JBJS REVIEWS

# Prevention of Anterior Cruciate Ligament Rupture in Female Athletes

## A Systematic Review

Rey N. Ramirez, MD

Keith Baldwin, MD, MPH, MSPT

Corinna C.D. Franklin, MD

*Investigation performed at Shriners Hospital of Philadelphia and Children's Hospital of Philadelphia, Philadelphia, Pennsylvania*

**Background:** A number of reports have been published on the effectiveness and design of intervention programs for the prevention of rupture of the anterior cruciate ligament (ACL) in female athletes. The purpose of this study was to systematically review the literature to determine the effectiveness of neuromuscular training programs in preventing ACL injury in female athletes.

**Methods:** A systematic review was performed with use of the PubMed, MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases. The search terms included "anterior cruciate ligament" and "ACL" combined with "prevention" and "intervention." The searches included material indexed by September 30, 2013. Data concerning study design, the characteristics of participants, the details of the neuromuscular programs, the types of sports, and number of ACL ruptures were extracted from the studies. Study heterogeneity was assessed with funnel plot and Egger regression methods. Pooled effects were calculated with use of a DerSimonian-Laird random-effects model. The number needed to treat was calculated on the basis of pooled incidence data.

**Results:** The risk of ACL rupture was 1.83 times higher for female athletes who did not participate in neuromuscular ACL-prevention training programs (odds ratio [OR], 1.83; 95% confidence interval [95% CI], 1.08 to 3.10; $p = 0.02$). In studies that focused exclusively on soccer, the risk of ACL rupture was 2.62 times higher for nonparticipating athletes (OR, 2.62; 95% CI, 1.59 to 4.32; $p < 0.01$). When the data were analyzed according to the timing of the intervention, no significant effects were found. In studies in which the program took place both preseason and in-season, the risk (odds ratio) of ACL rupture for nonparticipating athletes was 2.34 (95% CI, 0.82 to 6.7; $p = 0.11$). In studies in which the intervention took place in-season only, the risk (odds ratio) of ACL rupture for nonparticipating athletes was 1.25 (95% CI, 0.23 to 6.75; $p = 0.8$). The number needed to treat to prevent a single ACL rupture was 128.7 athletes. We found no significant heterogeneity among the included studies. The $I^2$ value was 35.40% ($p = 0.11$). No significant publication bias was found in our included studies.

**Conclusions:** The results of this systematic review and meta-analysis favor a protective effect of neuromuscular training programs on the risk of ACL rupture in female athletes. This protective effect is more pronounced in

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soccer players. Additional research is needed to design the optimal training program.

**Level of Evidence:** Therapeutic Level II. See Instructions to Authors for a complete description of levels of evidence.

It has been estimated that approximately 100,000 injuries of the anterior cruciate ligament (ACL) occur each year in the United States[1]. These injuries can be immediately debilitating to athletes and can increase the risk of future osteoarthritis[2,3]. ACL injuries are of particular concern to female athletes, who carry a four to six times increased risk of ACL rupture compared with their male counterparts[4]. Female athletes are estimated to sustain 0.06 to 0.24 ACL tear per 1000 hours of exposure in a variety of sports, with a rate as high as 0.9 per 1000 hours during a soccer game[5]. In the four decades since the passage of Title IX, there has been a dramatic increase in the participation of girls and women in sports—a tenfold increase in high school and a fivefold increase in college[2]—leading to a corresponding increase in ACL tears in female athletes.

A variety of factors have been suggested to play a role in the increased risk of ACL rupture in female athletes. Anatomic differences in the notch and excess ligamentous laxity as well as the effects of estrogen on ligaments have been proposed as possible explanations[2]. In addition, much recent work has focused on the identification of modifiable risk factors in order to attempt to ameliorate the risk of ACL injury in women and girls; because the vast majority of these injuries are noncontact injuries, they are at least theoretically avoidable[6]. Female athletes are thought to have increased valgus moments and angles at the knee along with greater quadriceps dominance and diminished flexion at the hip and knee[7,8]. Attempts to modify these factors have led to the design and implementation of training programs to reduce ACL injuries in female athletes who participate in a variety of sports.

In 1996, Caraffa et al. performed a study in which they demonstrated that proprioceptive training could reduce ACL injuries in soccer players[9]. While that study did not focus on female athletes, many subsequent studies, often exclusively involving women and girls, have described the results of proprioceptive or neuromuscular training programs designed to reduce the incidence of ACL injury. The purpose of this analysis was to systematically review the available studies describing the effects of ACL prevention programs in female athletes and to evaluate whether these programs are effective in reducing ACL injuries.

