CLINICAL PRACTICE GUIDELINES

AMELIA J. H. ARUNDALE, PT, PhD • **MARIO BIZZINI,** PT, PhD
AIRELLE GIORDANO, DPT • **TIMOTHY E. HEWETT,** PhD
DAVID S. LOGERSTEDT, PT, PhD • **BERT MANDELBAUM,** MD
DAVID A. SCALZITTI, PT, PhD • **HOLLY SILVERS-GRANELLI**, MPT
LYNN SNYDER-MACKLER, PT, ScD, FAPTA

Exercise-based Knee Injury Prevention

Clinical Practice Guidelines
Linked to the International Classification
of Functioning, Disability, and Health
from the Orthopaedic and Sports Sections of the
American Physical Therapy Association

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Reviewers: Roy D. Altman, MD • Paul Beattie, PT, PhD • Dean Caswell, PT, ATC, AT/L • Marie Charpentier**,** PT, DPT, ATC, LAT • John DeWitt, DPT • James Elliott, PT, PhD • Helene M. Fearon, PT • Amanda Ferland, DPT • G. Kelly Fitzgerald, PT, PhD • Jennifer S. Howard, ATC, PhD • David Killoran, PhD • Joanna Kvist, PT, PhD **•** Robert Marx, MD • Sean Stedeford Leslie Torburn, DPT • James Zachazewski, DPT

 Address correspondence to: Brenda Johnson, ICF-based Clinical Practice Guidelines Coordinator, Orthopaedic Section, APTA Inc., 2920 East Avenue South, Suite 200; La Crosse, WI 54601. Email:bjohnson@orthopt.org

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SUMMARY OF RECOMMENDATIONST*

THIS SECTION WILL BE COMPLETED AFTER FINAL REVIEW AND EDITING

*These recommendations and clinical practice guidelines are based on the scientific literature published prior to October 2017

<u>List of Acronyms</u>

ACL: anterior cruciate ligament

AEs: athletic exposures

AMSTAR: A Measurement Tool to Assess Systematic Reviews

APTA: American Physical Therapy Association

CI: confidence interval

CPG: clinical practice guideline

EMG: electromyography

FIFA: Fédération Internationale de Football Association; international soccer governing body

FIFA11+: An injury prevention program developed originally in association with the medical committee of FIFA

FIFA11: Also known as “the 11” an injury prevention program developed originally in association with the medical committee of FIFA and the predecessor to the FIFA11+

ICD: International Classification of Disease

ICF: International Classification of Functioning, disability and health

JOSPT: Journal of Orthopaedic & Sports Physical Therapy

KLIP: Knee Ligament Injury Prevention program

PEDro: Physioheray Evidence Database

PEP: Prevent Injury and Enhance Performance injury prevention program

RCT: randomized controlled trial

SIGN: Scottish Intercollegiate Guidelines Network

INTRODUCTION

AIM OF THE GUIDELINE

The Orthopaedic Section and the Sports Physical Therapy Section of the American Physical Therapy Association (APTA) have an ongoing effort to create evidence-based clinical practice guidelines (CPGs) for orthopaedic and sports physical therapy management and prevention of musculoskeletal impairments described in the World Health Organization's International Classification of Functioning, disability and health (ICF).[49] This particular guideline focuses on the exercise-based prevention of knee injuries. Exercise-based prevention was defined as an intervention requiring the participant(s) to be active and move. This could include physical activity, strengthening, stretching, neuromuscular, proprioceptive, agility, or plyometric exercises, other training modality, but excluded passive interventions such as bracing, or programs that only involved education. Knee injuries were defined as any knee joint pathology including damage to the joint (patellofemoral and/or tibiofemoral), ligaments, meniscus, or patella tendon. The recommendations can be followed and implemented by athletes, coaches, health and fitness professionals, athletic trainers, physical therapists, physicians, surgeons, and other clinicians.

The objectives of this CPG are:

- Review the evidence in the scientific literature for exercise-based knee injury prevention programs.
- Identify exercise-based knee injury prevention programs that are effective for specific sub-groups of athletes.
- Describe the evidence for the components, dosage, and delivery of exercise-based knee injury prevention programs.
- Provide suggestions for the implementation of exercise-based knee injury prevention programs.
- Create a reference publication for athletes, coaches, students, interns, residents, fellows, athletic trainers, orthopaedic and sports physical therapy clinicians, academic instructors, clinical instructors, and physicians and surgeons in orthopedics and sports, regarding the best current practice of exercise-based knee injury prevention programs.

