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## Evidence-Based Best-Practice Guidelines for Preventing Anterior Cruciate Ligament Injuries in Young Female Athletes: A Systematic Review and Meta-analysis

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### Abstract

**Background:** Injury prevention neuromuscular training (NMT) programs reduce the risk for anterior cruciate ligament (ACL) injury. However, variation in program characteristics limits the potential to delineate the most effective practices to optimize injury risk reduction.

**Purpose:** To evaluate the common and effective components included in ACL NMT programs and develop an efficient, user-friendly tool to assess the quality of ACL NMT programs.

**Study Design:** Systematic review and meta-analysis.

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A Video Supplement for this article is available online.

**Methods:** Study inclusion required (1) a prospective controlled trial study design, (2) an NMT intervention aimed to reduce incidence of ACL injury, (3) a comparison group, (4) ACL injury incidence, and (5) female participants. The following data were extracted: year of publication, study design, sample size and characteristics, and NMT characteristics including exercise type and number per session, volume, duration, training time, and implementer training. Analysis entailed both univariate subgroup and meta-regression techniques using random-effects models.

**Results:** Eighteen studies were included in the meta-analyses, with a total of 27,231 participants, 347 sustaining an ACL injury. NMT reduced the risk for ACL injury from 1 in 54 to 1 in 111 (odds ratio [OR], 0.51; 95% CI, 0.37–0.69). The overall mean training volume was 18.17 hours for the entire NMT (24.1 minutes per session, 2.51 times per week). Interventions targeting middle school or high school–aged athletes reduced injury risk (OR, 0.38; 95% CI, 0.24–0.60) to a greater degree than did interventions for college- or professional-aged athletes (OR, 0.65; 95% CI, 0.48–0.89). All interventions included some form of implementer training. Increased landing stabilization and lower body strength exercises during each session improved prophylactic benefits. A meta-regression model and simple checklist based on the aforementioned effective components (slope =  $-0.15$ ,  $P = .0008$ ; intercept =  $0.04$ ,  $P = .51$ ) were developed to allow practitioners to evaluate the potential efficacy of their ACL NMT and optimize injury prevention effects.

**Conclusion:** Considering the aggregated evidence, we recommend that ACL NMT programs target younger athletes and use trained implementers who incorporate lower body strength exercises (ie, Nordic hamstrings, lunges, and heel-calf raises) with a specific focus on landing stabilization (jump/hop and hold) throughout their sport seasons.

**Clinical Relevance:** Clinicians, coaches, athletes, parents, and practitioners can use the developed checklist to gain insight into the quality of their current ACL NMT practices and can use the tool to optimize programming for future ACL NMT to reduce ACL injury risk.

## Keywords

neuromuscular training; pediatric sports medicine; injury prevention; biomechanics; decision support

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Knee injuries are the most common severe<sup>13</sup> and season/ career-ending sport injury.<sup>72</sup> The anterior cruciate ligament (ACL) sustains the majority of these traumatic knee injuries, and surgical reconstruction is the common treatment approach (ie, 80%).<sup>28</sup> One ACL injury currently costs \$38,000, which includes long-term costs; thus, the economic burden to society is substantial.<sup>42</sup> Women's basketball, soccer, gymnastics, and lacrosse are the highest risk sports for ACL injury.<sup>20,69</sup> Women are approximately 3 times more likely than men to injure their ACL.<sup>20,58,62</sup> ACL injuries often result in concomitant injury (meniscus 55%–65%, cartilage 16%–46%),<sup>32,77</sup> which leads to a higher risk (4 times) for osteoarthritis,<sup>4,8,11,12,50</sup> total knee replacement,<sup>68</sup> and impaired knee-related quality of life at 5 to 25 years after injury.<sup>16</sup> Risk for a second ACL injury is also substantial (ie, 10%), and if the athletes return to their preinjury sport, risk doubles (ie, 20%).<sup>5,38,75,76</sup> The recovery time for ACL injury is approximately 1 year, and about 45% of athletes do not return to competitive sport.<sup>6,7,39</sup> If athletes return to their respective sport, their performance is likely to decrease.<sup>30,39</sup>

