

Osteoarthritis Prevalence Following Anterior Cruciate Ligament Reconstruction: A Systematic Review and Numbers-Needed-to-Treat Analysis

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Objective: To determine the prophylactic capability of anterior cruciate ligament (ACL) reconstruction in decreasing the risk of knee osteoarthritis (OA) when compared with ACL-deficient patients, as well as the effect of a concomitant meniscectomy. We also sought to examine the influence of study design, publication date, and graft type as well as the magnitude of change in physical activity from preinjury Tegner scores in both cohorts.

Data Sources: We searched Web of Science and PubMed databases from 1960 through 2012 with the search terms *osteoarthritis*, *meniscectomy*, *anterior cruciate ligament*, *anterior cruciate ligament reconstruction*, and *anterior cruciate ligament deficient*.

Study Selection: Articles that reported the prevalence of tibiofemoral or patellofemoral OA based on radiographic assessment were included. We calculated numbers needed to treat and relative risk reduction with associated 95% confidence intervals for 3 groups (1) patients with meniscal and ACL injury, (2) patients with isolated ACL injury, and (3) total patients (groups 1 and 2).

Data Extraction: A total of 38 studies met the criteria. Of these, 27 assessed the presence of tibiofemoral osteoarthritis in patients treated with anterior cruciate ligament reconstruction.

Data Synthesis: Overall, ACL reconstruction (ACL-R) yielded a numbers needed to treat to harm of 16 with a relative risk increase of 16%. Anterior cruciate ligament reconstruction along with meniscectomy yielded a numbers needed to treat to benefit of 15 and relative risk reduction of 11%. Isolated ACL-R showed a numbers needed to treat to harm of 8 and relative risk increase of 43%. Activity levels were decreased in both ACL-R ($d = -0.90$; 95% confidence interval = 0.77, 1.13) and ACL-deficient ($d = -1.13$; 95% confidence interval = 0.96, 1.29) patients after injury.

Conclusions: The current literature does not provide substantial evidence to suggest that ACL-R is an adequate intervention to prevent knee osteoarthritis. With regard to osteoarthritis prevalence, the only patients benefiting from ACL-R were those undergoing concomitant meniscectomy with reconstruction.

Key Words: knee, meniscectomy, activity level, absolute risk reduction

Key Points

- The current literature does not support the prophylactic benefit of anterior cruciate ligament reconstruction in reducing the prevalence of knee osteoarthritis after anterior cruciate ligament injury.
- Meniscal status and graft type affect the risk of knee osteoarthritis after anterior cruciate ligament injury and reconstruction.

The anterior cruciate ligament (ACL) is a major stabilizer of the knee, restricting anterior tibial translation and rotational forces at the tibiofemoral joint. Anterior cruciate ligament rupture occurs in approximately 250 000 Americans each year.^{1,2} Anterior cruciate ligament deficiency (ACL-D) results in pain, increased instability, and altered function in a large proportion of patients.³ Total medical costs encompassing diagnosis, surgical reconstruction, and postoperative rehabilitation of ACL injuries total \$3 billion in the United States annually.⁴

The development of posttraumatic knee osteoarthritis (OA) has been established as a significant risk after ACL injury.^{5,6} Knee OA is a chronic, progressive disease that leads to increased disability and significant economic burden

on the health care system.^{7,8} The mechanisms that contribute to the development of OA after ACL injury are not completely understood, yet current hypotheses have focused on influences from altered biochemical processes,⁹ biomechanical alterations,¹⁰ and deficits in neuromuscular function.^{8,11} It has been suggested that ACL reconstruction (ACL-R) may aid patients in regaining proper joint kinematics, possibly minimizing the abnormal stresses that could occur with ACL-D.^{8,12,13} Although ACL-R is primarily performed to regain stability after ACL rupture, a long-term goal of this procedure is to decrease the risk of developing knee OA and improve long-term joint health.^{12,13}

Concomitant meniscal injury requiring meniscectomy after ACL rupture cannot be ignored as a contributing

factor to knee OA. Meniscal damage is associated with approximately 25% to 45% of ACL ruptures^{8,14-16} and has been reported to be as high as 50%.¹⁷ Meniscal damage and ACL injury increase the risk of knee OA, likely a result of diminished intra-articular energy attenuation and altered arthrokinematics.¹⁸ Isolated ACL-R and ACL-R with meniscectomy are common surgical procedures, but we do not completely understand the ability of these procedures to decrease the risk of OA development.

Therefore, the purpose of our article is to systematically review the literature to determine the prophylactic capacity of ACL-R in decreasing the prevalence of knee OA compared with ACL-D patients receiving only conservative treatment.

METHODS

Search Strategies

We performed an exhaustive search of all databases associated with the Web of Science (BIOSIS Citation Index, BIOSIS Previews, Derwent Innovations Index, MEDLINE, and Journal Citations Report) and PubMed databases from 1960 through June 6, 2012. Search terms were *osteoarthritis* and *meniscectomy* or *anterior cruciate ligament* or *anterior cruciate ligament reconstruction* or *anterior cruciate ligament deficient*. We included only studies published in English that evaluated the presence of tibiofemoral or patellofemoral OA in patients who sustained an ACL rupture and underwent an ACL-R or had ACL-D. Investigations were included if the presence of OA was assessed radiographically using a standardized assessment tool in either the medial or lateral tibiofemoral or the patellofemoral compartment. A study was excluded if the grade of OA was based upon the contralateral knee or if it was documented that participants had OA at the time of initial ACL rupture. Additionally, research that assessed only the development of OA in participants with rerupture of the ACL graft was excluded. We cross-referenced bibliographies from all relevant studies to identify articles that had not been located during the initial Web of Science search (Figure 1). If the presence of OA could not be determined directly from the study,¹⁹ we e-mailed the authors in an attempt to acquire this information.

Publication Bias

Publication bias was assessed for both ACL-R and ACL-D through the creation of 2 funnel plots. The percentage of OA developed in the sample was plotted against the sample size in each study. Funnel plots were then assessed for symmetry, with greater skewness away from the funnel shape indicating a greater degree of publication bias.²⁰

Data Extraction and Analysis

Radiographic Assessment of Knee Osteoarthritis. From each included study, we extracted the number of patients diagnosed radiographically with tibiofemoral OA and the total number with ACL-R or ACL-D. Similarly, from articles reporting concomitant meniscectomy procedures, we extracted the number of ACL-R and ACL-D patients with OA who underwent meniscectomy and the total number of patients in the ACL-R and ACL-D groups. To determine the progression of OA over time, the data were

separated into subgroups based on the decade post-ACL injury in which the radiographs were taken. Studies were partitioned based upon the mean or median time point at which outcomes were assessed; subgroups consisted of the first decade (0–10 years), second decade (11–18 years), and third decade (19–35 years) postinjury. Although Ventura et al²¹ reported mean follow-up times of 19 years post-ACL-R, the range of follow-up times extended into the third decade, so we included their results in the third-decade group to allow ACL-R comparison with the ACL-D study's²² third-decade OA prevalence data. Results were also separated by study design (retrospective versus prospective), publication year, and graft type chosen for reconstruction to evaluate their effect on the prevalence of knee OA after ACL injury.