STATEMENT OF INTENT

These guidelines are not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual athlete/patient and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every athlete or patient, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular injury prevention plan, clinical procedure, or treatment plan must be made based on experience and expertise in light of the presentation of the athlete or patient, the available evidence, available diagnostic and treatment options, and the athlete or patient's values, expectations, and preferences. However, when providing care for athletes/patients, we suggest that significant departures from accepted guidelines should be documented in the athlete/patient's medical records at the time the relevant clinical decision is made.

Methods

The Orthopaedic Section and the Sports Physical Therapy Section of the APTA appointed content experts with relevant physical therapy, medical, and surgical expertise as developers and authors of the clinical practice guidelines for exercise-based knee injury prevention. These experts were given the task of describing the interventions and evidence for exercise-based knee injury prevention. The authors declared relationships and developed a conflict management plan, which included submitting a Conflict of Interest form to the Orthopaedic Section, APTA, Inc. Funding was provided by the Orthopaedic and Sports Physical Therapy Sections, APTA and the APTA to the CPG development team for travel and expenses for CPG development training. The CPG development team maintained editorial independence.

With the assistance of a research librarian (TH), the authors systematically searched PubMed, Scopus, SportDiscus, CINAHL, and the Cochrane databases for relevant articles. Literature searches were performed on June 2015 and updated in April 2016 and October 2017. Reference lists of included sources were hand-searched for additional articles not identified in the searches. [See **APPENDIX A** for full search strategies and **APPENDIX B** for search dates and results].
Inclusion and exclusion criteria used to select relevant articles were:

<u>Inclusion criteria:</u>

- Exercise-based knee injury prevention
    - Studies needed to expressly state that knee injuries of any kind were the specific target of the program and outcome measure of the study.
    - Exercise-based prevention was defined as an intervention requiring the participant to be active and move their body. This could include physical activity, strengthening, stretching, neuromuscular, proprioceptive, agility, or plyometric exercises, other training modality, but excluded passive interventions such as bracing, or programs that only involved education.
    - Knee injuries were defined as any knee joint pathology including damage to the joint (patellofemoral and/or tibiofemoral), ligaments, meniscus, or patella tendon.
        - Articles that only focused on one type of knee injury, eg. anterior cruciate ligament (ACL) injuries, were included
        - Mechanism of injury included both contact (injuries as a result of collision with another person or object) and non-contact (injuries that do not involve another individual or object).[16] (This CPG discusses contact and non-contact injuries together, unless specifically noted in the text.)
- Meta-analyses
- Systematic reviews
- Randomized controlled trials (RCTs)
- High-level cohort studies (critical appraisal score on Scottish Intercollegiate Guidelines Network (SIGN) checklist ≥ 5)
- Published in a peer-reviewed journal
- Able to access full-text article
- Published and accessible in English

<u>Exclusion criteria:</u>

- Injury prevention programs aimed at preventing all lower extremity injuries
- Injury prevention programs aimed at preventing lower extremity injuries other than knee injuries (eg, ankle injury prevention programs)
- Injury prevention programs aimed at modifying risk factors for knee injuries (eg, modifying peak knee abduction moment)
- Non-exercise-based interventions (eg, prophylactic bracing)
- Case series
- Case-control studies
- Case studies

This guideline focuses on exercise-based *knee* injury prevention programs, and excludes broader programs aimed at preventing *lower extremity* injuries. *Lower extremity* injury prevention programs target a wide range of pathologies, thus select different exercises or focus athlete feedback on joints other than the knee. Further, mechanisms of prevention may also differ. Programs targeting risk factors for knee injuries (for example, programs focused on modifying knee biomechanics during jump landing) were also excluded from this CPG. There are a number of modifiable and non-modifiable risk factors for knee injuries. However, the size of each risk factor for an athlete can be dependent on many other variables. For example, hormonal changes as a result of menstruation may affect women but not men,[20] similarly asymmetries in jump landing have been associated with knee injuries in women[30] but not, to date, in men. As an international group of experts in prevention, familiar with the prevention literature as a whole as well as specific to knee injuries, the authors felt these were appropriate restrictions.