Well-controlled neuromuscular training (NMT) for ACL injury prevention reduces the risk for such injury by roughly 50% in female athletes.<sup>46,61,66,67</sup> Historically, NMT programs have included various modalities such as strength training, plyometrics, balance exercises, and stretching to manipulate muscle activation or imbalances. Numerous studies and simulations indicate that NMT is a cost-effective prevention strategy.<sup>36,41</sup> However, NMT programs vary, thus warranting increased effort to determine the common and most effective components. In addition, to create useful best-practice guidelines, effective intervention components need to be explicitly documented, which has yet to be done through the use of robust quantitative and statistical methods.<sup>54</sup> Thus, the goal of this study was to (1) determine the common and effective components of ACL NMT programs and (2) create an efficient, user-friendly tool to assess the quality of ACL NMT programs. This tool not only will provide transparent best-practice information regarding the most effective program components but also can be used as a feedback system to assess current programs or a decision support tool to develop effective ACL NMT programs in the future.

## METHODS

### Search Methods for the Identification of Studies

A literature search was performed with PubMed and EBS-COhost (CINAHL Plus and MEDLINE), on January 31, 2018. The keyword search was performed with a combination of keywords related to ACL, knee, injury, prevention, neuromuscular, and training. Language was limited to English, and all participants were human. The following inclusion criteria were applied: (1) a prospective controlled trial study design was used, (2) an NMT intervention aimed to reduce ACL incidence was applied, (3) a comparison group was used, (4) the number of ACL injuries was reported, and (5) females were included as participants. Two authors (D.S. and E.J.P.) performed the literature search. Abstracts, posters, review papers, and irrelevant studies were excluded. When eligibility of certain studies was questionable, the 2 authors discussed and determined the status based on the 5 inclusion criteria. During the literature search, cross-referencing was performed when studies that met inclusion criteria cited other studies.

### Data Extraction

The following information was extracted from each article identified for inclusion: year of publication, study design, sample size including number of ACL injuries, sample characteristics including age and sport, and NMT characteristics including exercise type and number per session, volume, duration, training time, and implementer training. The Physiotherapy Evidence Database (PEDro) scale was used to assess methodological quality and risk of bias. Data were independently extracted by 3 individuals (D.S., E.J.P., G.S.). Discrepancies between classifications or values were discussed and resolved between the extractors.

### Statistical Analysis

The primary outcome of interest was ACL injury odds ratio (OR). To determine the most effective components of ACL NMT programs, both univariate subgroup and meta-regression techniques were used. Specifically, random-effects models (using restricted maximum

likelihood estimators) were used to calculate the ORs and statistical parameters (95% CIs, regression slopes, and intercepts) for the various program characteristics.<sup>9,37</sup> For univariate comparisons, only the exercises or components (eg, squat, calf raise, hip flexor stretch) that were included in at least 25% ( $k = 5$ ) of the studies were included in the analysis in order to reduce biases associated with largely unequal sample sizes. Publication bias was assessed via regression tests for funnel plot asymmetry using standard error, sample size, and sample variance as predictors.<sup>15</sup> All statistical calculations and analyses were performed by use of the *metafor* and *meta* packages with the statistical software environment R.

## RESULTS

### Overall Effects

Eighteen studies were included in the analyses (Table 1 and Figure 1).<sup>‡‡</sup> Because 2 studies had program changes after the first year/phase<sup>47,52</sup> but reported injury outcomes for both years/phases, these studies were analyzed separately. Cumulative evidence gathered over time (from 1999 to the present) indicates that NMT has been an effective intervention to reduce ACL injury risk since approximately 2008 (Figure 2A). Specifically, Figure 2A shows how the accumulation of studies over time changes the effect estimate (eg, after each study is included, a new OR is calculated). As a whole, NMT reduced the risk for ACL injury from 1 in 54 to 1 in 111 (OR, 0.51; 95% CI, 0.37–0.69) (Figure 2B). Statistical heterogeneity ( $I^2$ ) for the random-effects model was 23.3% ( $Q_{19} = 24.81$ ,  $P = .17$ ). Because substantial heterogeneity was found in programming characteristics between studies (training exercises, target population, etc) and moderate statistical heterogeneity was noted, subgroup and meta-regression analyses were conducted. No significant publication bias or funnel plot asymmetry was found when standard error ( $Z = 0.92$ ,  $P = .36$ ), sample size ( $Z = -1.86$ ,  $P = .06$ ), and sample variance ( $Z = -1.07$ ,  $P = .28$ ) were used as predictors. Grouped ORs were similar between randomized trials ( $k = 11$ ; OR, 0.54; 95% CI, 0.35–0.83) and nonrandomized trials ( $k = 9$ ; OR, 0.46; 95% CI, 0.28–0.76). The average  $\pm$  SD PEDro score across all studies was  $5.45 \pm 2.31$  out of a possible score of 10. No significant meta-regression effects were found for the PEDro score on ACL injury risk (slope =  $-0.002$ ;  $P = .98$ ).