The number of patients with knee OA in each group was divided by the total number of participants in each group and then multiplied by 100. Rates from the ACL-R and ACL-D groups were used to calculate absolute risk reduction (ARR; Equation 1) and relative risk reduction (RRR; Equation 2) with associated 95% confidence intervals (CIs).²³ When ACL-R increased the risk of tibiofemoral OA, we reported absolute risk increase (ARI) and relative risk increase (RRI). Absolute risk reduction and ARI were used to calculate the numbers needed to treat (NNT; Equation 3) with 95% CIs (Equation 4).²⁴ Comparisons which indicated a beneficial effect for ACL-R in preventing tibiofemoral OA were termed *number needed to treat to benefit* (NNT), whereas comparisons depicting an increased rate of OA after ACL-R were reported as *number needed to treat to harm* (NNH). We calculated odds ratios (Equation 5)²³ and their 95% CIs (Equation 6) to identify the magnitude of risk of incurring tibiofemoral OA depending on the inclusion of patients in the ACL-R and ACL-D groups.

$$ARR = (ACL_R\% - ACL_D\%) * 100 \quad (1)$$

$$RRR = \left(1 - \left(\frac{ACL_R\%}{ACL_D\%} \right) \right) * 100 \quad (2)$$

$$NNT = \frac{1}{(ACL_D\%)(RRR)} \quad (3)$$

$$NNT \text{ Lower CI} = \frac{1}{ARR \text{ Lower CI}} \quad (4)$$

$$NNT \text{ Upper CI} = \frac{1}{ARR \text{ Upper CI}} \quad (4)$$

$$\text{Odds Ratio} = \frac{(ACL_R\#_{OA} * ACL_D\#_{NOA})}{(ACL_D\#_{OA} * ACL_R\#_{NOA})} \quad (5)$$

$$SE(\log OR) = \sqrt{\left(\frac{1}{ACL_R\#_{OA}} \right) + \left(\frac{1}{ACL_R\#_{NOA}} \right) + \left(\frac{1}{ACL_D\#_{OA}} \right) + \left(\frac{1}{ACL_D\#_{NOA}} \right)} \quad (6)$$

where

ACL_R% = percentage of ACL-R patients with OA;
ACL_D% = percentage of ACL-D patients with OA;

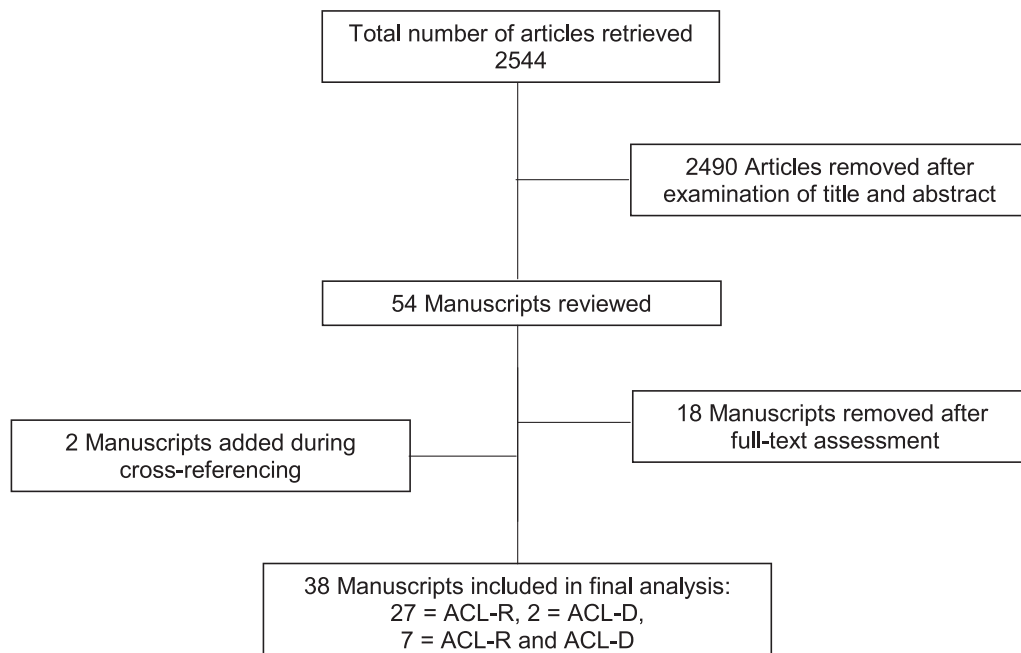


Figure 1. Search for included studies. Abbreviations: ACL-D, anterior cruciate ligament deficiency; ACL-R, anterior cruciate ligament reconstruction.

$ACL_{R\#OA}$ = number of ACL-R patients with OA;
 $ACL_{R\#NOA}$ = number of ACL-R patients without OA;
 $ACL_{D\#OA}$ = number of ACL-D patients with OA; and
 $ACL_{D\#NOA}$ = number of ACL-D patients without OA.

Assessment of Change in Physical Activity Level.

Because we were unable to characterize all confounding factors that might have led to the development of OA after ACL injury, we sought to determine if activity levels differed between the ACL-R and ACL-D patients in an attempt to identify possible group differences. The Tegner scale was used to determine the magnitude of change in physical activity level from preinjury baseline levels determined at the time of injury compared with postinjury levels at follow-up. Means and standard deviations for Tegner activity level scores were collected at baseline and follow-up time points. For studies reporting medians and ranges for Tegner scores, we used Equations 7 and 8 for conversion into means and standard deviations, respectively.²⁵ After standard deviations were converted to variance, means and variances for each study were weighted based upon sample sizes from each study. Weighted grand means and variances from baseline and follow-up time points were used to calculate standardized effect sizes (Cohen d) to determine the deleterious effects of ACL-R and ACL-D on the Tegner score (Equations 9 and 10). Preinjury and postinjury weighted means and standard deviations were then used to calculate effect sizes and 95% confidence intervals (CIs) for each group (Equations 8 and 10).

$$x \approx \frac{a + 2m + b}{4} \quad (7)$$

$$S \approx \frac{b - a}{4} \quad (8)$$

where

m = median;
 a = range minimum; and
 b = range maximum.

$$d = \frac{\text{grand mean preinjury} - \text{grand mean postinjury}}{\text{pooled SD}} \quad (9)$$

$$95\% \text{ CI} = d \pm \left(\frac{SD}{\sqrt{n}} * 1.96 \right) \quad (10)$$

where d = effect size.