Components of training programs were defined as different exercise approaches involved in the prevention program. For example, a program that only involved balance exercises was considered to only have one component, where a program that involved strengthening and plyometric exercises was considered to have multiple components. Common components include flexibility, strengthening, plyometrics, balance, agilities.

One author (DS) screened articles for full-text availability, publication in English, and in peer reviewed journals. Two authors (AA and AG or DL) then independently screened articles for inclusion based on title and abstract. The authors then discussed their findings. Articles that clearly did not meet inclusion criteria based on title and abstract were excluded at this point, any article that the authors were unsure of or seemed to clearly meet inclusion criteria were then full-text reviewed. Full-text reviews were performed independently by the same authors. The authors met to review their findings, and all disagreements on inclusion/exclusion were resolved by discussion. Consensus was reached on all articles. [See **APPENDIX C** for flowchart of articles and **APPENDIX D** for the citations of articles included in this guideline]

All authors were involved in the quality assessment and data extraction process. Two authors independently assessed the quality of each article. . The A Measurement Tool to Assess Systematic Reviews (AMSTAR) tool was used to assess the quality of meta-analyses and systematic reviews.[58] The Physiotherapy Evidence Database (PEDro) scale was used to assess the quality of RCTs,[75] the SIGN checklist the quality of cohort studies,[59] and the Drummond checklist the quality of cost effectiveness analyses.[11] Authors established reliability in the use of each quality appraisal tool by independently assessing articles not included in the CPG, discussing their scoring, and coming to consensus on areas of disagreement. Discrepancies in quality ratings were resolved through discussion of the 2 authors. Studies that were authored by a reviewer were assigned to an alternate reviewer. Studies with a quality score less than 5 on any scale were considered low quality and were not used in the development of these guidelines.[38] [See **APPENDIX E** for quality assessment scores] Recommendations were written based on the included articles and were agreed upon by all authors. **APPENDIX A** through **I** are available on the CPGs web page at www.orthopt.org.

This guideline was issued in 2018 based on the published literature up to October 2017. This guideline will be considered for review in 2022, or sooner if new evidence becomes available. Any updates to the guideline in the interim period will be noted on the Orthopaedic Section of the APTA website: www.orthopt.org

LEVELS OF EVIDENCE

Articles were graded according to criteria adapted from the Centre for Evidence-Based Medicine, Oxford, United Kingdom for diagnostic, prospective, and therapeutic studies.[56] In 4 teams of 2, authors came to consensus to assign a level of evidence based on the quality assessment of each articles. [See **APPENDIX F** and **G** for evidence table and details on procedures used for assigning levels of evidence]. An abbreviated version of the grading system is provided below.

I	Evidence obtained from high quality diagnostic studies, prospective studies, randomized controlled trials, or systematic reviews
II	Evidence obtained from lesser-quality diagnostic studies, prospective studies, systematic reviews, or, randomized controlled trials (eg, weaker diagnostic criteria and reference standards, improper randomization, no blinding, less than 80% follow-up)
III	Case controlled studies or retrospective studies
IV	Case series
V	Expert opinion

GRADES OF EVIDENCE

In teams of 2, the authors developed recommendations based on the strength of evidence, including how directly the studies addressed exercise-based knee injury prevention programs. The strength of the evidence supporting each recommendation was graded according to the previously established methods and is provided below. In developing their recommendations, the authors considered the strengths and limitations of the body of evidence and the health benefits and risks of interventions.