### Training Duration and Timing

No significant meta-regression effects were found for total training duration on ACL injury risk (total training time estimate/slope =  $-0.02$ ;  $P = .28$ ). The overall mean training amount was 57 sessions totaling 18.17 hours (roughly 24 minutes per session, 2.5 times per week).<sup>§§</sup> NMT interventions conducted only in the preseason did not reduce the risk for ACL injury (OR, 0.59; 95% CI, 0.16–2.15); however, only 2 studies were included in this estimate.<sup>21,24</sup> NMT interventions conducted in-season only or both preseason and in-season reduced the risk for ACL injury (OR, 0.50; 95% CI, 0.36–0.70). Thus, continued exposure to

<sup>‡‡</sup>References 1, 10, 17, 19, 21, 24, 31, 34, 40, 47, 51, 52, 55–57, 59, 63, 74.

<sup>§§</sup>These numbers are based on the prescribed amount and not actual compliance. The average number of sessions per week typically varied for NMT interventions conducted in both preseason and in-season (fewer sessions per week during the season). Training session duration was substantially longer for the studies conducted during preseason only (eg, 75 minutes per session).

neuromuscular training throughout the sport season seems to enhance prophylactic effects of NMT, but more preseason-only studies may help elucidate this finding.

### Target Population

NMT interventions were effective for female basketball (OR, 0.33; 95% CI, 0.16–0.69), soccer (OR, 0.46; 95% CI, 0.24–0.88), and handball (OR, 0.66; 95% CI, 0.45–0.97) athletes, and interventions including various athletes were potentially effective (eg, soccer, basketball, and volleyball) (OR, 0.60; 95% CI, 0.25–1.44); however, only 4 small studies were included in the estimate for combined-sport investigations.<sup>17,24,34,57</sup> Interventions targeting middle and high school-aged athletes (13–19 years old) reduced injury risk (OR, 0.38; 95% CI, 0.24–0.60) to a greater degree than did interventions for college- or professional-aged athletes (19–24 years old) (OR, 0.65; 95% CI, 0.48–0.89).

### Neuromuscular Training Program Characteristics

All interventions included some form of implementer training (eg, instructional workshop, video, or brochure) on proper program implementation (eg, exercise instruction and progression, feedback). All but 1 program<sup>59</sup> focused on proper movement technique including knee control during landing and other dynamic movements. Programs including more landing stabilization and lower body strength exercises during each session were most effective (Figure 3). Programs including balance, core-strengthening, stretching, or agility exercises were no more effective than programs that did not incorporate these components (Figure 3). Specifically, programs that included more landing stabilization exercises (eg, drop landings, jump/hop and holds), hamstring strength (eg, Nordic hamstring), lunges, and heel-calf raises reduced the risk for ACL injury to a greater degree than did programs without these exercises.

### Best-Practice Model

A final additive meta-regression model was made and a simple checklist was created based on the aforementioned effective components and characteristics of ACL injury prevention programs (Figure 4). Sensitivity analysis was conducted by removing a potential outlier,<sup>59</sup> and results or interpretations did not change. Because (1) each of the components displayed similar protective effects (eg, subgroup and meta-regression effect sizes), (2) the programs had multiple components, and (3) we wanted to create a simple, user-friendly tool for coaches and practitioners, a simple additive model was created by summing the inclusion of the various effective components. Scoring for this tool was as follows: all “yes” responses were considered 1 point; the numbers of landing stabilization exercises were counted as indicated (eg, if the program contained 3 landing stabilization exercises, the number of points was 3); middle or high school age was 1 point; college or professional age was 0 points; preseason only was 0 points; in-season or both preseason and in-season was 1 point; “no” for implementer training was 0 points; and “yes” for implementer training was 1 point. Thus, the maximum score was 11. As seen in Figure 4, a score of approximately 5 would result in the average meta-analytic effect of the combined interventions (eg, OR of approximately 0.5). It was determined that based on the CIs for the meta-regression model, a score of greater than 3 is likely to lead to protective effects. These findings were corroborated by qualitatively synthesizing the program components of the top 5 most