RESULTS

Included Studies and Quality Assessment

Thirty-eight studies^{6,11–17,21,22,26–53} met the specified criteria and were independently rated by 2 evaluators using the Critical Appraisal Skills Program⁵⁴ to identify methodologic concerns (Table 1). If the evaluators disagreed on the methodologic quality of a study, they discussed their concerns until they agreed on a consensus score. Twenty-seven* of the included studies specifically evaluated the presence of tibiofemoral OA in patients treated with ACL-R, whereas 2 studies^{13,22} assessed OA in only ACL-D patients who received conservative treatment without reconstruction. Additionally, 9 studies† evaluated the presence of tibiofemoral OA in both ACL-R and ACL-D patient populations. Of the 38 included studies, 12 studies‡ also reported the prevalence of meniscectomy and the presence of tibiofemoral OA in ACL-R and ACL-D patients, allowing us to evaluate the effect of meniscectomy in ACL-R and ACL-D patients on the prevalence of tibiofemoral OA. One study¹⁹ was excluded because we

*References 6, 12, 15, 21, 26, 30–39, 41, 43–53.

†References 11, 14, 16, 27–29, 40, 42, 55.

‡References 11, 14, 16, 17, 22, 26, 28–31, 33, 53.

were unable to determine the presence of OA without a response from the authors. Twelve studies§ included preinjury and postinjury Tegner scores that were used to assess the change in activity level.

Point estimates and 95% CIs for all outcome measures are reported in Tables 2 through 4. Confidence intervals crossing zero or infinity were interpreted as inconclusive, whereas CIs not crossing zero or infinity were interpreted as conclusive. The mean Critical Appraisal Skills Program score was 9.23 of 12 possible points (range = 7 to 11, mode = 9, median = 9; Table 2). Using the Centre for Evidence Based Medicine guidelines,⁵⁴ which is a rating system assessing both study design and homogeneity of results, we assigned a level of 2a to the data in this review. Looking at the data overall, we assigned a level of 2a based on the homogeneous findings from the cohort studies included in the overall sample analysis (Table 3). Separating the prevalence of OA by time postinjury resulted in heterogeneous findings and a Centre for Evidence Based Medicine grade of 2a-. Similarly, after we stratified by publication year, study design, and graft type, the heterogeneous results received a Centre for Evidence Based Medicine level of 2a-.

Radiographic Assessment of Knee Osteoarthritis

All Patients Included. The 38 studies consisted of 2837 patients, including 2500 ACL-R patients and 337 ACL-D patients. Overall, patients with ACL-R demonstrated a slightly greater prevalence of knee OA than ACL-D patients, resulting in a moderate NNH with conclusive CIs (Table 3). Additionally, ARI and RRI were low and had conclusive CIs, indicating a minimal increase in risk from ACL-R (Table 3). Odds ratios demonstrated that ACL-R patients were 1.29 times (95% CI = 1.06, 1.52) more likely to have knee OA compared with the ACL-D cohort. Data pertaining to the first decade after ACL rupture yielded a very small increase in OA development in ACL-R patients over those with ACL-D patients (2%); however, the percentage of OA in ACL-D patients was 34% greater than in ACL-R patients in the third decade (Table 3). Confidence intervals for ARR and RRR in the third decade were wide but did not cross zero (Table 3).

Patients with ACL Injury and Meniscectomy. Fifty-two percent of patients who underwent ACL-R and a meniscectomy demonstrated knee OA. Of patients who underwent meniscectomy and remained ACL-D, 59% developed knee OA (Table 4). The NNT for ACL-R with meniscectomy was moderate, with inconclusive CIs (Table 4). Additionally, ARR and RRR were low, and the CI for ARR was inconclusive (Table 4). Odds ratios demonstrated that ACL-R patients who underwent a concomitant meniscectomy were less likely to have knee OA than patients who underwent a meniscectomy but had ACL-D (OR = 0.75; 95% CI = 0.31, 1.21). Patients who had ACL-R along with meniscectomy continued to show a decrease in OA in the third decade compared with ACL-D patients who had a meniscectomy, resulting in a small NNT and moderate ARR and RRR (Table 4).

Patients with Isolated ACL Injury. Overall, the prevalence of OA was higher in patients with isolated ACL-R compared with isolated ACL-D patients. For

isolated ACL-R, the NNH was small and the CIs were conclusive (Table 5). Moderate ARI and RRI with conclusive CIs were noted for patients with isolated ACL-R (Table 5). Those who underwent an isolated ACL-R were 1.73 (95% CI = 1.44, 2.02) times more likely to have OA than patients who had ACL-D. Small to moderate NNH, ARI, and RRI with inconclusive CIs for ARI and RRI were seen 1 and 3 decades after ACL injury (Table 5).

Influence of Study Design

The numbers of ACL-R and ACL-D patients were similar between retrospective and prospective designs, but ACL-D populations were significantly smaller than ACL-R populations (retrospective ACL-R n = 1455, ACL-D n = 213; prospective ACL-R n = 1099, ACL-D n = 80). Between prospective and retrospective studies, results conflicted. Prospective studies demonstrated that ACL-R patients had an increased rate of OA compared with those who remained ACL-D; NNH was small and CIs were conclusive (Table 6). Conversely, retrospective studies demonstrated that ACL-R patients had a decreased rate of OA compared with those who had ACL-D; NNT was moderate and CIs were inconclusive (Table 6).

Influence of Publication Year

We divided the study results into 3 subgroups based upon publication year (1990s, 2000s, 2010s). Only 1 study was published in the 1990s, and it assessed a small number of ACL-R patients (n = 114). For studies published between 2000 and 2009, there were significantly more ACL-R patients (n = 1105) than ACL-D patients (n = 199). A 1% ARR in OA presence was seen in the ACL-R patients compared with ACL-D patients; NNT was large and the CI crossed zero (Table 7). For studies published between 2010 and 2012, there was an increase in the presence of OA in patients who underwent ACL-R, yielding a moderate NNH with conclusive CIs (Table 7).