## Materials and Methods

A systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement[10].

### *Search Strategy*

We performed an electronic search of the PubMed, MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) databases on September 30, 2013. The search terms included "anterior cruciate ligament" and "ACL" combined with "prevention" and "intervention." The search was not restricted by language or date. We then performed a meta-analysis of the pooled data from eligible studies to answer our study questions.

### *Eligibility Criteria*

Studies that were published in the English language and that involved prospective controlled trials of interventions to prevent ACL injury in women were eligible. Studies involving patients of both sexes were included if sufficient data were included to determine the separate effects on women. Interventions had to include neuromuscular training programs. Studies evaluating functional braces as prophylaxis against ACL injury were not included.

### *Study Selection*

Two authors (R.N.R. and C.C.D.F.) performed all study reviews in parallel. The first pass involved screening of the studies by title. The second pass involved a review of abstracts. The third pass involved a review of the full text. These three steps were repeated for potentially relevant studies listed in the bibliographies of the selected studies. This process was repeated recursively until no additional studies were identified. Efforts were made to be broadly inclusive at each level. At each level of screening, the remaining list of studies was compared between the two authors reviewing the studies (R.N.R. and C.C.D.F.). A study was subjected to the next level of review if either author determined that it met the criteria for inclusion. The final set of included studies was determined on the basis of a full-text review and agreement of all authors.

### *Extraction of Relevant Data*

Data concerning study design, the characteristics of participants, details of the neuromuscular programs, the types of sports, and the number of ACL ruptures were extracted from the studies.

### *Publication Bias*

Publication bias is the tendency for studies showing zero or negative effects to remain unpublished. This bias tends to skew the set of studies available for meta-analysis. Studies included in the meta-analysis were analyzed for publication bias on the basis of a funnel plot as well as the weighted regression technique of Egger et al.[11]. Funnel plots rely on the assumption that larger studies have more precision for calculating actual effects. Plotting calculated effect on the x axis against sample size on the y axis generates a funnel-shaped plot that narrows onto the actual effect with increasing sample size. Asymmetry in the plot suggests "missing" studies. The weighted regression technique described

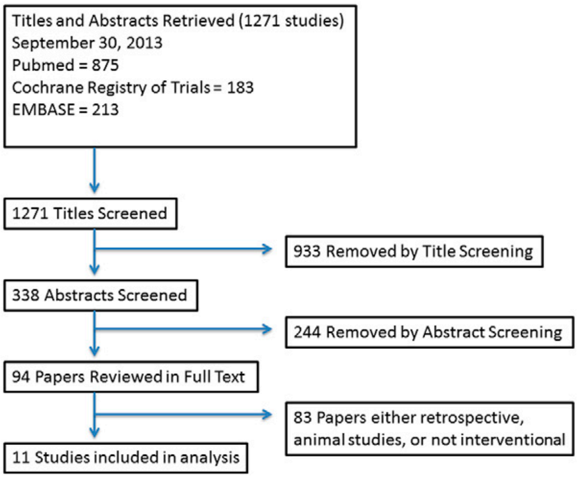


Fig. 1
Flowchart demonstrating the strategy that was used to select studies for inclusion in the systematic review.

by Egger et al. is a quantitative method to assess this asymmetry.

### *Study Heterogeneity*

Heterogeneity refers to differences in the true effects being measured when there is variation between studies in terms of design and conduct as well as in terms of participants and interventions. The presence of study heterogeneity was assessed qualitatively with the Cochrane Q test and quantitatively with the $I^2$ index[12].

### *Quantitative Data Analysis*

Data from the included studies were pooled to calculate a pooled risk ratio and risk difference with use of a DerSimonian-Laird random-effects model[13]. This method provides a weighted average of the calculated risks while assuming considerable study heterogeneity. A random-effects model was chosen on the basis of the high variability of the included studies in terms of methodology as well as the level of heterogeneity as calculated with the $I^2$ index.

Data were analyzed with use of Mix 2.0 (Bax L: MIX 2.0 – Professional software for meta-analysis in Excel. Version 2.0.1.4. BiostatXL, 2011. http://www.meta-analysis-made-easy.com).

## Results

### *Included Studies*

Our initial search retrieved 1271 studies, of which 933 were removed after title screening. The abstracts of the remaining 338 studies were reviewed, and 244 were removed. Ninety-four full papers were reviewed, and eighty-three were removed because they were retrospective studies, were animal studies, or were not interventional studies. Ultimately, eleven studies were found to be appropriate for inclusion (Fig. 1). The following is a brief summary of the included studies and their results.

