55–0.99) with low–moderate heterogeneity

530 ($I^2 = 28.8\%$).531 *PRP, platelet-rich plasma; RR, risk ratio; CI, confidence interval.*

532

533 Figure 3. Retear risk by PRP formulation

534 Caption: Forest plot of subgroup analyses by PRP formulation. Leukocyte-poor PRP (LP-PRP)

535 showed the clearest and most precise reduction (RR 0.37, 95% CI 0.19–0.73); excluding the

536 single critically biased study (*Auregan 2019*) reduced LP-PRP heterogeneity from 53.3% to

537 0.0%, clarifying the formulation-specific signal. Leukocyte-rich PRP (LR-PRP) trended
538 protective but was not significant (RR 0.76, 95% CI 0.52–1.12); PRFM/PRP matrix showed no
539 consistent advantage, while PRP gel favored PRP (RR 0.42, 95% CI 0.22–0.82). Diamonds
540 indicate random-effects pooled estimates for each subgroup; the test for subgroup differences
541 was not significant ($\chi^2 = 7.76$, $df = 4$, $p = 0.100$).

542 *LP-PRP, leukocyte-poor PRP; LR-PRP, leukocyte-rich PRP; PRFM, platelet-rich fibrin matrix;*
543 *RR, risk ratio; CI, confidence interval.*

544

545 Figure 4. Retear risk stratified by tear size

546 Caption: Forest plot of imaging-confirmed retears after arthroscopic rotator cuff repair, grouped
547 by baseline tear size. Medium tears showed a significant reduction with PRP (RR 0.68, 95% CI
548 0.48–0.96), whereas large (RR 0.80, 95% CI 0.41–1.57) and massive tears (RR 0.89, 95% CI
549 0.46–1.69) were not significant. Diamonds indicate random-effects pooled estimates within each
550 subgroup; the test for subgroup differences was not significant ($\chi^2 = 0.62$, $df = 2$, $p = 0.730$).

551 *PRP, platelet-rich plasma; RR, risk ratio; CI, confidence interval.*

552

553 Figure 5A-D. Patient-reported outcomes following PRP augmentation during rotator cuff repair
554 Forest plots of pooled mean differences (MD) comparing PRP versus control for (A) Constant-
555 Murley score (MD 0.7, 95% CI –0.2 to 1.6; $p = .112$); (B) ASES score (MD 1.5, 95% CI –1.7 to
556 4.7; $p = .363$); (C) UCLA Shoulder Rating Scale (MD 0.3, 95% CI 0.0 to 0.6; $p = .439$); and (D)
557 Visual Analog Scale (VAS) for pain (MD –0.1, 95% CI –0.2 to –0.0; $p = .028$). All outcomes
558 were pooled using random-effects models (REML; Hartung–Knapp confidence intervals). PRP
559 augmentation did not result in clinically meaningful improvement in patient-reported outcomes.

560 Although small statistically significant differences were observed for UCLA score and VAS
561 pain, effect sizes were below established minimal clinically important difference thresholds and
562 are unlikely to be clinically meaningful. Squares represent study weights, and diamonds indicate
563 pooled effects.

564

565 Figure 6. Cost-consequence schematic for LP-PRP augmentation during arthroscopic rotator cuff
566 repair.

567 Decision-analytic flow diagram showing the modeled structural retear reduction with leukocyte-
568 poor platelet-rich plasma (LP-PRP) versus standard repair and the downstream economic
569 consequences when only a fraction of structural failures proceed to revision surgery. Using a
570 control structural retear rate of 18.7% and an LP-PRP structural retear rate of 6.9% (ARR 11.8%;
571 NNT = 9), the model estimates cost-neutral (break-even) total PRP cost thresholds and net cost
572 impact per repair and nationally under a base-case revision probability of 6% and scenario
573 analyses at 9% and 12%. Model inputs (including revision cost, PRP preparation/consumable
574 cost, and unit-cost assumptions) are provided in Supplementary Table 1. Net cost impact values
575 are presented at a PRP consumable cost of \$52.27 per case and assume 300,000 rotator cuff
576 repairs performed annually in the United States.