effective programs based on 3 ranking systems: (1) 95% CI upper bound (Figure 2B), (2) OR, and (3) meta-regression checklist ranking. The majority of the top 5 programs included multiple landing stabilization exercises (forward and backward hop and hold, single-legged hop and hold, and vertical jump with landing stabilization), Nordic hamstrings, lunges, and heel-calf raises.

## DISCUSSION

The goal of this investigation was to use robust quantitative analyses to determine the key components for optimizing ACL injury prevention programs. Through the development of a meta-analytic driven checklist, the current results provide specific guidelines for ACL injury prevention programming. Overall, the most effective ACL injury prevention programs included trained or informed personnel (eg, coaches, trainers), targeted younger athletes, exposed athletes to NMT throughout the sport season, and included lower body strengthening and landing stabilization exercises. Significant effectiveness was not found in programs including balance, core strengthening, stretching, or agility compared with NMT programs that did not incorporate these components. Including these other components may not be harmful but may be an ineffective use of time if ACL injury prevention is a primary goal. A potential important caveat is that these other components, such as balance training, have been shown to be effective for preventing ankle sprains<sup>73</sup>; thus, a more holistic perspective must be considered when designing overall sport injury prevention programs. In addition, proper exercise progression, especially for landing stabilization, was used throughout the majority of the ACL NMT programs.

Previous meta-analyses regarding ACL injury prevention have found consistently effective component results<sup>67,70</sup>; however, this analysis provides explicit characteristics for prevention programs that previous analyses lacked. The overall quality of the studies included in this analysis was moderate, based on PEDro scores; thus, more high-quality studies may help improve the strength of recommendations. Our results are also consistent with theoretical and empirical evidence on the mechanisms of action for these prevention programs/components as related to ACL injury mechanisms and risk factors. Specifically, stiff landings and improper alignment of the knee joint in the frontal plane, which are influenced by hip and trunk control, are likely to increase the risk for ACL injury.<sup>25,26,33,35</sup> Thus, properly performed exercises that engage hip muscles (eg, gluteal muscles, hamstrings) and ACL agonist knee muscles (eg, calf and hamstrings), such as Nordic hamstrings, lunges, heel-calf raises, and landing stabilization exercises, should protect the ACL and limit hip internal rotation and adduction motions, which contribute to improper knee alignment. Landing stabilization exercises directly focus on optimizing muscle activation to ensure proper technique and alignment (landing softly and knee-over-toe positioning). Acute feedback interventions as well as some longer term training studies have shown muscular adaptations in response to NMT.<sup>23,44,45,71</sup>

Although between-study assessment of dosage effects seems to result in null or small effects, various within-study results of actual adherence to injury prevention have been found.<sup>60,65,74</sup> Thus, adherence is key and should not be assumed or ignored. Despite the substantial evidence documenting the efficacy and societal benefit of prevention programs,



ACL injury rates have not decreased.<sup>2,3,18,22</sup> A primary reason is that athletes are not engaging in this prevention training. The use of ACL injury prevention through NMT by female high school teams is low nationally (13%–20%) and very low in rural areas (4%).<sup>29,48,64</sup> Knowledge and comprehension of evidence-based prevention strategies have been documented to be the most important modifiable barriers to implementation.<sup>14,27,43,48,49,53</sup> Thus, improving understanding of effective components of NMT should translate to greater implementation of NMT (see the online Video Supplement for a summary). Furthermore, the tool developed in this investigation will help coaches and practitioners to assess their current programs or design future NMT programs that optimize ACL injury prevention.