Hewett et al.[14] prospectively compared two groups of female athletes (including one group in which the athletes participated in a neuromuscular training program and one group in which they did not) as well as a group of untrained male athletes. The program consisted of flexibility, plyometrics, and weight-training and took place during the preseason. The incidence of ACL injury was two of 366 in the trained group, compared with five of 463 in the control group.

Heidt et al.[15] evaluated the injury rates in a group of forty-two female high school players who participated in a preseason conditioning program and a control group of 258 players who were not conditioned. The program included cardiovascular conditioning, plyometric work, resistance cord drills, and strength and flexibility exercises. The incidence of ACL injury was one of forty-two in the trained group, compared with eight of 258 in the control group.

Söderman et al.[16] performed a prospective, randomized trial in which sixty-two female soccer players performed balance-board exercises in season and seventy-eight players served as controls. The rate of ACL injury was four of sixty-two in the intervention group, compared with one of seventy-eight in the control group.

Petersen et al.[17] performed a prospective case-controlled study of female handball players to examine the effects of a program that included balance board and jumping exercises that were performed both before and during the season. The rate of ACL injury was one of 134 in the trained group, compared with five of 142 in the control group.

Mandelbaum et al.[18], in a study involving a cohort of female soccer players, examined the effect of a program involving stretching, strengthening, plyometrics, and agility exercises. The rate of ACL injury was six of 1885 in the intervention group, compared with sixty-seven of 3818 in the control group.

Pfeiffer et al.[19] performed a prospective cohort study to examine whether a plyometric program would decrease the incidence of noncontact ACL injury in female soccer, basketball, and volleyball players. This study did not demonstrate a difference; the rate of noncontact ACL injury was three of 577 in the intervention group, compared with three of 862 in the control group.

Steffen et al.[20] performed a cluster-randomized controlled trial to determine whether a set of exercises focusing on core stability, lower extremity strength, neuromuscular control, and agility would reduce the rate of ACL injuries in female soccer players. The