Influence of Graft Type Used in Reconstruction

A total of 1285 patients underwent patellar tendon autograft reconstruction, 476 underwent hamstrings tendon autograft reconstruction, and 125 underwent an open patellar tendon reconstruction. Open reconstruction using a patellar tendon graft resulted in the greatest risk of OA, and the NNH was small (7). Similarly, the arthroscopic patellar tendon autograft had a high OA prevalence, with a small NNH (10), and a conclusive CI (Table 8). Reconstruction using a hamstrings autograft demonstrated a decrease in the presence of OA when compared with the ACL-D group; the NNT was small and the CI was conclusive. However, ARI and RRI were moderate with conclusive CIs (Table 8).

Magnitude of Change in Physical Activity Level

Both ACL-R and ACL-D had a strong negative effect on the level of physical activity from the preinjury time points to follow-up, reflecting decreases in activity level (ACL-R

§References 6, 11, 13, 16, 21, 28–30, 39, 40, 42, 55.

Table 1. Details of Included Studies Extended on Next Page

Study	Study Design	Patient Population	Assessment Time Point, y
Ichiba and Kishimoto, ¹² 2009	Retrospective	ACL-R	3.9
Ferretti et al, ²⁶ 1991	Retrospective	ACL-R	5
Sajovic et al, ⁵² 2006	Prospective	ACL-R	5
Keays et al, ⁴⁵ 2007	Prospective	ACL-R	6
Liden et al, ³⁰ 2008	Retrospective	ACL-R	7
Ahlden et al, ³⁹ 2009	Retrospective	ACL-R	7
Roe et al, ⁵⁰ 2005	Retrospective	ACL-R	7
Hart et al, ²⁷ 2005	Retrospective	ACL-R	10
Mueffels et al, ⁴⁰ 2009	Retrospective	Both	10
Holm et al, ⁴³ 2010	Retrospective	ACL-R	10
Sutherland et al, ³⁸ 2010	Retrospective	ACL-R	10
Hoffelner et al, ⁴² 2012	Retrospective	ACL-R	10
van der Hart et al, ⁴⁹ 2008	Prospective	ACL-R	10.3
Hertel et al, ⁴¹ 2005	Retrospective	ACL-R	10.7
Seon et al, ³³ 2006	Prospective	ACL-R	11
Kessler et al, ¹¹ 2008	Retrospective	Both	11
Lebel et al, ³² 2008	Prospective	ACL-R	11
Sajovic et al, ⁵¹ 2011	Prospective	ACL-R	11
Cohen et al, ¹⁵ 2007	Retrospective	ACL-R	11.2
Segawa et al, ¹³ 2001	Retrospective	ACL-D	12
Lohmander et al, ¹⁴ 2004	Retrospective	Both	12
Oiestad et al, ³⁴ 2011	Prospective	ACL-R	12.1
Murray et al, ⁵³ 2012	Retrospective	ACL-R	13
Salmon et al, ⁴⁷ 2006	Retrospective	ACL-R	13
Struwer et al, ⁵ 2012	Retrospective	ACL-R	13.5
Meunier et al, ¹⁶ 2007	Prospective	Both	15
Neuman et al, ¹⁷ 2008	Prospective	Both	15
Oiestad et al, ³⁵ 2010	Prospective	ACL-R	15
Oiestad et al, ³⁶ 2010	Prospective	ACL-R	15
Hui et al, ⁴⁴ 2011	Retrospective	ACL-R	15
Streich et al, ²⁸ 2011	Retrospective	Both	15
Bourke et al, ³⁷ 2012	Retrospective	ACL-R	15
Drogset et al, ⁴⁶ 2006	Prospective	ACL-R	16
Selmi et al, ³¹ 2006	Retrospective	ACL-R	17
Mihelic et al, ²⁹ 2011	Retrospective	Both	17
Ventura et al, ²¹ 2010	Prospective	ACL-R	19
Strand et al, ⁴⁸ 2005	Retrospective	ACL-R	23
Nebelung et al, ²² 2005	Retrospective	ACL-D	35

Abbreviations: ACL-D, anterior cruciate ligament deficient; ACL-R, anterior cruciate ligament reconstruction; HS, hamstrings; IKDC, International Knee Documentation Committee; N/A, not applicable; OA, osteoarthritis; PT, patellar tendon.

$d = -0.90$, 95% CI = $-0.77, -1.133$; ACL-D $d = -1.13$, 95% CI = $-0.96, -1.29$.

DISCUSSION

It is estimated that 12% of the United States population has diagnosed knee OA.⁵⁶ For patients with ACL injury, however, the OA percentage is much greater than that for the overall population and can be as high as 60% to 90%.¹⁶ Our results provide further evidence of a similarly high prevalence of OA after ACL injury. In the total sample, the percentage of patients with knee OA was slightly increased in patients who underwent ACL-R (44%) compared with those who had ACL-D (37%), demonstrating an RRI of 7%. Specifically, those patients with patellar tendon reconstruction technique demonstrated the highest prevalence of OA, with minimal difference in OA between open (49%) and arthroscopic (47%) procedures. However, patients who had ACL-R with a concomitant meniscectomy displayed a definitive reduction in OA prevalence compared with those who remained ACL-D and underwent a meniscectomy.

In the first decade after injury, the ACL-R group continued to show a greater prevalence of OA (36%) than

the ACL-D group (34%), with this trend continuing into the second decade after ACL injury. In the third decade after injury, ACL-D patients had a significantly greater rate of OA compared with ACL-R patients, but only a small cohort of ACL-D patients was assessed during this time. These results seem to suggest that ACL-R may decrease the likelihood of maintaining long-term joint health compared with ACL-D. Additionally, it should be noted that decrements in physical activity were similar between ACL-R and ACL-D cohorts. Although we cannot identify other confounding differences between cohorts that might have led to OA, the reductions in physical activity were likely not a factor.