The checklist was developed based on descriptive meta-analytic findings and not randomized comparison trials; thus, results should be interpreted with caution. Future studies should directly compare program content (dosage, timing, exercises) and the associated injury prevention effects. However, because ACL injuries do not occur as frequently as one might think (eg, overall injury rate is approximately 1 in 80 athletes per season in these high-risk sports), large sample sizes (eg, > 8000) are needed to conduct a sufficiently powered randomized controlled or comparison trial. Given the amount of resources needed to conduct such a trial and considering the evidence found in this meta-analysis, it may be more appropriate to ensure that individuals are engaging in NMT (consisting of these best-practice components) rather than invest in additional large, randomized controlled trials. Ultimately, the goal of developing this tool is to ensure that athletes routinely engage in and adhere to evidence-based ACL injury prevention activities.

## CONCLUSION

Various programmatic components of ACL NMT are associated with injury reduction. We recommend that ACL NMT programs target younger athletes and use trained implementers who incorporate lower body strength exercises (ie, Nordic hamstrings, lunges, and calf raises) and focus specifically on landing stabilization exercises (jump and hold, drop and land) throughout the sport season. Coaches, athletes, parents, and practitioners can use the developed checklist to gain insights into the quality of their current ACL NMT practices as well as to inform modification or development of future ACL NMT.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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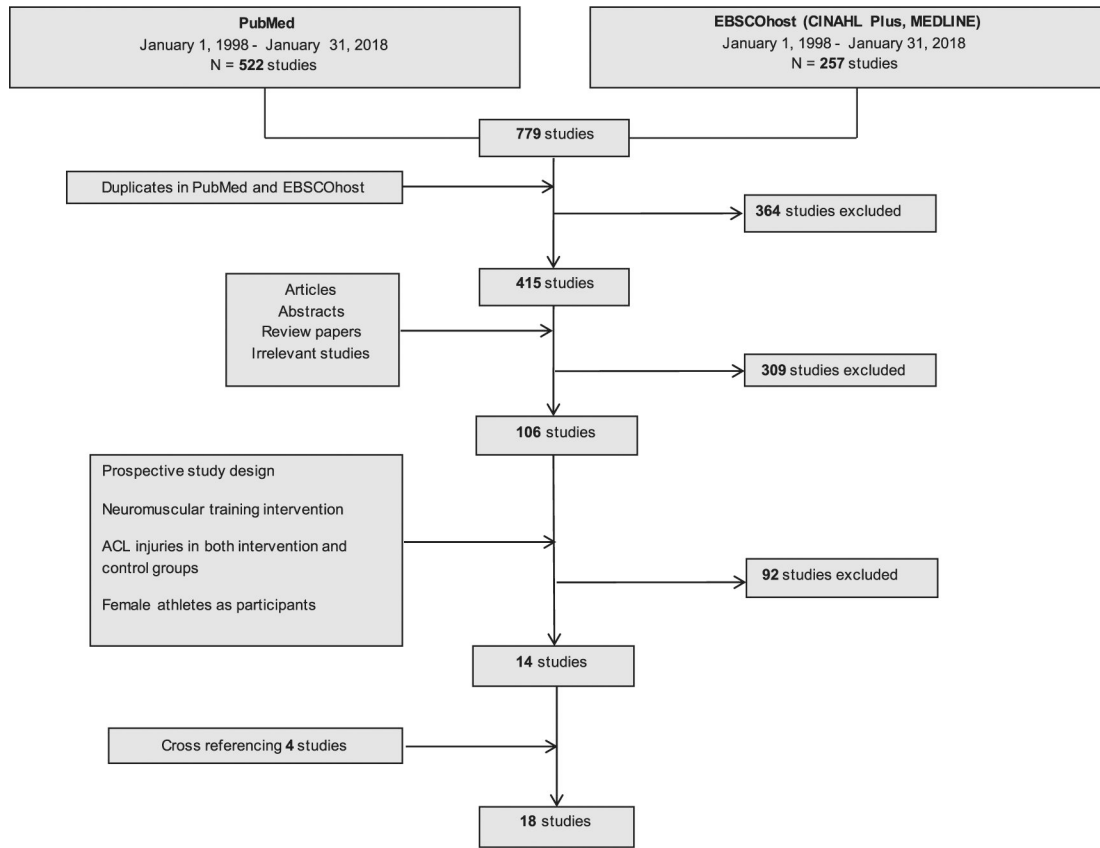