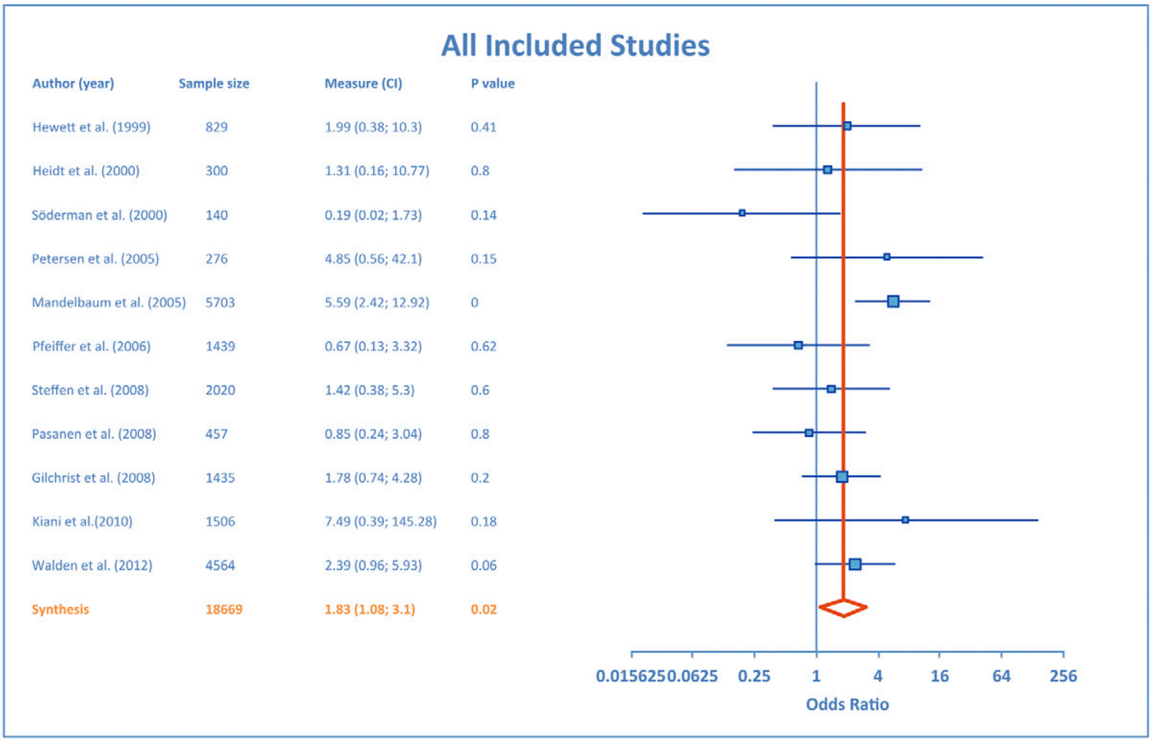


Fig. 2

Forest plot comparing the risk of ACL rupture for female athletes who did not participate in neuromuscular training programs with the risk for those who did. The odds ratio is plotted on the x axis on a logarithmic scale. The pooled odds ratio of 1.83 is represented by the vertical orange line. The diamond represents the 95% confidence interval of 1.08 to 3.1. An odds ratio of 1 is represented by the vertical blue line. Each study is represented by a horizontal line showing the 95% confidence interval and a square representing the odds ratio. The size of the square represents the size of the study population.

rate of ACL injury was four of 1073 in the intervention group, compared with five of 957 in the control group.

Pasanen et al.[21] performed a cluster-randomized controlled trial to evaluate the effect of a neuromuscular training program on motor skills and body control in female floorball players. The rate of ACL injury was six of the 256 (with three noncontact injuries) in the intervention group, compared with four of 201 (with three noncontact injuries) in the control group.

Gilchrist et al.[22] performed a randomized controlled study of National Collegiate Athletic Association Division-I soccer players who were managed with the same program as that used in the study by Mandelbaum et al.[18]. The rate of ACL injury was seven of 583 in the intervention group, compared with eighteen of 852 in the control group.

Kiani et al.[23] performed a prospective cohort study of female soccer players to evaluate the effect of a program aimed at improving motor skills, body control, and motor activation. The rate of ACL injury was zero of 777 in the intervention group, compared with three of 729 in the control group.

Waldén et al.[24] performed a cluster-randomized controlled trial of female soccer players to examine the effect of an in-season plyometrics training program. The rate of ACL injury was seven of 2479 in the intervention group, compared with fourteen of 2085 in the control group.

A summary of the included studies is provided in Table I.

### *Pooled Effect*

The meta-analysis of the pooled data demonstrated that neuromuscular training programs have a significant protective effect against ACL injury. The risk of ACL rupture was 1.83 times higher for athletes who did not participate in such a program (odds ratio [OR], 1.83; 95% confidence interval [95% CI], 1.08 to 3.10; $p = 0.02$) (Fig. 2).

When the analysis included data from randomized studies only, a slightly lower effect was seen. The risk of ACL rupture was 1.46 times higher for athletes who did not receive neuromuscular training (OR, 1.46; 95% CI, 0.87 to 2.44). This difference was not found to be significant ($p = 0.15$) (Fig. 3).

In studies that focused exclusively on soccer, there was a significant protective effect of neuromuscular training. The risk of ACL rupture was 2.62 times higher in patients who did not receive such training (OR, 2.62; 95% CI, 1.59 to 4.32; $p < 0.01$) (Fig. 4).

When the data were analyzed according to the timing of the intervention, no significant effects were