GRADES OF RECOMMENDATION		STRENGTH OF EVIDENCE
A	Strong evidence	A preponderance of level I and/or level II studies support the recommendation. This must include at least one level I study
B	Moderate evidence	A single high-quality randomized controlled trial or a preponderance of level II studies support the recommendation
C	Weak evidence	A single level II study or a preponderance of level III and IV studies, including statements of consensus by content experts, support the recommendation
D	Conflicting evidence	Higher-quality studies conducted on this topic disagree with respect to their conclusions. The recommendation is based on these conflicting studies
E	Theoretical/ foundational evidence	A preponderance of evidence from animal or cadaver studies, from conceptual models/principles, or from basic sciences/bench research support this conclusion
F	Expert opinion	Best practice based on the clinical experience of the guidelines development team

DESCRIPTION OF GUIDELINE REVIEW PROCESS AND VALIDATION

Identified reviewers who are experts in knee injury prevention reviewed the CPG draft for integrity, accuracy, and to ensure that it fully represented the current evidence for the condition. The guideline draft was also posted for public comment and review on www.orthopt.org and a notification of this posting was sent to the members of the Orthopaedic Section, APTA, Inc. In addition, a panel of consumer/patient representatives and external stakeholders, such as claims reviewers, medical coding experts, academic educators, clinical educators, physician specialists, and researchers also reviewed the guideline. All comments, suggestions, and feedback from the expert reviewers, public, and consumer/patient representatives were provided to the authors and editors for consideration and revisions. Guideline development methods policies, and implementation processes are reviewed at least yearly by the Orthopaedic Section, APTA's ICF-based Clinical Practice Guideline Advisory Panel, including consumer/patient representatives, external stakeholders, and experts in physical therapy practice guideline methodology.

DISSEMINATION AND IMPLEMENTATION TOOLS

In addition to publishing this guideline in the Journal of Orthopaedic & Sports Physical Therapy (JOSPT), it will be highlighted and posted on the CPG webpage of the JOSPT and the Orthopaedic Section, APTA websites. These webpages have unrestricted public access. The CPG has been submitted for inclusion on the Agency for Healthcare Quality and Research's publicly accessible website (guideline.gov). Implementation tools and associated implementation strategies that will be made available for athletes, coaches, patients, physicians, surgeons, clinicians, educators, payors, policy makers, and researchers include:

Tool	Strategy
• "Patient Perspectives"	• Patient-oriented guideline summary available on jospt.org and orthopt.org
• Mobile applications of guideline-based exercises for patient/clients, athletes, coaches, and healthcare practitioners	• Marketing and distribution of app using orthopt.org
• Clinician's Quick-Reference Guide	• Summary of guideline recommendations available on orthopt.org
• Read-for-credit continuing education content	• Continuing Education content available for physical therapists and athletic trainers from JOSPT
• Webinar-based educational offerings for healthcare practitioners	• Guideline-based instruction available for practitioners on orthopt.org
• Mobile and web-based applications for healthcare practitioner training	• Marketing and distribution of app using orthopt.org
• Non-English versions of the guidelines and guideline implementation tools	• Development and distribution of translated guidelines and tools to JOSPT's international partners and global audience via jospt.org

CLASSIFICATION

The primary International Classification of Disease-10 (ICD-10) codes and conditions associated with exercise-based knee injury prevention are S83.2 Tear of the (medial) (lateral) meniscus of the knee, S83.4 Sprain and strain involving (fibular) (tibial) collateral ligament of knee, S83.5 Sprain and strain involving (anterior)(posterior) cruciate ligament of knee, S83.7 Injury to multiple structures of knee, Injury to (lateral)(medial) meniscus in combination with (collateral)(cruciate) ligaments and M22.2 Patellofemoral disorders.

The primary ICF activities and participation codes associated with exercise-based knee injury prevention are d450 walking, d4552 running, d4553 jumping, d4559 moving around, specified as direction changes while walking or running, d9200 play, d9201 sports, and d9202 arts and culture.

ORGANIZATION OF THE GUIDELINES

Topics are arranged in relation to the CPG objectives. For each objective, the summaries of the evidence, levels of evidence, recommendation(s), and grade of recommendation(s) are provided.

Guidelines

A summary of the studies on exercise-based knee injury prevention programs that met the inclusion criteria for this CPG are found in the **Table**. Studies are organized by program.

Objective: Review the evidence in the scientific literature for exercise-based knee injury prevention programs. Systematic reviews and meta-analyses that look at prevention programs across populations (**Appendix H** available at www.orthopt.org and **Table)**.

Evidence

I

Three meta-analyses have examined exercise-based knee injury prevention programs across populations.[8, 17, 57] One meta-analysis examined the efficacy in reducing all knee injuries as well as reducing ACL injuries specifically, 2 focused only on ACL injuries.[17, 57] All of the studies included in these meta-analyses included athletes (sporting or tactical/military), with participants being men and women, of different ages and races, as well as different sports and skill levels.