577

578 Supplemental Figure S1. Retear risk by PRP formulation (Auregan included)

579 Caption: Forest plot of subgroup analyses by formulation with the critically biased trial by
580 Auregan et al., 2019 retained. LP-PRP shows a nonsignificant trend toward benefit (RR 0.53,
581 95% CI 0.21–1.31) with higher heterogeneity ($I^2 \approx 53\%$) versus the 0% seen when Auregan is

582 excluded in the main text. LR-PRP is nonsignificant (RR 0.76, 95% CI 0.52–1.12). PRFM/PRP
583 matrix shows no advantage (RR 0.95, 95% CI 0.55–1.66), PRP gel favors PRP (RR 0.42, 95%
584 CI 0.22–0.82), and L-PRF favors PRP (RR 0.71, 95% CI 0.53–0.95). Diamonds denote random-
585 effects pooled estimates; study weights are inverse-variance.

586

587 Supplemental Figure S2. Retear risk by follow-up duration.

588 Caption: Subgroup forest plot stratified by follow-up duration. Effects were directionally
589 consistent across time windows: short-term (≤ 6 mo) RR 0.78 [0.51–1.20], mid-term (>6 –12 mo)
590 RR 0.78 [0.50–1.22], long-term (>12 mo) RR 0.42 [0.15–1.21], and extended-term (latest
591 follow-up in two studies) RR 0.33 [0.01–7.75]. Test for subgroup differences: $\chi^2 = 1.46$, $df = 3$, p
592 = 0.690 (no evidence of effect modification by time).

593

594 Supplemental Figure S3. Funnel plot for publication bias in retear outcomes (unadjusted)

595 Caption: Funnel plot (SE vs. log RR) for all studies. Visual asymmetry suggests small study
596 effects; Egger's regression $p = 0.017$. Dashed vertical line marks the null; dotted lines outline
597 pseudo 95% CIs.

598

599 Supplemental Figure S4. Trim-and-fill funnel plot for retear outcomes (imputed studies in white)

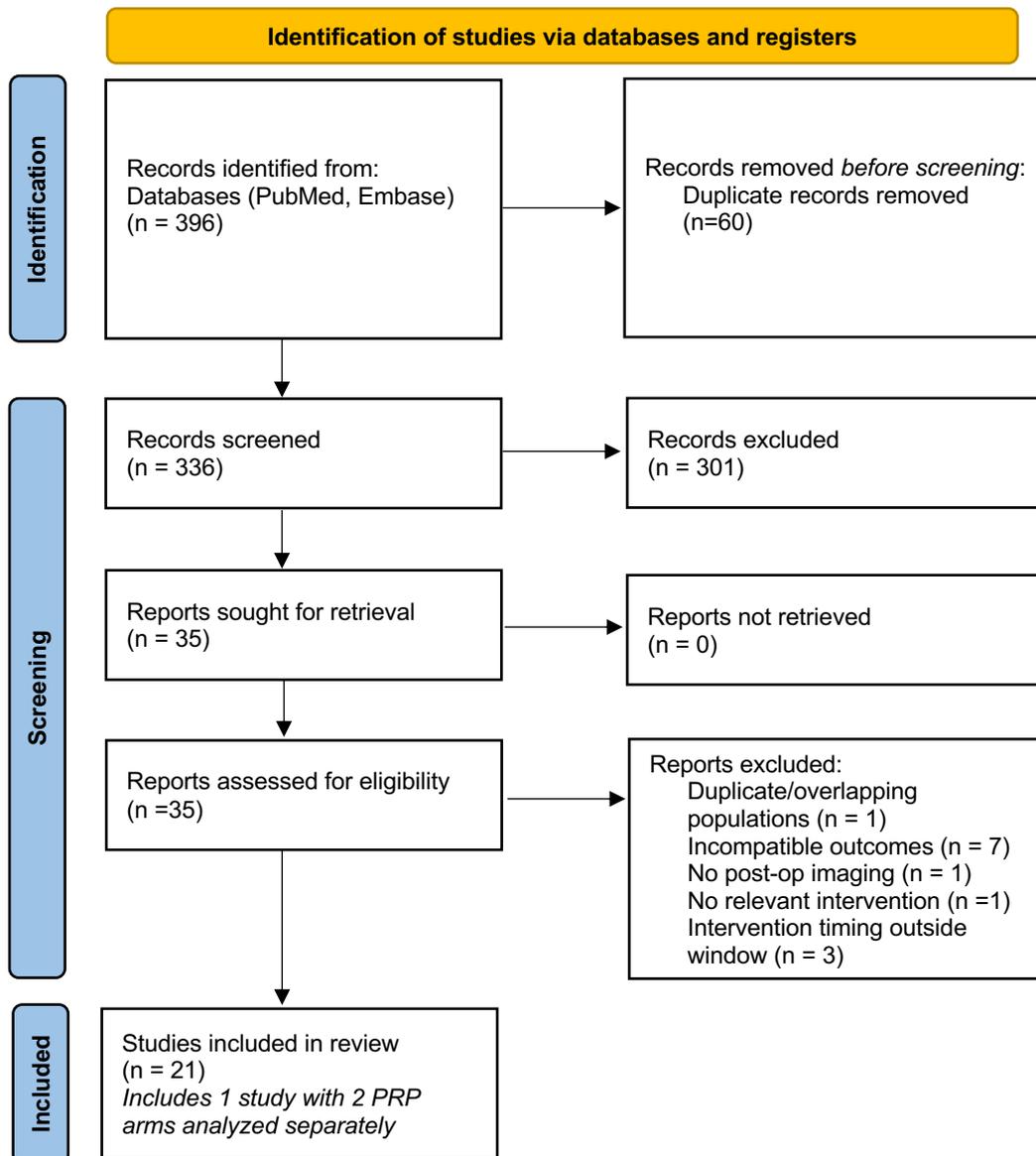
600 Caption: Trim-and-fill analysis imputing $k_0=8$ potentially missing studies (open circles). The
601 bias-adjusted pooled effect attenuates to RR 0.91 (95% CI 0.69–1.19). Interpreted as a sensitivity
602 analysis rather than a corrected estimate.