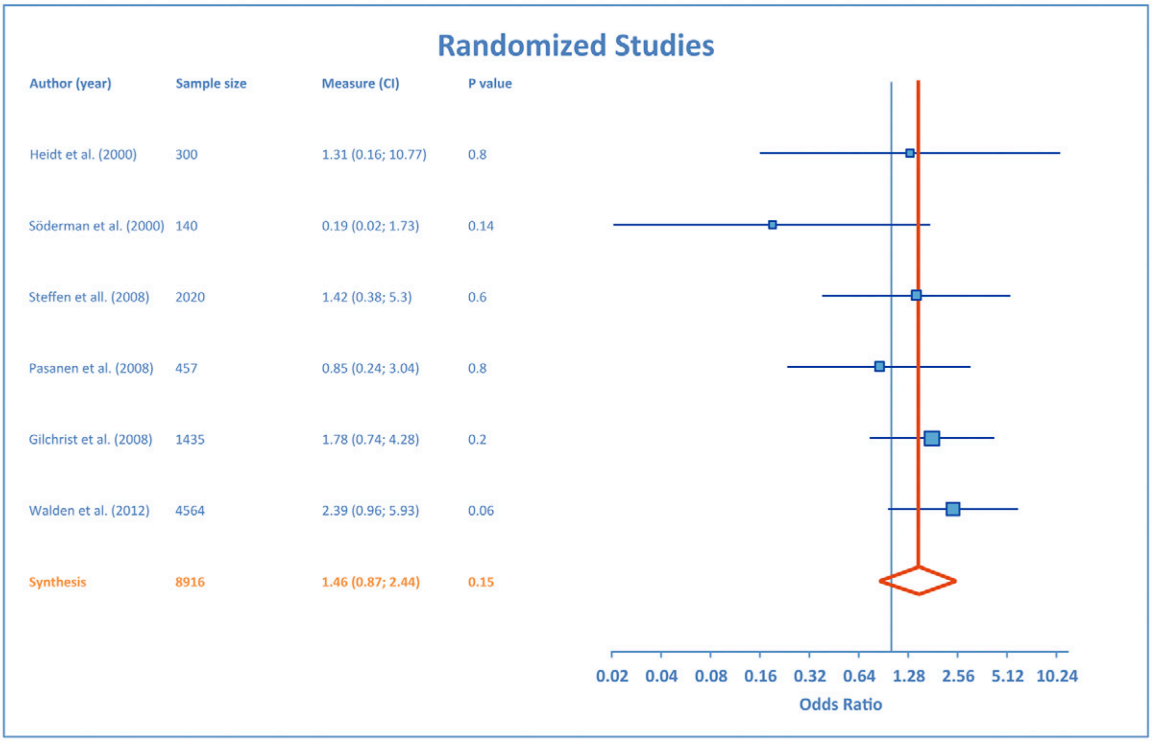


Fig. 3
Forest plot showing a sensitivity analysis of the effect of ACL injury prevention programs as shown in randomized prospective studies only. The pooled odds ratio was 1.46 (95% CI, 0.87 to 2.44; p = 0.15).

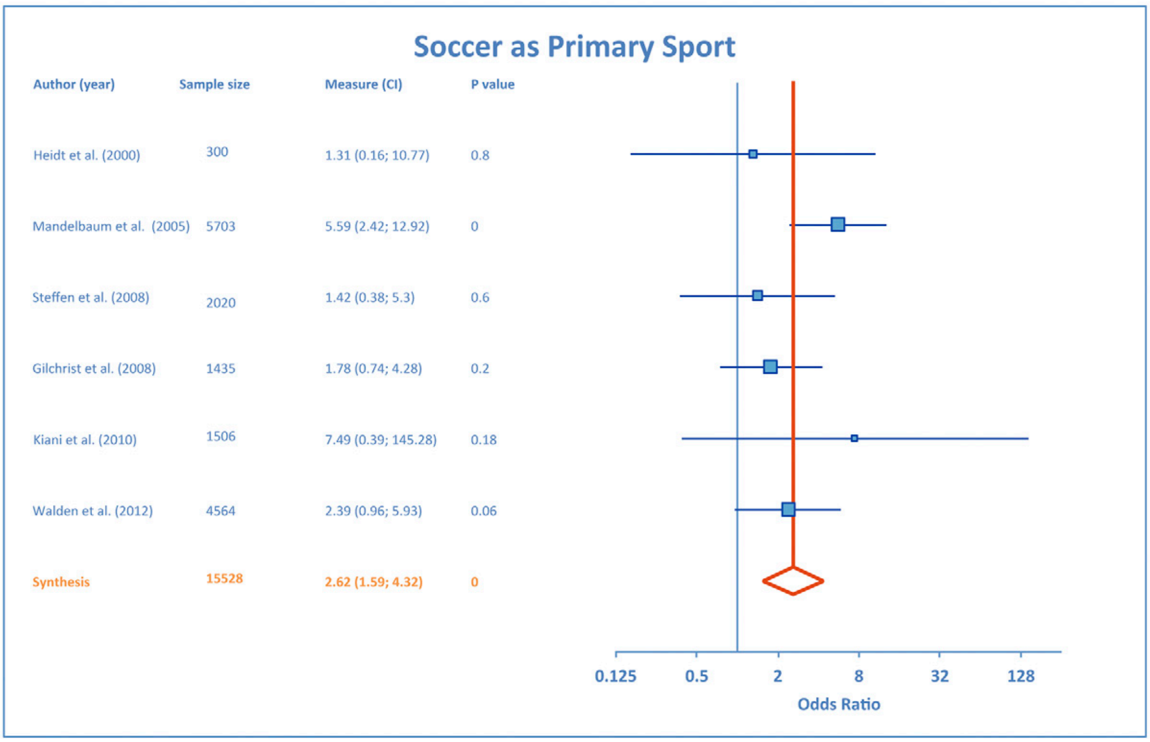


Fig. 4
Forest plot showing a sensitivity analysis of the effectiveness of ACL injury prevention programs in studies that involved soccer players only. The pooled odds ratio was 2.62 (95% CI, 1.59 to 4.32; $p < 0.01$).