The exercise-based prevention programs included in these analyses employed a number of different intervention strategies, from neuromuscular and proprioceptive training to strengthening, stretching, and plyometric exercises. Many of these programs employed more than one of these strategies, and gave participants feedback on their form during exercises, particularly jump landings.[8, 17, 57]

The pooled incidence rate ratio based on 19 studies (N= 19 143) indicated that exercise-based prevention programs are effective in reducing the incidence of knee injuries (incidence rate ratio 0.73 [95% confidence interval (CI) 0.61, 0.87]).[8] Programs in the meta-analysis showing efficacy in reducing knee injuries included: Emery et al,[13] FIFA11+,[24, 61] FIFA11 (The 11),[73] Goodall et al,[19] HarmoKnee,[34] Junge et al,[33] Knakontrol,[77] LaBella et al,[35] Malliou et al,[40] Olsen et al,[48] Pasanen et al,[51] Petersen et al,[52] Wedderkop et al.[78]

Pooled rate and risk ratios from the three meta-analyses[8, 17, 57] examining the impact of exercise-based knee injury prevention programs on incidence of primary ACL injuries indicate these programs are effective.[17, 57] Gagnier et al[17] examined 14 studies (N=27 000) and found a pooled rate ratio of 0.46 (95% CI 0.36, 0.60). Sadoghi et al[57] examined 8 studies (N=10 839) and found a pooled risk ratio of 0.38 (95% CI 0.20, 0.72). Donnell-Fink et al[8] examined 14 studies (N= 17 735) and found a rate ratio of 0.49 (95% CI 0.29, 0.85). This study narrowed their analysis to examine non-contact injuries, and found a rate ratio of 0.51 (95% CI 0.30, 0.88). Programs in the meta-analysis showing efficacy in reducing ACL injuries included: Caraffa et al,[5] HarmonKnee,[34] Heidt et al,[26] Knakontrol,[77] LaBella et al,[35] Myklebust et al[45] Olsen et al,[48] PEP,[18] Petersen et al,[52] Sportsmetrics.[28]

Evidence Synthesis
There is strong evidence that of important benefits of exercise-based knee injury prevention programs, including reduction in risk for all knee injuries and for ACL injuries specifically, with little risk of adverse events and minimal cost.

Recommendation
A
Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and ACL injuries including: *Programs for reducing all knee injuries:* Emery et al, FIFA11+, FIFA11, Goodall et al, HarmoKnee, Junge et al, Knäkontroll, LaBella et al, Malliou et al, Olsen et al, Pasanen et al, Petersen et al, Wedderkop et al. *Programs for reducing ACL injuries:* Caraffa et al, HarmoKnee, Heidt et al, Knäkontroll, LaBella et al, Myklebust et al, Olsen et al, PEP, Petersen et al, Sportsmetrics.

Objective: Identify exercise-based knee injury prevention programs that are effective for specific sub-groups of athletes. Systematic reviews, meta-analyses, and cohort studies that specifically delineate populations.

Appendices I and J (available at www.orthopt.org) summarize the evidence in this section.

Evidence
Men
II
One systematic review examined the effects of exercise-based prevention programs on ACL injuries in only men.[2] The review, by Alentorn-Geli et al[2] found that studies of exercise-based knee prevention programs in men were primarily performed on soccer teams. The review identified one program successful in reducing ACL injury rates. The Caraffa et al[5] program reported ACL injury rates in the intervention group of 0.15 ACL injuries/team/year and in the control group of 1.15 ACL injuries/team/year. The review also identified a study by Grooms et al[24] that examined the FIFA11+ program. Using a one season historical control, Grooms et al [24] did not observe an ACL injury in either the control or intervention season.