603

604 Supplemental Table 1. Per-patient supply and equipment costs for manual LP-PRP preparation
605 (U.S. 2025 dollars)

606 Caption: Itemized consumables and amortized capital used to prepare leukocyte-poor PRP intra-
607 operatively. Quantities reflect a single case; costs are shown as lowest / average / highest
608 observed across common U.S. vendors. Capital items listed as “Fixed (amortized)” contribute
609 <\$0.01/patient under 5-year straight-line amortization. The summed average total cost per patient
610 is \$52.27 (range \$19.93–\$79.84).

611 *Abbreviations:* ACD-A, anticoagulant citrate dextrose solution A; PRP, platelet-rich plasma.



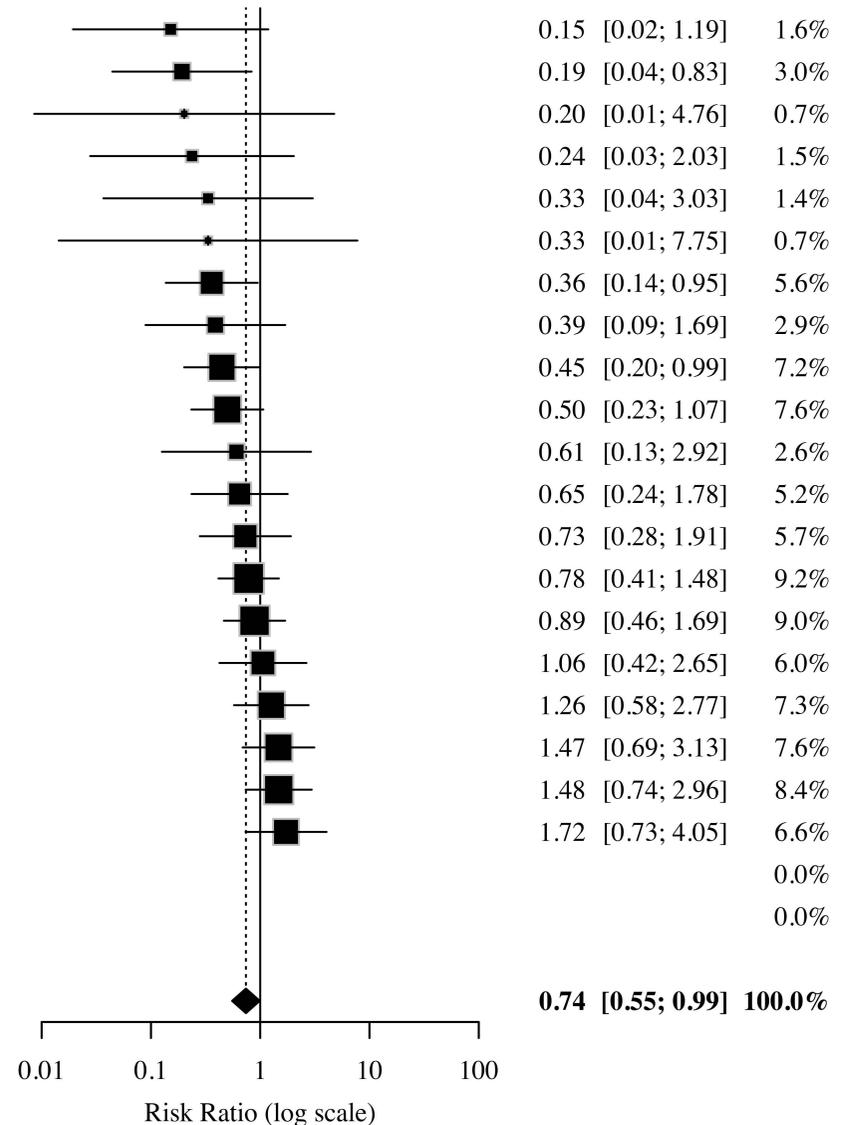
Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