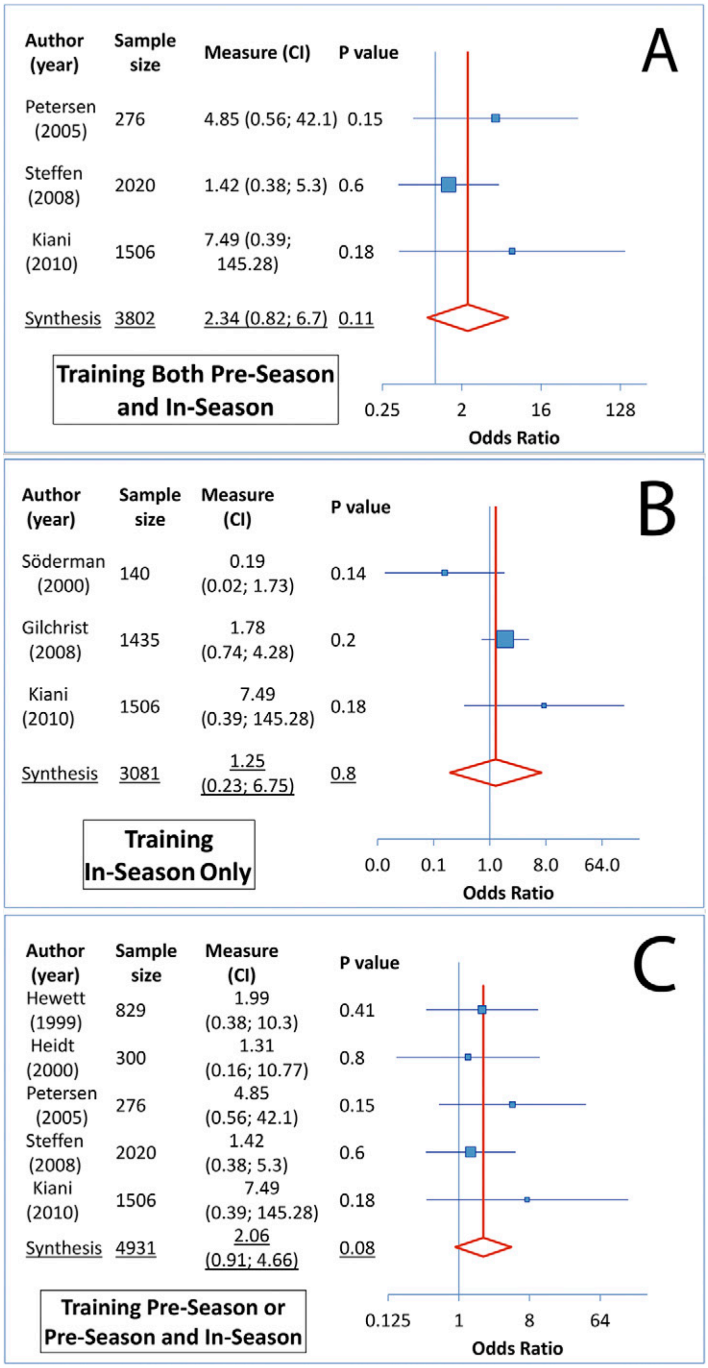


Fig. 5

**Fig. 5A** Forest plot showing a sensitivity analysis of the effect of ACL injury-prevention programs in which training began before the season and continued during the season. The pooled odds ratio was 2.34 (95% CI, 0.82 to 6.7; p = 0.11). **Fig. 5B** Forest plot showing sensitivity analysis of the effect of ACL injury-prevention programs in which training was in-season only. The pooled odds ratio was 1.25 (95% CI, 0.23 to 6.75; p = 0.8). **Fig. 5C** Forest plot showing sensitivity analysis of the effect of ACL injury prevention programs in which training was began preseason, including whether the training continued in-season. The pooled odds ratio was 2.06 (95% CI, 0.91 to 4.66; p = 0.08).

found. For studies in which the programs took place before and during the season, the pooled odds ratio was 2.34 (95% CI, 0.82 to 6.7; p = 0.11). For studies in which the intervention was in-season only, the odds ratio was 1.25 (95% CI, 0.23 to 6.75; p = 0.8). When all studies that included preseason activities (whether preseason activities only or both preseason and in-season activities) were considered, the odds ratio was 2.06 (95% CI, 0.91 to 4.66; p = 0.08). Some studies were not included in this analysis because they did not clearly differentiate between in-season and preseason training (Fig. 5, *A, B, and C*).