Women
I
Three meta-analyses indicate that, in women, exercise-based injury prevention programs are effective in reducing the risk of all ACL injuries with pooled odds ratios ranging from 0.40 to 0.64. [44, 72, 80] More specifically, when reporting on only non-contact ACL injuries, the pooled odds ratio was 0.38.[72, 80]

Programs identified by meta-analyses[44, 72, 80] as being effective in reducing the risk for ACL injuries in women were the PEP, Sportsmetrics, Knäkontroll, and HarmoKnee programs, as well as the programs used in the studies by Myklebust et al[45] and Petersen et al[52] Common themes of these successful programs were use of multiple types of exercises, participation during preseason or preseason and in-season, performance *prior* to training sessions/practices or games, and an emphasis on proper lower extremity alignment.[18, 26, 28, 34, 35, 41, 45, 48, 52, 63, 77]

Two programs were identified as being ineffective at preventing ACL injuries.[72, 80] The KLIP exercise-based knee injury prevention program, used by Pfeiffer et al[54] with high school aged women was used *after* practices and games. Despite an odds ratio of 2.05 suggesting a greater risk of incurring a non-contact ACL injury for the athletes in their intervention group, the wide 95% CI (0.21, 21.7) indicates a lack of statistical significance. Soderman et al[60] found that a greater percentage of athletes in their intervention group incurred non-contact ACL injuries (intervention 6.5%, control 1.3%, no p-value reported) and severe knee injuries (intervention 12.9%, control 7.7%, no p-value reported) than their control group. Unlike the effective programs that involved multiple exercise modalities, the Soderman et al[60] program only involved balance board training.

I
Adolescent female athletes seem to gain the most benefit from exercise-based knee injury prevention programs.[44, 67, 80] Two meta-analyses examined the effect of age, finding that women under 18 years of age have a greater reduction in ACL injuries (odds ratio 0.27-0.28) compared to women over 18 years old (odds ratio 0.78-0.84).[44, 80] One study analyzed age based on tertiles. Using 3 age groups, Myer et al[44] found a statistically significant reduction in ACL injuries for the youngest group but not for the older 2 groups: ages 14-18 (odds ratio 0.28, 95% CI 0.18, 0.42), ages 18-20 (odds ratio 0.48, 95% CI 0.21, 1.07), ages >20 (odds ratio 1.01, 95% CI 0.62, 1.64).[44] An additional study analyzed age in quartiles. Sugimoto et al[67] found that female athletes 14-18 years old had greater reduction in ACL injury incidence (odds ratio 0.29, 95% CI 0.19, 0.44, P=.01) compared to those < 14 years old (odds ratio 0.29, 95% CI 0.01, 7.09, P=.45), 18-20 (odds ratio 0.48, 95% CI 0.21, 1.07, P=.07), and > 20 years old (odds ratio 1.01, 95% CI 0.62, 1.64, P=.97).

Soccer
I
A meta-analysis of RCTs found a protective effect of exercise-based knee injury prevention programs in soccer players (men and women) for knee injuries (relative risk 0.74, 95% CI 0.55, 0.98). The study found a reduction in ACL injuries, though this decrease in incidence was not statistically significant (relative risk 0.66, 95% CI 0.33, 1.32).[21] Three prevention programs, however, were successful in significantly decreasing the incidence of ACL injuries in soccer players when compared to a control group (PEP, Knäkontroll, and the program used by Caraffa et al).[5, 41, 77]

Three individual studies included in this CPG (using the PEP, Knäkontroll, and HarmoKnee programs) examined the incidence of serious knee injuries.[28, 34, 77] While all 3 studies showed a decrease in the incidence of serious knee injuries,[28, 34, 77] the reduction was only statistically significant with the Knäkontroll program.[77] All 7 individual studies included in this CPG that examined ACL injury incidence in soccer players (PEP, Knäkontroll, KLIP, the program by Caraffa et al, Sportsmetrics), found a decrease in ACL injuries.[5, 18, 28, 34, 41, 54, 77]

II
In women soccer players (N=4564) between the ages of 12-17, the Knäkontroll program reduced ACL injuries in the intervention group by 64% (rate ratio 0.36, 95% CI 0.15, 0.85) and severe knee injuries by 30% (rate reduction 0.70, 95% CI 0.42, 1.18). [77]