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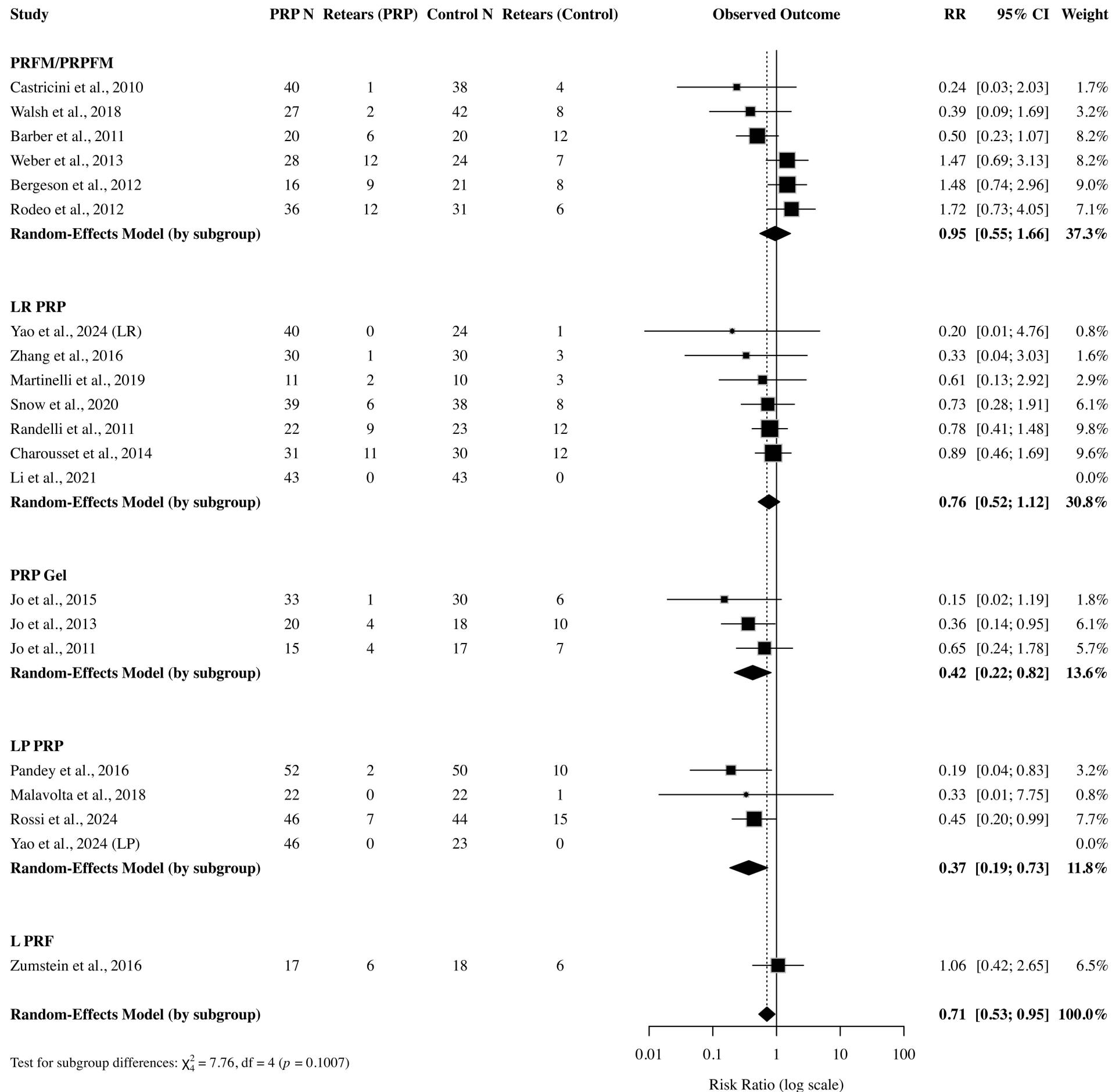
Study	PRP N	Retears (PRP)	Control N	Retears (Control)	Observed Outcome	RR	95% CI	Weight
Jo et al., 2015	33	1	30	6		0.15	[0.02; 1.19]	1.6%
Pandey et al., 2016	52	2	50	10		0.19	[0.04; 0.83]	3.0%
Yao et al., 2024 (LR)	40	0	24	1		0.20	[0.01; 4.76]	0.7%
Castricini et al., 2010	40	1	38	4		0.24	[0.03; 2.03]	1.5%
Zhang et al., 2016	30	1	30	3		0.33	[0.04; 3.03]	1.4%
Malavolta et al., 2018	22	0	22	1		0.33	[0.01; 7.75]	0.7%
Jo et al., 2013	20	4	18	10		0.36	[0.14; 0.95]	5.6%
Walsh et al., 2018	27	2	42	8		0.39	[0.09; 1.69]	2.9%
Rossi et al., 2024	46	7	44	15		0.45	[0.20; 0.99]	7.2%
Barber et al., 2011	20	6	20	12		0.50	[0.23; 1.07]	7.6%
Martinelli et al., 2019	11	2	10	3		0.61	[0.13; 2.92]	2.6%
Jo et al., 2011	15	4	17	7		0.65	[0.24; 1.78]	5.2%
Snow et al., 2020	39	6	38	8		0.73	[0.28; 1.91]	5.7%
Randelli et al., 2011	22	9	23	12		0.78	[0.41; 1.48]	9.2%
Charousset et al., 2014	31	11	30	12		0.89	[0.46; 1.69]	9.0%
Zumstein et al., 2016	17	6	18	6		1.06	[0.42; 2.65]	6.0%
Auregan et al., 2019	26	10	23	7		1.26	[0.58; 2.77]	7.3%
Weber et al., 2013	28	12	24	7		1.47	[0.69; 3.13]	7.6%
Bergeson et al., 2012	16	9	21	8		1.48	[0.74; 2.96]	8.4%
Rodeo et al., 2012	36	12	31	6		1.72	[0.73; 4.05]	6.6%
Li et al., 2021	43	0	43	0				0.0%
Yao et al., 2024 (LP)	46	0	23	0				0.0%