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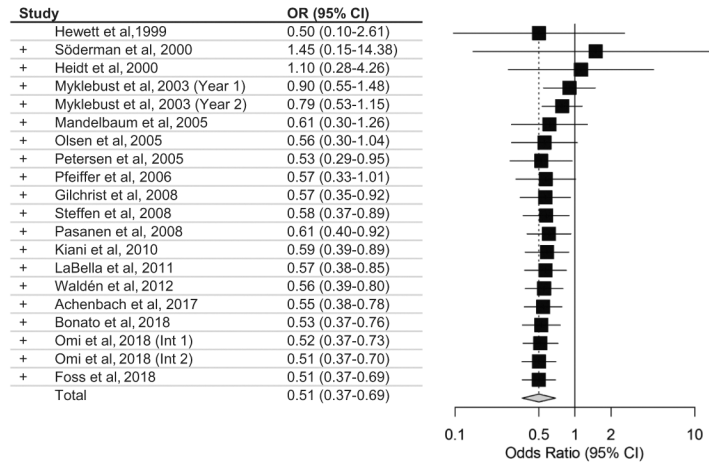
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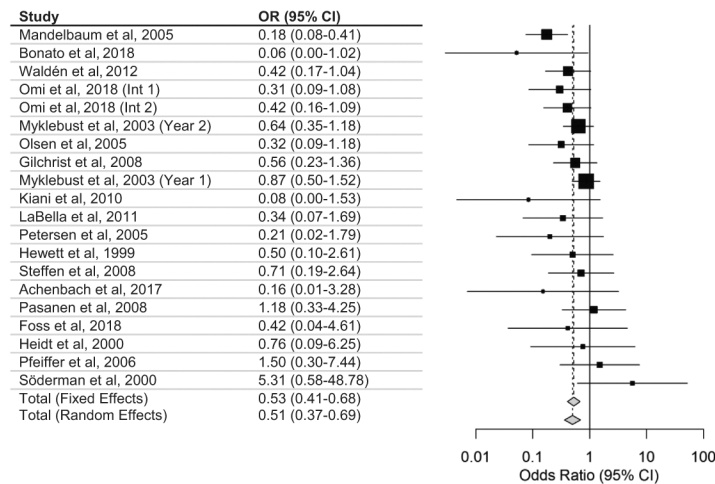


**Figure 1.** Flowchart of the literature review. ACL, anterior cruciate ligament.

**A** Cumulative meta-analytic effects across publication date



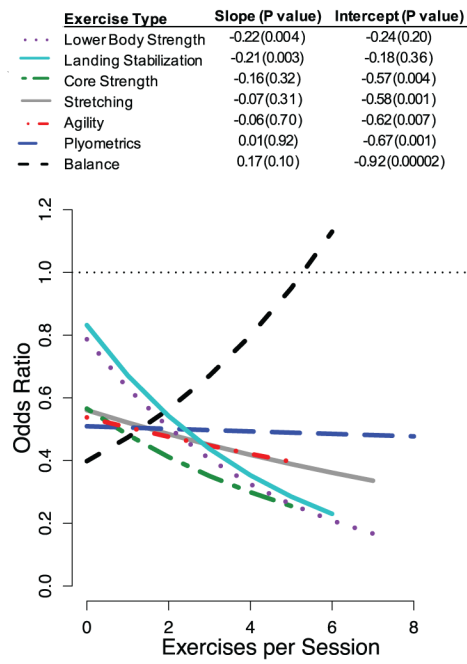
**B** Meta-analytic effects ordered by OR 95% CI upper bound