Similarly, the subset of patients with isolated ACL-R and no concomitant meniscectomy were 1.73 times more likely to develop OA than ACL-D patients with an isolated ACL injury. Our results demonstrate that ACL-R was not an adequate prophylactic intervention for decreasing knee OA development after an isolated ACL rupture. However, it is possible that these patients sustained meniscal damage that did not require a meniscectomy and was not reported by the authors. Anterior cruciate ligament reconstruction is

Table 1. Extended From Previous Page

Graft Type	Total No. of Patients	No. of Patients With/Without OA	OA Grading System and Inclusion of OA
PT autograft	ACL-R = 49	28/21	International Cartilage Repair Society
HS autograft	ACL-R = 114	29/85	Fairbank 3 or 4
HS and PT autograft	ACL-R = 54	18/36	IKDC B or C
HS and PT autograft	ACL-R = 56	26/30	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 58	25/33	Ahlbach 2–4
HS and PT autograft	ACL-R = 44	30/14	Fairbank 3 or 4
HS and PT autograft	ACL-R = 53	31/22	IKDC B or C
PT autograft	ACL-R = 31	9/22	Ahlbach 2 or 3
PT autograft	ACL-R = 25 ACL-D = 25	ACL-R = 12/13 ACL-D = 7/18	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 57	34/23	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 79	36/43	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 28	15/13	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 28	13/15	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 67	25/42	IKDC C or D
PT autograft	ACL-R = 58	25/33	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 60 ACL-D = 49	ACL-R = 27/33 ACL-D = 12/37	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 101	18/83	IKDC C or D
HS and PT autograft	ACL-R = 52	38/14	IKDC B or C
PT autograft	ACL-R = 62	24/38	Fairbank 3 or 4
N/A	ACL-D = 36	11/25	Kellgren and Lawrence 2 or 3
N/A	ACL-R = 41 ACL-D = 26	ACL-R = 23/18 ACL-D = 11/15	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 164	114/50	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 83	28/55	IKDC B or C
PT autograft	ACL-R = 43	11/32	IKDC B or C
PT autograft	ACL-R = 73	40/33	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 42 ACL-D = 36	ACL-R = 17/25 ACL-D = 11/25	Ahlback and Fairbank 2 or 3
N/A	ACL-R = 17 ACL-D = 44	ACL-R = 6/11 ACL-D = 13/31	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 181	133/48	Kellgren and Lawrence 2 or 3
HS and PT autograft	ACL-R = 210	149/61	Kellgren and Lawrence 2 or 3
PT autograft	ACL-R = 90	46/44	IKDC B or C
PT autograft	ACL-R = 40 ACL-D = 40	ACL-R = 25/15 ACL-D = 22/18	IKDC C or D
HS autograft	ACL-R = 117	8/109	IKDC C or D
HS and PT autograft, allograft	ACL-R = 85	9/76	Ahlbach
Open PT	ACL-R = 89	24/65	IKDC C or D
Open PT	ACL-R = 36 ACL-D = 18	ACL-R = 23/13 ACL-D = 10/8	IKDC C or D
Synthetic allograft, PT autograft	ACL-R = 51	51/0	Ahlbach
N/A	ACL-R = 61	9/53	IKDC C or D
N/A	ACL-D = 19	18/1	Ahlbach

performed at a rate of approximately 250 000 cases per year.² The cost of ACL-Rs, including diagnosis, surgery and rehabilitation, is around \$17 000, with a total annual cost of approximately \$3 billion in the United States.⁴ These data demonstrate the low potential that ACL-R offers prophylactic benefit in maintaining long-term joint health. The entire data set demonstrated an NNH of 16, suggesting that for every 16 patients that undergo ACL-R, 1 more patient will develop OA compared with the ACL-D group. This relatively low NNH indicates the increased risk for developing OA after reconstruction compared with remaining ACL-D.

When an ACL injury occurs in combination with meniscal damage warranting a meniscectomy, performing an ACL-R along with meniscectomy may be beneficial for reducing the risk of OA. In meniscectomy patients, ACL-R and meniscectomy decreased the rate of knee OA by 7% compared with ACL-D patients who received a meniscectomy; however, the CI for ARR crossed zero. This trend continued in the third decade postinjury, with ACL-R and meniscectomy patients exhibiting 61% less OA than patients with ACL-D and meniscectomy. However, it should be noted that results in the third decade postsurgery

were extrapolated from only 1 study²² that had a small sample size of ACL-D patients at the farthest time from injury (35 years). This may be further evidence that the meniscus is a vital component of maintaining joint health and that removing the meniscus can decrease force transmission and increase degeneration of bony tissue,¹⁸ which may be hastened by an unreconstructed ACL rupture. Isolated meniscectomy has previously been shown to increase the risk of developing knee OA.⁵ It has been suggested that removing a portion of the meniscus may decrease the ability to attenuate energy within the knee joint.¹⁸ Additionally, partial meniscectomy has been associated with decreased quadriceps strength, which may alter lower extremity biomechanics and complicate the already decreased ability to attenuate energy at the knee.⁵⁷ We found that in patients with ACL rupture and meniscal damage, ACL-R and meniscectomy demonstrated greater prophylactic benefits in decreasing knee OA than in those with ACL-D who underwent meniscectomy.

Isolated ACL-R increased the risk of knee OA compared with ACL-D patients within the entire population as well as in each decade after injury. This increased risk of OA may be evidence that although ACL-R is effective in restoring