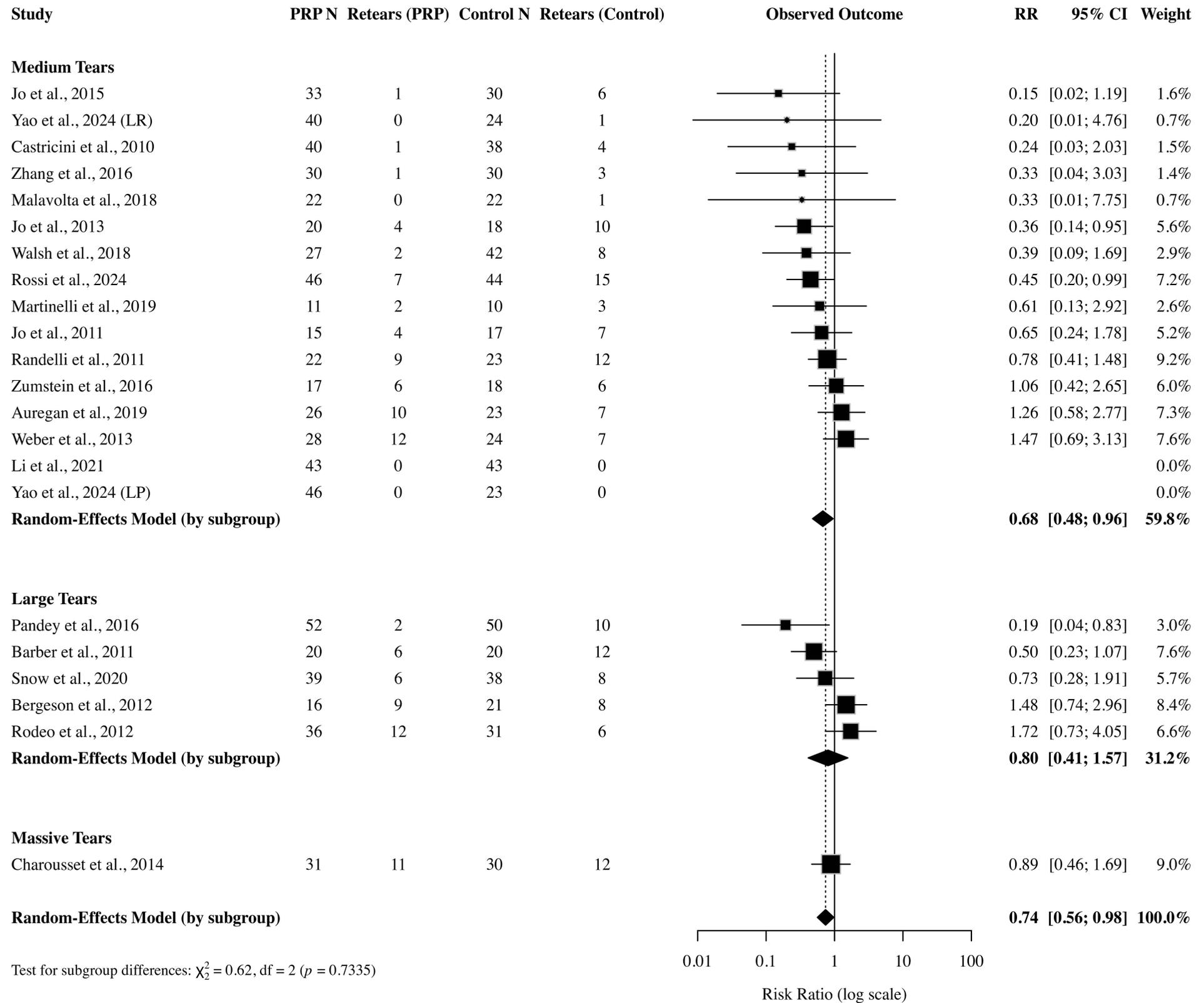
Random-Effects Model

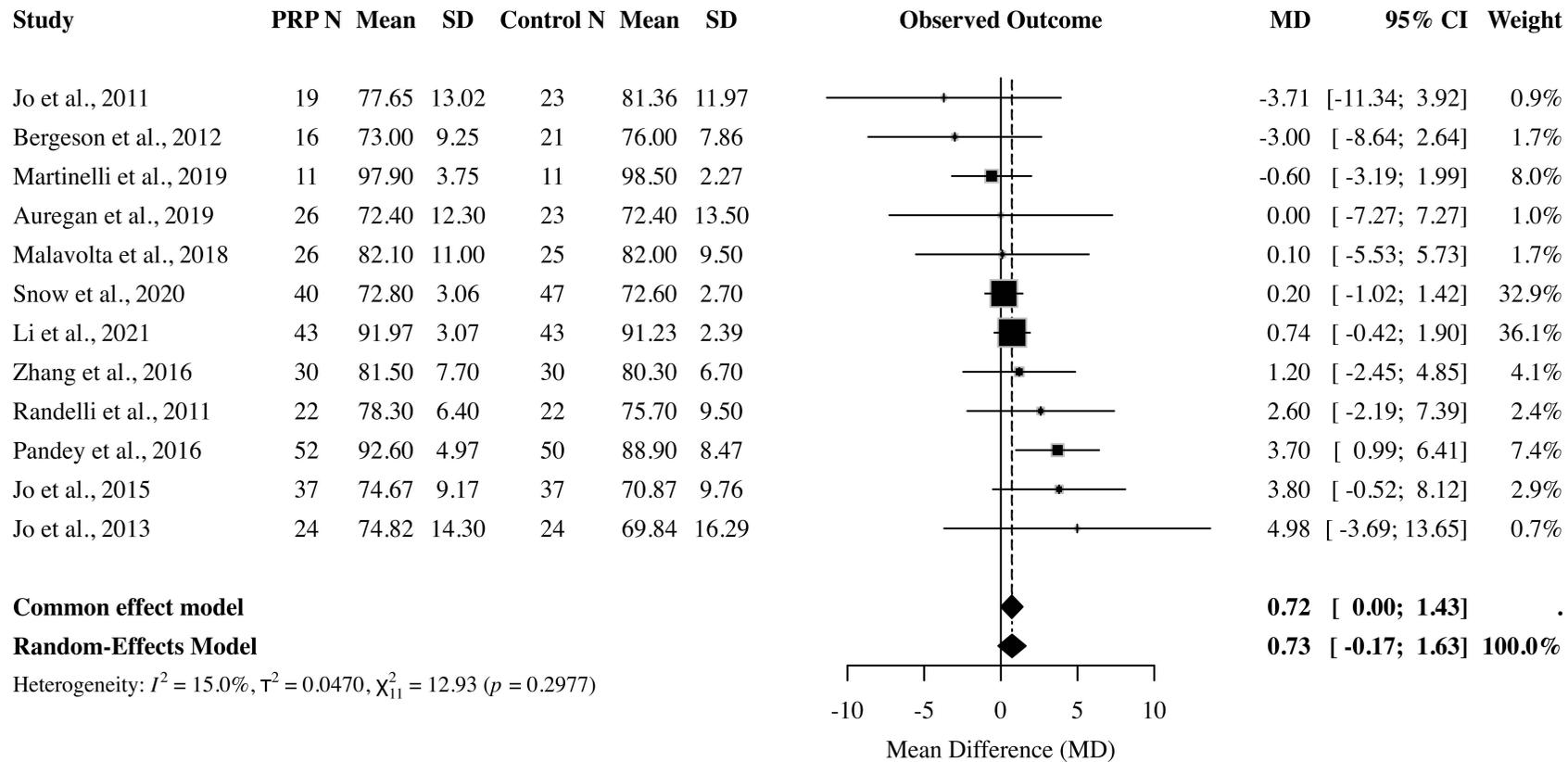
Heterogeneity: $I^2 = 28.8\%$, $\tau^2 = 0.1113$, $\chi^2_{19} = 26.67$ ($p = 0.1125$)