II
Two studies examined the efficacy of the PEP program in reducing ACL injuries in women soccer players. Mandelbaum et al[41] examined 14-18 year old women and found an 88% decrease (rate ratio 0.11, 95% CI 0.03, 0.48) in ACL injuries compared to age and skill matched control athletes in the first season of the PEP program and a 74% decrease (rate ratio 0.28, 95% CI 0.09, 0.85) in the second season of use. Gilchrist et al[18] examined college age women and found lower, but non-significant differences in rates of ACL injuries in their intervention (0.20/1000 athletic exposures (AEs)) compared to their

control (0.34/1000 AES) group (P=.20).[18] The results were similar, lower but non-significant rates, when they examined non-contact ACL injuries specifically (Intervention = 0.06/1000 AES, Control = 0.19/1000AEs). There was a higher rate, though not significant, of overall knee injuries in their intervention group (1.14/1000 AEs) as compared to their control group (1.10/1000 AEs, P=.86).

II
Studies that have examined women soccer and handball players have shown effectiveness in reducing ACL injuries (soccer: odds ratio 0.32, 95% CI 0.19, 0.56; handball: odds ratio 0.54, 95% CI 0.30, 0.97).[80] However, making a direct comparisons of effectiveness between sports needs to be done with caution, because the exercise-based knee injury prevention programs used in each cohort were not identical.

Handball
II
Olsen et al[48] found significant reductions in acute knee injuries (relative risk 0.45, 95% CI 0.25, 0.81), and knee ligament injuries (relative risk 0.2, 95% CI 0.06, 0.70) in 15-17 year old male and female handball athletes after implementing an exercise-based knee injury prevention program. However, they noted no change in meniscal injuries (relative risk 0.27, 95% CI 0.06, 1.28).

II
Achenbach et al[1] found significant reductions in severe (injuries that cause ≥ 28 days absence from sport) knee injuries (odds ratio 0.11 [95% CI 0.01, 0.90], P=.02) in 15-17 year old male and female handball athletes.

II
In women handball players, Myklebust et al[45] did not find a significant decrease in ACL injuries after performing an exercise-based knee injury prevention program for 2 seasons. However, when comparing teams that were compliant with the program (performed the intervention 15+ times over the course of the season with at least 75% of players participating) to the teams who were not compliant, they found a significant decrease in ACL injuries in amongst the compliant elite handball athletes (odds ratio 0.06, 95% CI 0.01, 0.54).

Basketball
II
There is conflicting evidence on the effectiveness of exercise-based knee injury prevention programs in female basketball players. Hewett et al[28] observed fewer serious knee injuries in their female basketball intervention group. Although this was not a statistically significant difference in incidence (intervention 0.42 injuries/1000 AEs, control 0.48 injuries/1000 AEs, P=.17), it was a positive trend following their 6-week, preseason, 60-90 minute, plyometric based program. Female basketball players who had performed their intervention had significantly fewer non-contact knee injuries compared to untrained female basketball players (P=.02). In contrast, Pfeiffer et al[54] observed a 4 times greater risk of ACL injury in their intervention group compared to the control group (intervention 0.48 ACL injuries per 1000 AEs, control 0.11/1000 AEs,), following their 15-20 minute program that was performed after training sessions.

Volleyball
II

No conclusions can be drawn with regards to exercises-based knee injury prevention programs in female volleyball players. Two studies have included volleyball players, but neither study observed the outcome of interest (serious knee injury or ACL injury) in either the intervention or the control group.[28, 54]

Evidence Synthesis
There is evidence of important benefits of exercise-based knee injury prevention programs, including reduction of risk for knee and ACL injuries, with little risk of adverse events and minimal cost.

Recommendations
A
Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs prior to athletic training sessions/practices or games in women athletes to reduce the risk of ACL injuries, especially in women athletes under age 18. *Programs that should be implemented*: PEP, Sportsmetrics, Knäkontroll, HarmoKnee, Olsen et al, Petersen et al.

A
Soccer players, especially women, should use exercise-based knee injury prevention programs to reduce the risk of severe knee and ACL injuries. *Programs that could be beneficial for preventing knee injuries*: PEP, Knäkontroll, and HarmoKnee programs. *Programs that could be beneficial for preventing ACL injuries*: Caraffa et al, Sportsmetrics.

B
Men and women handball players, particularly those 15-17 years old, should implement exercise-based knee injury prevention programs. *Programs that could be beneficial for preventing knee injuries*: Olsen et al, Achenbach et al

Gaps in Knowledge
Although large scale prospective or randomized control trials are costly, the benefits of identifying programs effective in reducing knee injuries in men playing various sports outweigh these financial costs.