***Number Needed to Treat***

The risk of ACL rupture in the pooled group that received training was 0.00498. The risk of ACL rupture in the pooled control group was 0.0127. The absolute risk reduction was 0.0078, and the number needed to treat was 128.7.

***Heterogeneity***

There was considerable heterogeneity among the included studies, although this finding did not reach significance.

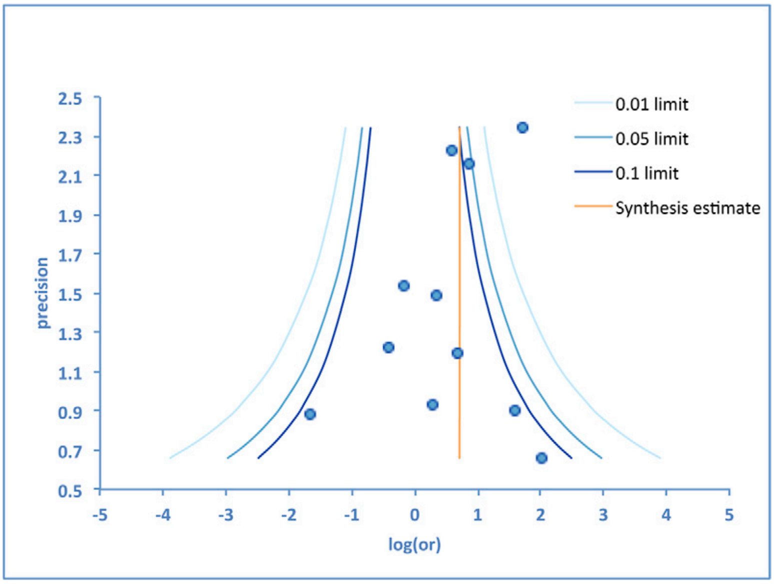


Fig. 6
Funnel plot showing all included studies to assess for publication bias. The pooled odds ratio is represented by the vertical yellow line. The curved lines represent the 99%, 95%, and 90% confidence intervals. While not all studies fall within the 95% funnel, Egger regression did not suggest that there was a significant publication bias (p = 0.27).

The $I^2$ value was 35.40% (p = 0.11). The Cochrane Q value was 15.72. For this reason, a random-effects model was used for quantitative meta-analysis.

### *Publication Bias*

No publication bias was found in our included studies. The funnel plot was partially skewed toward showing a protective effect for neuromuscular training. The Egger test did not suggest the existence of significant publication bias (p = 0.27) (Fig. 6).

## Discussion

Eleven studies were found to be appropriate for inclusion in our systematic review of ACL injury prevention programs for female athletes. Our analysis of the pooled data provides evidence of a positive effect of neuromuscular ACL injury prevention programs. The overall odds ratio associated with no protective neuromuscular training was 1.83. The number of female athletes that would have to be treated to prevent one ACL rupture was found to be 129.

Overall, we did not find significant publication bias. The study by Kiani et al.[23] showed the strongest predictive effect, whereas the study by Söderman et al.[16] showed the weakest. Kiani et al.[23] found a 77% reduction in the risk of ACL injuries in teenage female soccer players, whereas Söderman et al.[16] actually found a higher rate of knee injury in the intervention group. One possible reason for this considerable difference is that the intervention in the study by Kiani et al.[23] was much more extensive, involving warm-up, muscle activation, balance, strength, and core stability training. The study by Söderman et al.[16] is notable in that it demonstrated a large negative effect of neuromuscular training in preventing ACL injuries. One explanation is that the study had the smallest number of subjects and a dropout rate of 37%. The relevance of the findings is thus questionable. Another explanation may lie in the intervention characteristics. The athletes in the study received balance board training only. Although an earlier study by Caraffa et al.[9] showed a beneficial effect in association with balance board training, most studies that have shown a beneficial effect of neuromuscular training have incorporated plyometrics[14,15,18,20,22,24]. In general, however, given the variety of different training regimens, we are unable to comment on which set of exercises or style of training is most effective.

The quality of the eleven included studies was variable. Six of the eleven studies were randomized (Steffen et al.[20], Pasanen et al.[21], Heidt et al.[15], Söderman et al.[16], Gilchrist et al.[22], and Waldén et al.[24]); of these, four were cluster-randomized (Steffen et al.[20], Pasanen et al.[21], Gilchrist et al.[22], and Waldén et al.[24]), and one did not clearly state the method of randomization (Heidt et al.[15]). Six of the eleven studies recorded compliance with the training regimen (Steffen et al.[20], Pasanen et al.[21], Kiani et al.[23], Söderman et al.[16], Mandelbaum et al.[18], and Gilchrist et al.[22]), and six of the eleven studies compared player characteristics (Pasanen et al.[21], Kiani et al.[23], Söderman et al.[16], Mandelbaum et al.[18], Gilchrist et al.[22], and Waldén et al.[24]).