Table 2. Methodologic Assessment for All Included Studies

Study	Critical Appraisal Skills Program Score: Methodologic Assessment
Ichiba and Kishimoto, ¹² 2009	9: Cohort not recruited in acceptable way, outcome not accurately measured to minimize bias, results cannot be applied to general population
Ferretti et al, ²⁶ 1991	8: Exposure not accurately measured to minimize bias, confounding factors not identified, results cannot be applied to general population, results do not fit with other available evidence
Sajovic et al, ⁵² 2006	11: Results cannot be applied to general population
Keays et al, ⁴⁵ 2007	8: Cohort not recruited in acceptable way, outcome not accurately measured to reduce bias, results are not precise, results cannot be applied to general population
Liden et al, ³⁰ 2008	8: Cohort not recruited in acceptable way, exposure not accurately measured to minimize bias, confounding factors not identified, results cannot be applied to general population
Ahlden et al, ³⁹ 2009	9: Cohort not recruited in acceptable way, confounding factors not identified, confounding factors not accounted for
Roe et al, ⁵⁰ 2005	10: Results cannot be applied to general population, confounding factors not identified
Hart et al, ²⁷ 2005	8: Cohort not recruited in acceptable way, confounding factors not identified, results cannot be applied to general population, results do not fit with other evidence
Mueffels et al, ⁴⁰ 2009	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
Holm et al, ⁴³ 2010	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
Sutherland et al, ³⁸ 2010	10: Confounding factors not accounted for, results not applied to general population
Hoffelner et al, ⁴² 2012	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
van der Hart et al, ⁴⁹ 2008	11: Confounding factors not accounted for
Hertel et al, ⁴¹ 2005	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
Seon et al, ³³ 2006	9: Cohort not recruited in acceptable way, confounding factors not identified, results cannot be applied to general population
Kessler et al, ¹¹ 2008	8: Cohort not recruited in acceptable way (ie, body mass index), no blinding, confounding factors not identified, results cannot be applied to general population
Lebel et al, ³² 2008	7: Cohort not recruited in acceptable way, confounding factors not identified, results not precise, results not believable, results do not fit with other evidence
Sajovic et al, ⁵¹ 2011	11: Results cannot be applied to general population
Cohen et al, ¹⁵ 2007	9: No control comparison, no definite data to support conclusions, results cannot be applied to general population
Segawa et al, ¹³ 2001	9: Cohort not recruited in acceptable way, confounding factors not identified, high dropout rate
Lohmander et al, ¹⁴ 2004	10: Exposure not accurately measured, results cannot be applied to general population
Oiestad et al, ³⁴ 2011	10: Confounding factors not accounted for, results cannot be applied to general population
Murray et al, ⁵³ 2012	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
Salmon et al, ⁴⁷ 2006	11: Confounding factors not accounted for
Struwer et al, ⁶ 2012	10: Confounding factors not accounted for, results cannot be applied to general population
Meunier et al, ¹⁶ 2007	8: Cohort not recruited in acceptable way, outcome not accurately measured to minimize bias, confounding factors not accounted for
Neuman et al, ¹⁷ 2008	9: Results are not precise, cannot be applied to general population, results are not believable
Oiestad et al, ³⁵ 2010	11: Confounding factors not accounted for
Oiestad et al, ³⁶ 2010	10: Confounding factors not accounted for, results cannot be applied to general population
Hui et al, ⁴⁴ 2011	9: Confounding factors not identified, cohort not recruited in acceptable way, results cannot be applied to general population
Streich et al, ²⁸ 2011	10: Results are not precise, cannot be applied to general population
Bourke et al, ³⁷ 2012	11: Confounding factors not accounted for
Drogset et al, ⁴⁶ 2006	10: Results do not fit with other available evidence, results cannot be applied to general population
Selmi et al, ³¹ 2006	10: Confounding factors not identified, results cannot be applied to general population
Mihelic et al, ²⁹ 2011	7: Cohort not recruited in acceptable way, confounding factors not identified, results not precise, results not believable
Ventura et al, ²¹ 2010	9: Confounding factors not identified, outcome not accurately measured to reduce bias, results cannot be applied to general population
Strand et al, ⁴⁸ 2005	9: Results do not fit with other available evidence, results cannot be applied to general population, confounding factors not accounted for
Nebelung et al, ²² 2005	7: Cohort not recruited in acceptable way, outcome was not measured correctly to minimize bias, confounding factors not identified, results cannot be applied to general population, results do not fit with other evidence

joint stability after injury, it may not be the most efficient treatment in decreasing the development of posttraumatic OA when the ACL is the only involved structure. An NNH of 9 suggests that for every 9 patients undergoing ACL-R, 1

additional patient will develop knee OA compared with the ACL-D group. Although ACL-R is common for much of the population incurring ACL injury in the United States, it is not the standard of care in countries other than the United

Table 3. Osteoarthritis Data for All Patients in Included Studies

	Anterior Cruciate Ligament Reconstruction	Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)	Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	Relative Risk Reduction (RRR), %; Relative Risk Increase (RRI), % (95% Confidence Interval)
Total					
No. of patients	2500	337	NNH = 16 (NNH = 208 to 9)	ARI = 6 (ARI = 12 to 0.5)	RRR = 16 (RRI = 22 to 11)
No. OA/NOA	1088/1412	126/211			
% OA	44	37			
Decade 1, 0–10 y					
No. of patients	795	53	NNH = 50 (NNH = 7 to ∞ to NNT = 9)	ARI = 2 (ARI = 15 to ARR = 11)	RRI = 6 (RRI = 20 to RRR = 7)
No. OA/NOA	286/527	18/35			
% OA	36	34			
Decade 2, 11–18 y					
No. of patients	1468	247	NNH = 7 (NNH = 12 to 5)	ARI = 15 (ARI = 21 to 8)	RRI = 48 (RRI = 54 to 41)
No. OA/NOA	702/766	80/167			
% OA	48	32			
Decade 3, 19–35 y					
No. of patients	237	37	NNT = 3 (NNH = 2 to 6)	ARR = 33 (ARR = 48 to 18)	RRR = 44 (RRR = 59 to 29)
No. OA/NOA	100/137	28/9			
% OA	42	76			

Abbreviations: NOA, no osteoarthritis; OA, osteoarthritis.

Table 4. Osteoarthritis Data for Patients with Anterior Cruciate Ligament Injury and Meniscectomy

	Anterior Cruciate Ligament Reconstruction	Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)	Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	Relative Risk Reduction (RRR), %; Relative Risk Increase (RRI), % (95% Confidence Interval)
Total					
No. of patients	451	94	NNT = 15 (NNH = 24 to ∞ to NNT = 6)	ARR = 7 (ARI = 4 to ARR = 18)	RRR = 11 (RRR = 0.04 to 22)
No. OA/NOA	234/217	55/39			
% OA	52	59			
Decade 1, 0–10 y					
No. of patients	81	N/A	N/A	N/A	N/A
No. OA/NOA	31/50	N/A			
% OA	38	N/A			
Decade 2, 11–18 y					
No. of patients	288	76	NNH = 9 (NNH = 4 to ∞ to NNT = 64)	ARI = 11 (ARI = 24 to ARR = 2)	RRI = 22 (RRI = 10 to 35)
No. OA/NOA	176/112	38/38			
% OA	61	50			
Decade 3, 19–35 y					
No. of patients	82	19	NNT = 2 (NNH = 1 to 4)	ARR = 41 (ARR = 26 to 56)	RRR = 65 (RRR = 50 to 80)
No. OA/NOA	27/55	18/1			
% OA	33	94			

Abbreviations: N/A, not applicable; NOA, no osteoarthritis; OA, osteoarthritis.