0.74 [0.55; 0.99] 100.0%





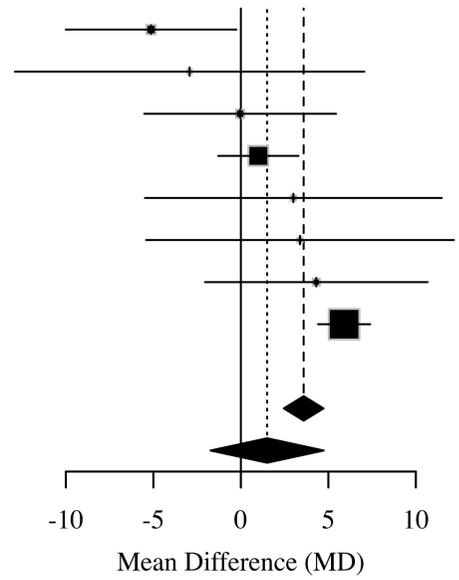


Study	PRP N	Mean	SD	Control N	Mean	SD	Observed Outcome	MD	95% CI	Weight
Rodeo et al., 2012	19	91.30	9.53	22	96.43	5.55		-5.13	[-10.00; -0.26]	13.9%
Jo et al., 2011	19	86.26	19.95	23	89.19	10.73		-2.93	[-12.91; 7.05]	6.3%
Weber et al., 2013	29	82.48	8.77	30	82.52	12.45		-0.04	[-5.52; 5.44]	12.7%
Pandey et al., 2016	52	87.40	5.46	50	86.40	6.30		1.00	[-1.29; 3.29]	19.6%
Bergeson et al., 2012	16	87.00	10.00	21	84.00	16.19		3.00	[-5.48; 11.48]	7.9%
Jo et al., 2013	24	88.94	13.61	24	85.56	17.26		3.38	[-5.41; 12.17]	7.5%
Jo et al., 2015	37	87.96	13.10	37	83.65	14.76		4.31	[-2.05; 10.67]	11.0%
Snow et al., 2020	40	80.10	3.39	47	74.20	3.70		5.90	[4.41; 7.39]	21.0%

Common effect model

Random-Effects Model

Heterogeneity: $I^2 = 76.5\%$, $\tau^2 = 10.3499$, $\chi^2_7 = 29.82$ ($p = 0.0001$)



3.59 [2.45; 4.72] .
1.50 [-1.73; 4.73] **100.0%**