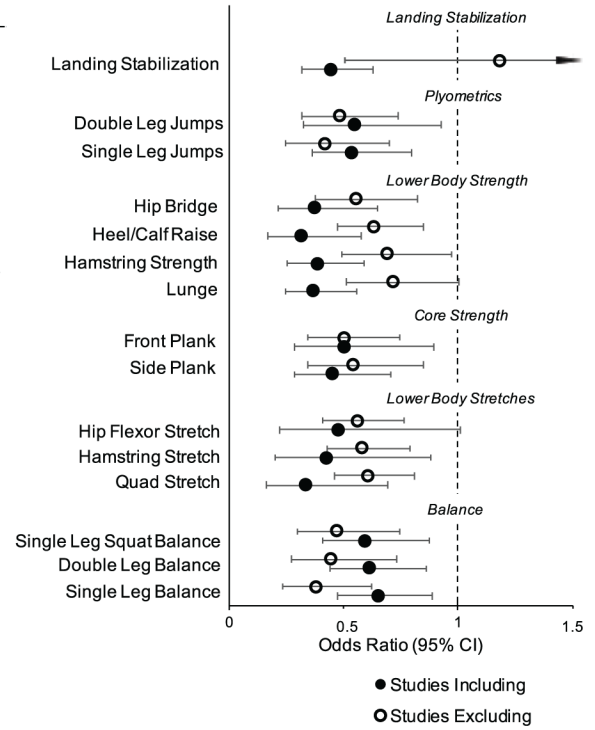
**Figure 2.** Odds of anterior cruciate ligament injury compared with control group. (A) Cumulative effects over time and (B) effects ordered by upper bound CI of the odds ratio (OR).



**A** Meta-regression results for amount of various NMT exercises

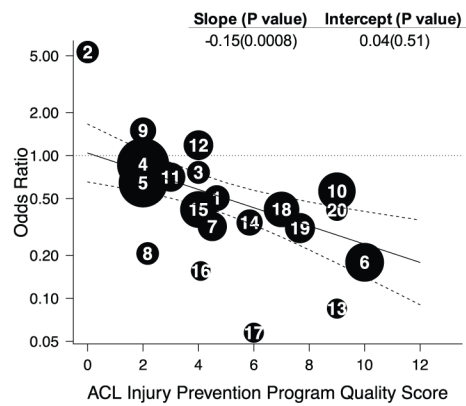


**B** Subgroup results for specific type of NMT exercise



**Figure 3.** Exercise-based (A) meta-regression and (B) subgroup analyses. NMT, neuromuscular training.

**A** Checklist based meta-regression model



- |                                   |                             |
|-----------------------------------|-----------------------------|
| 1. Hewett et al, 1999             | 11. Steffen et al, 2008     |
| 2. Söderman et al, 2000           | 12. Pasanen et al, 2008     |
| 3. Heidt et al, 2000              | 13. Kiani et al, 2010       |
| 4. Myklebust et al, 2003 (Year 1) | 14. LaBella et al, 2011     |
| 5. Myklebust et al, 2003 (Year 2) | 15. Waldén et al, 2012      |
| 6. Mandelbaum et al, 2005         | 16. Achenbach et al, 2017   |
| 7. Olsen et al, 2005              | 17. Bonato et al, 2017      |
| 8. Petersen et al, 2005           | 18. Omi et al, 2018 (Int 1) |
| 9. Pfeiffer et al, 2006           | 19. Omi et al, 2018 (Int 2) |
| 10. Gilchrist et al, 2008         | 20. Foss et al, 2018        |

**B** ACL injury prevention program best practice checklist

**Does your program/training include?**

	No	Yes
Lunges	<input type="checkbox"/> 0	<input checked="" type="checkbox"/> 1
Hamstring Exercises (e.g., Nordic Hamstring)	<input type="checkbox"/> 0	<input checked="" type="checkbox"/> 1
Heel/Calf Raises	<input type="checkbox"/> 0	<input checked="" type="checkbox"/> 1

Total number of **landing stabilization** exercises **per session** (e.g., drop landings, jump/hop and holds)

0     1     2     3     4     5

Number of exercises

---

What is the age of athletes you work with?

Middle/High School     College/Professional

---

How often do you perform the program?

Pre-Season Only     In-Season or Both Pre/In-Season

---

Has the person implementing the program (e.g., Coach) been trained or educated on ACL injury prevention programming (e.g., workshop, video/brochure)?

No     Yes

Total Score: \_\_\_/11

Checklist Score	0	1	2	3	4	5	6	7	8	9	10	11
Interpretation	No Benefit		Small Benefit			Intermediate Benefit			Large Benefit			

**Figure 4.** Meta-regression based, best-practice checklist. (A) Regression model characteristics and (B) checklist. All dichotomous items are scored as 0 or 1, and continuous measures (landing stabilization exercises) are scored as indicated by the exact number. ACL, anterior cruciate ligament.