Table 5. Osteoarthritis Data for Patients with Isolated Anterior Cruciate Ligament Injury

	Anterior Cruciate Ligament Reconstruction	Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)	Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	Relative Risk Reduction (RRR), %; Relative Risk Increase (RRI), % (95% Confidence Interval)
Total					
No. of patients	2094	243	NNH = 9 (NNH = 17 to 6)	ARI = 12 (ARI = 18 to 6)	RRR = 43 (RRI = 37 to 49)
No. OA/NOA	854/1195	71/172			
% OA	42	29			
Decade 1, 0–10 y					
No. of patients	714	53	NNH = 57 (NNH = 7 to ∞ to NNT = 9)	ARI = 2 (ARI = 15 to ARR = 11)	RRR = 5 (RRI = 18 to RRR = 8)
No. OA/NOA	255/459	18/35			
% OA	36	34			
Decade 2, 11–18 y					
No. of patients	1180	171	NNH = 5 (NNH = 8 to 4)	ARI = 20 (ARI = 27 to 12)	RRR = 80 (RRI = 87 to 73)
No. OA/NOA	526/654	42/129			
% OA	45	25			
Decade 3, 19–35 y					
No. of patients	155	19	NNT = 9 (NNH = 8 to ∞ to NNT = 3)	ARR = 11 (ARI = 13 to ARR = 35)	RRR = 19 (RRI = 5 to RRR = 43)
No. OA/NOA	73/82	11/8			
% OA	47	57			

Abbreviations: NOA, no osteoarthritis; OA, osteoarthritis.

Table 6. Osteoarthritis Data for Patients by Study Design

Study Design	Anterior Cruciate Ligament Reconstruction	Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)	Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	Relative Risk Reduction (RRR), %; Relative Risk Increase (RRI), % (95% Confidence Interval)
Retrospective studies					
No. of patients	1455	213	NNT = 24 (NNH = 32 to ∞ to NNT = 9)	ARR = 4 (ARI = 3 to ARR = 11)	RRR = 10 (RRI = 3 to 17)
No. OA/NOA	562/893	91/122			
% OA	39	43			
Prospective studies					
No. of patients	1099	80	NNH = 4 (NNH = 7 to 2)	ARI = 26 (ARI = 36 to 16)	RRR = 87 (RRI = 97 to 77)
No. OA/NOA	617/482	24/56			
% OA	56	30			

Abbreviations: NOA, no osteoarthritis; OA, osteoarthritis.

Table 7. Osteoarthritis Data for Patients by Publication Year

Publication Year	Anterior Cruciate Ligament Reconstruction	Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)	Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	Relative Risk Reduction (RRR), %; Relative Risk Increase (RRI), % (95% Confidence Interval)
1990–1999					
No. of patients	114	N/A	N/A	N/A	N/A
No. OA/NOA	29/85	N/A			
% OA	25	N/A			
2000–2009					
No. of patients	1105	199	NNT = 230 (NNH = 15 to ∞ to NNT = 13)	ARR = 1 (ARI = 7 to ARR = 8)	RRR = 1.2 (RRI = 6 to RRR = 8)
No. OA/NOA	395/710	72/127			
% OA	35	36			
2010–2012					
No. of patients	1327	58	NNH = 30 (NNH = 38 to 22)	ARI = 3 (ARI = 16 to ARR = 10)	RRI = 6 (RRI = 19 to RRR = 7)
No. OA/NOA	776/551	32/26			
% OA	58	55			

Abbreviations: N/A, not applicable; NOA, no osteoarthritis; OA, osteoarthritis.

Table 8. Osteoarthritis Data for Patients by Graft Type

Graft Type	Anterior Cruciate Ligament Reconstruction		Anterior Cruciate Ligament Deficiency	Number Needed to Treat to Benefit (NNT); Number Needed to Treat to Harm (NNH) (95% Confidence Interval)		Absolute Risk Reduction (ARR), %; Absolute Risk Increase (ARI), % (95% Confidence Interval)	
	No.	%		NNT	NNH	ARR	RRI
Patellar tendon autograft							
No. of patients	1285		337	NNH = 10 (NNH = 32–7)	ARI = 9 (ARI = 14–3)	RRI = 26 (RRI = 32–20)	
No. OA/NOA	606/679		126/211				
% OA	47		37				
Hamstrings autograft							
No. of patients	476		337	NNT = 12 (NNT = 5–42)	ARR = 9 (ARR = 2–16)	RRR = 21 (RRR = 14–28)	
No. OA/NOA	140/336		126/211				
% OA	29		37				
Open patellar tendon autograft							
No. of patients	141		337	NNH = 7 (NNH = 4–23)	ARI = 14 (ARI = 5–24)	RRI = 38 (RRI = 28–48)	
No. OA/NOA	73/68		126/211				
% OA	51		37				

Abbreviations: NOA, no osteoarthritis; OA, osteoarthritis.

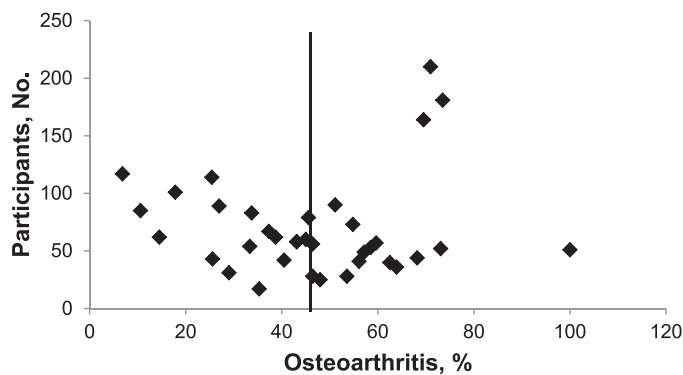


Figure 2. Anterior cruciate ligament reconstruction publication bias. Vertical line indicates mean prevalence (%) of osteoarthritis among all studies.

States.⁵⁸ Early reconstruction may not be more advantageous in improving patient-reported outcomes compared with conservative treatment with delayed reconstruction.⁵⁹ Therefore, conservative treatment for patients with isolated ACL ruptures may be prudent before deciding whether to reconstruct the ligament. More patients with isolated ACL ruptures may be able to cope without an intact ligament. Many factors enter into the decision to undergo ACL-R or conservative treatment, and the risk of OA development should be a major concern. If isolated ACL-D patients are able to achieve their desired physical activity levels and accomplish activities of daily living, they may benefit from conservative treatment rather than ACL-R. Copers are patients who can remain ACL-D and return to preinjury levels of physical activities without reconstruction.³ Noncopers are not able to return to preinjury levels of activity and are likely to benefit from ACL-R to regain normal arthrokinematics before returning to full activity.³ It may be more cost-effective to screen and treat noncopers with ACL-R as a matter of ACL injury management. Recent evidence⁶⁰ has suggested that the functional status of the knee after ACL rupture may indicate if a patient is a better candidate for repair than conservative treatment. However, most young athletes forego an initial bout of conservative treatment in order to immediately regain ligamentous stability of the knee and return to activity as soon as possible. Determining if a patient can cope with ACL-D may save health care costs, reduce time spent recovering from surgery, and prolong long-term joint health after injury.