Our sensitivity analysis demonstrated a greater effect in soccer players. This finding may be due to the particular stresses of the sport, which include frequent cutting and pivoting maneuvers. These maneuvers may be especially amenable to modification through neuromuscular training. We did not have sufficient data to perform subgroup analyses for other sports. While the results were not significant, we did find a trend toward a greater effect for programs that began before the season and continued throughout the season; conceptually,

**TABLE I Characteristics of Included Studies**

| Study | Design | Level of Evidence | Sport | Age*† (yr) | Type of Rehabilitation | Training Program | | No. of Athletes | | No. of ACL Injuries | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Preseason | In-Season | Control Group | Training Group | Control Group | Training Group |
| Hewett et al.[14] (1999) | Prospective cohort | II | Soccer, volleyball, basketball | High school | Flexibility, plyometrics, weight-training | 3×/wk | None | 463 | 366 | 5 | 2 |
| Heidt et al.[15] (2000) | Randomized | II | Soccer | 14 to 18 | Cardiovascular, plyometrics, strengthening, flexibility | 3×/wk | None | 258 | 42 | 8 | 1 |
| Söderman et al.[16] (2000) | Prospective randomized | I | Soccer, basketball, volleyball | 20.4/20.5 (intervention/ control) | Balance board | None | Daily × 30 days, then 3×/wk | 78 | 62 | 1 | 4 |
| Petersen et al.[17] (2005) | Prospective case-controlled | II | Handball | NA | Balance board, jump | 3×/wk | 1×/wk | 142 | 134 | 5 | 1 |
| Mandelbaum et al.[18] (2005) | Cohort | II | Soccer | 14 to 18 | Warm-up, stretching, strengthening, plyometrics, agility exercises | Unclear | Unclear | 3818 | 1885 | 67 | 6 |
| Pfeiffer et al.[19] (2006) | Prospective cohort | II | Soccer, basketball, volleyball | High school | Plyometrics | Unclear | 2×/wk | 862 | 577 | 3 | 3 |
| Steffen et al.[20] (2008) | Cluster-randomized controlled | I | Soccer | 13 to 17 | Core stability, balance, plyometrics, strength | 15 sessions | 1×/wk | 947 | 1073 | 5 | 4 |
| Pasanen et al.[21] (2008) | Cluster-randomized controlled | I | Floorball | 24.2/23.3 (intervention/ control) | Running, balance, plyometrics, strengthening and stretching | Variable | Variable | 201 | 256 | 4 | 6 |
| Gilchrist et al.[22] (2008) | Randomized controlled | I | Soccer | 19.88 | Warm-up, stretching, strengthening, plyometrics, agilities | None | 3×/wk | 852 | 583 | 18 | 7 |
| Kiani et al.[23] (2010) | Prospective cohort | II | Soccer | 12.7 to 17.6 | Warm-up, muscle activation, balance, strength, core stability | 2×/wk | 1×/wk | 729 | 777 | 3 | 0 |
| Waldén et al.[24] (2012) | Cluster-randomized | I | Soccer | 12 to 17 | Plyometrics | None | 2×/wk | 2085 | 2479 | 14 | 7 |

*The values are given as the mean (if available) or the range. †NA = not available.

it seems probable that maintaining the training program throughout the season would be beneficial. We also were not able to examine whether specific types of programs—those using a balance board or plyometrics, for example—were more effective.

The present study was limited, as are all meta-analyses, by the limitations of the included studies. Our analysis showed significant heterogeneity among the included studies. This is not surprising given the variety of training types, duration, sports, and timing. Further research is needed to determine the most effective form of neuromuscular training as well as its appropriate timing.

## Conclusion

The results of the present systematic review and meta-analysis favor a protective effect of neuromuscular training programs on the risk of ACL rupture in female athletes. The data analysis suggested that this protective effect is more pronounced in soccer players. Additional research is needed to design the optimal training program.

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Rey N. Ramirez, MD[1],
Keith Baldwin, MD, MPH, MSPT[2],
Corinna C.D. Franklin, MD[1]

[1]Shriners Hospitals for Children, 3551 North Broad Street, Philadelphia, PA 19140

[2]Children's Hospital of Philadelphia, 34th Street and Civic Boulevard, Philadelphia, PA 19140

E-mail address for C.C.D. Franklin: corinna@post.harvard.edu

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