## Individual Study Characteristics

Table 1

Lead Author (Year)	Study Design	Training: Noninjured/ Injured, n	Control: Noninjured/ Injured, n	Country: Level/Division	Participant Age, y	Sport Types	Total Training Time, h <sup>d</sup>	Total Training Sessions <sup>d</sup>
Hewett (1999) <sup>24</sup>	Prospective nonrandomized cohort	364/2	458/5	US: high school	Range 14–18	Soccer, volleyball, and basketball	13.4	18
Söderman (2000) <sup>59</sup>	Prospective randomized controlled	58/4	77/1	Sweden: Divisions 2 and 3	Mean 20.4	Soccer	22.5	108
Heidt (2000) <sup>21</sup>	Prospective randomized controlled	41/1	250/8	US: high school	Range 14–18	Soccer	21.8	30
Myklebust (2003), <sup>47</sup> year 1	Prospective nonrandomized observation-intervention	832/23	913/29	Norway: Divisions 1–3	Range 21–22	Handball	13.8	55
Myklebust (2003), <sup>47</sup> year 2	Prospective nonrandomized observation-intervention	833/17	913/29	Norway: Divisions 1–3	Range 21–22	Handball	13.8	55
Mandelbaum (2005) <sup>40</sup>	Prospective nonrandomized cohort	1879/6	3751/67	US: Coast Soccer League (14- to 18-year-olds)	Range 14–18	Soccer	11.4	36
Olsen (2005) <sup>51</sup>	Prospective cluster randomized controlled	805/3	769/9	Norway: 16- to 17-y divisions	Range 16–17	Handball	13.5	45
Petersen (2005) <sup>56</sup>	Prospective matched cohort	133/1	137/5	Germany: semiprofessional and amateur	Mean ~19	Handball	9.8	59
Pfeiffer (2006) <sup>57</sup>	Prospective nonrandomized cohort	574/3	859/3	US: high school	Range 14–18	Soccer, volleyball, and basketball	10	30
Gilchrist (2008) <sup>19</sup>	Prospective cluster randomized controlled	576/7	834/18	US: college Division 1	Mean 19.9	Soccer	11.4	36
Steffen (2008) <sup>63</sup>	Prospective block randomized controlled	1073/4	947/5	Norway: under 17	Mean 15.4	Soccer	10	40
Pasanen (2008) <sup>55</sup>	Prospective cluster randomized controlled	250/6	197/4	Finland: top level	Mean 24	Floorball	12.4	42
Kiani (2010) <sup>31</sup>	Prospective cluster nonrandomized cohort	777/0	724/5	Sweden: various levels	Mean 15	Soccer	12.8	51
LaBella (2011) <sup>34</sup>	Prospective cluster randomized controlled	735/2	749/6	US: high school	Mean 16	Soccer and basketball	13.6	43
Waldén (2012) <sup>74</sup>	Prospective cluster randomized controlled	2472/7	2071/14	Sweden: under 14 to under 18	Mean 14	Soccer	15	60
Achenbach (2017) <sup>1</sup>	Prospective block randomized controlled	98/0	76/2	Germany: under 16 and under 18	Range 13–18	Handball	13.9	56
Bonato (2018) <sup>10</sup>	Prospective cluster randomized controlled	86/0	74/7	Italy: Premier National League	Mean 20	Basketball	64	128
Orni (2018), <sup>52</sup> intervention 1	Prospective nonrandomized observation-intervention	268/6	309/16	Japan: collegiate Division 2	Mean 19.6	Basketball	34.3	103
Orni (2018), <sup>52</sup> intervention 2	Prospective nonrandomized observation-intervention	180/3	309/16	Japan: collegiate Division 2	Mean 19.6	Basketball	34.8	104
Foss (2018) <sup>17</sup>	Prospective cluster randomized controlled	259/1	215/2	US: middle and high school	Mean 14	Soccer, volleyball, and basketball	11.32	44

<sup>d</sup>Training time and number of sessions are displayed according to protocol and not actual compliance.