Although ACL-D patients demonstrated a greater decrease in physical activity than ACL-R patients after injury, the 2 were not significantly different from each other because their CIs overlapped. Because this decrease in physical activity was statistically similar among ACL-R and ACL-D patients, altered levels of physical activity may not be the most critical factor to explain the development of OA after ACL injury with similar risks in reconstructed and deficient patients.

Most studies had a wide range of patient populations, ages, activity levels, and follow-up times, but not all authors reported all demographics,^{11,16,17,26,29} which made comparisons among studies difficult. Because of the differences in study design and outcomes assessed in individual studies, we were unable to determine if all potential OA risk factors were similar between ACL-R and

ACL-D patients. Although not knowing the equivalency of risk between groups remains a limitation to the current study, we found that each group displayed a similar magnitude of decreased activity. The number of ACL-R patients was significantly greater ($n = 2500$) than the ACL-D patients ($n = 337$), which may reflect the bias in standard-of-care practices and might have affected the variability in our calculations. In addition, a very small number of patients were assessed during the third decade after ACL injury. This could indicate a lack of information about patient outcomes beyond the first 2 decades postinjury or possible publication bias against the studies with a follow-up greater than 20 years. Different ACL-R procedures could lead to differences in OA development, as it has been reported⁶¹ that graft types affect patient outcomes. Anterior cruciate ligament reconstruction with a hamstrings tendon graft has demonstrated better self-reported function and decreased anterior knee pain compared with reconstruction with a patellar tendon graft.⁶² In a recent study by Frobell et al,⁶³ patients reconstructed with a patellar tendon graft demonstrated a significant increase in patellofemoral OA but not tibiofemoral OA compared with patients who received hamstrings tendon grafts, suggesting that graft choice and the potential effects on long-term joint health should be considered when patients elect to undergo ACL-R. With regard to the relationship between OA development and the type of graft used for reconstruction, hamstrings autografts seem to be associated with lower OA prevalence and lower NNT than other graft types, which may indicate the importance of graft selection for patients undergoing reconstruction.

Also, recent advancements in the ACL-R procedure may lead to different outcomes than the older procedures used in the reviewed studies. Publication dates ranged from 1991 through 2011; therefore, a large range of techniques was likely used in these studies. Articles published after 2010 demonstrated more OA in patients undergoing ACL-R than in ACL-D patients compared with articles published between 2000 and 2009. However, the studies published between 2010 and 2012 had small cohorts of ACL-D patients ($n = 58$) and also tended to have longer follow-up times (mean = 13.6 years) after injury, during which the rate of OA would be expected to increase. Radiographic OA grading scales were also not consistent across all studies (Table 1); however, we were not concerned about the grade of OA in this study but rather the presence of the disease. Authors of all included studies diagnosed OA through radiologic examination. Although OA was graded using different scales, the criteria for determining OA were consistent across all scales.

Both ACL-R (Figure 2) and ACL-D (Figure 3) studies had the potential for publication bias, as shown by the skewness of the funnel plots. Skewness of the plots may be due to small sample sizes or participant-recruitment processes.

The demonstrated publication bias suggests that investigations with results yielding greater increases in OA development after ACL-R may be less likely to be published. Specifically, the ACL-R funnel plot demonstrates that the studies with the greatest sample sizes were to the right of the mean. This may indicate that even though these studies had the greatest sample sizes, they did not represent the entire ACL-R population. Furthermore,

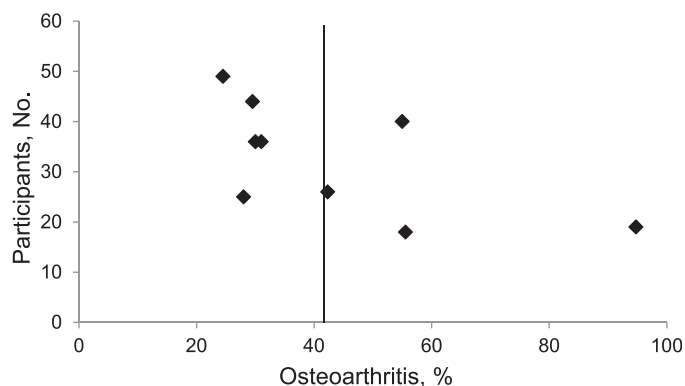


Figure 3. Anterior cruciate ligament deficiency publication bias. Vertical line indicates mean prevalence (%) of osteoarthritis among all studies.

authors of 2 of the studies^{26,30} with the highest numbers of participants did not report patient demographics, which could have led to selection bias if only the patients with the best outcomes were included. The ACL-D funnel plot identified 1 potential outlier²²; according to that report, 98% of patients developed knee OA 35 years postinjury. This study had a small sample size ($n = 19$) and evaluated outcomes at the longest time postinjury, thus potentially reflecting publication bias in indicating worse OA outcomes after ACL-D. More than half of the included articles were retrospective in nature, which may have led to greater variability in the measures of OA development after ACL injury. Retrospective designs showed a decreased risk of OA development in patients undergoing ACL-R compared with the ACL-D group. Conversely, prospective designs showed more OA in patients undergoing ACL-R than in the ACL-D cohort, with an NNH of 4.

Furthermore, we were unable to identify the individual factors that resulted in a patient's choice to reconstruct or not. Another factor that may influence outcomes is the effectiveness of nonsurgical rehabilitation after injury. It is difficult to determine if OA development is mainly explained by factors related to the surgical intervention or if the nonsurgical rehabilitation performed after ACL-R and ACL-D is critical in obtaining optimal therapeutic outcomes.

In conclusion, the current literature does not provide substantial evidence to suggest that ACL-R is an adequate intervention to prevent knee OA. Overall, the risk of knee OA was slightly higher in patients undergoing ACL-R than in the ACL-D group, with ACL-R resulting in an NNH of 16. Isolated ACL-R increased the risk of OA, yielding an NNH of 8. With regard to OA prevalence, the only patients benefiting from ACL-R were those undergoing concomitant meniscectomy with reconstruction, compared with ACL-D patients undergoing meniscectomy, with an NNT of 15; however, the CIs were inconclusive. Although both populations demonstrated decreased activity levels, they did not differ from each other, showing that decreased activity level may not be a confounding factor for OA development when comparing ACL treatment options. These analyses may provide evidence for clinicians working with young athletes that the long-term goal of prolonging joint health after ACL injury is of critical importance.

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