Researchers and clinicians should further evaluate the efficacy of exercise-based knee injury prevention programs in men of various ages and sports. *Programs that could be beneficial*: Caraffa et al

Researchers and clinicians should further evaluate the efficacy of exercise-based knee injury prevention programs in basketball and volleyball athletes.

Objective: Describe the evidence for components, dosage and delivery of exercise-based knee injury prevention programs.

Evidence
Components:
I
Exercise-based injury prevention programs are effective in reducing ACL injuries in young women when the programs incorporate multiple exercise components. Programs with multiple components resulted in ACL injury reductions (odds ratio 0.32, 95% CI 0.22, 0.46). In contrast, programs with only a single exercise component did not result is a significant reduction of injuries (odds ratio 1.15, 95% CI 0.70, 1.89).[69]

I

Exercise-based knee injury prevention programs in women that include proximal control exercises, such as trunk/core strengthening and stability exercises, led to significantly lower ACL injury rates (odds ratio 0.33, 95% CI 0.23, 0.47). In contrast, programs that did not include proximal control exercises did not reduce injury rates (odds ratio 0.95, 95% CI 0.60, 1.50).[69]

II

Programs that incorporate both plyometric and strengthening components are more effective at reducing ACL injuries in women than programs without both of these components.[64, 69, 80] Stevenson et al[64] noted that studies which have demonstrated statistically significant decreases in ACL injuries have all included strengthening, flexibility, and plyometric components in their program (PEP, Sportsmetrics, and the program used by Myklebust et al),[18, 28, 41, 45] and only one program with a plyometric component (the KLIP program used *after* training session and games)[54] has not resulted in a decrease in ACL injuries. Sugimoto et al[69] determined that when quantitatively comparing programs with and without plyometric components there was no significant difference in the ACL injury risk. However, when comparing programs with and without strengthening components there was a significant reduction in the number of ACL injuries only in those programs with strengthening exercises (odds ratio 0.32, 95% CI 0.23, 0.46). Those without strengthening exercises failed to reduce ACL injuries (odd ratio 1.02, 95% CI 0.63, 1.64).[69]

II

Programs without balance training components (Sugimoto et al[69] odds ratios 0.34, CI 0.20, 0.56; Yoo et al[80] odds ratios 0.27) are effective in preventing ACL injuries in women. There are differing results as to whether programs with balance training components are effective (Sugimoto et al[69] odds ratio 0.59, CI 0.42, 0.83; Yoo et al[80] odds ratio 0.63, CI 0.37, 1.09). Taylor et al[72] found that as the duration spent performing balance exercises increased the protective effect of the program decreased. One program, Soderman et al,[60] was included in all 3 meta-analyses examining the components of prevention program.[69, 72, 80] Soderman et al[60] only included balance exercises and observed a greater rate of ACL injuries in the intervention group.

II

Sadoghi et al[57] performed a meta-regression to determine the factors that influence the effect of an exercise-based knee injury prevention program in women. They found that use of balance boards (P=.71), use of video assistance (P=.91), duration of follow-up (P=.44), or year of study publication (P=.36) did not influence a program's ACL injury risk reduction.

Dosage and Delivery:

I

Gagnier et al[17] performed a meta-analysis, including men and women which indicated that programs with a longer duration (>14 months, incidence rate ratio estimate 0.41, 95% CI 0.20, 0.84, P=.01), more hours of training per week (≥75 hours per week, incidence rate ratio estimate 0.38, 95% CI 0.18, 0.77, P<.01), higher compliance (≥64%, incidence rate ratio estimate 0.39, 95% CI 0.17, 0.89, P=.03), and no participant drop-out (incidence rate ratio estimate 0.30, 95% CI 0.15, 0.62, P<.01) were more effective at reducing ACL injury incidence than programs that did not have these qualities.

I

Sugimoto et al[66] performed a meta- and subgroup analysis on clinical trials and evaluated potential dosage effects of exercise-based injury prevention training for ACL injury reduction in female athletes.

Exercise-based injury prevention programs implemented multiple times per week had an odds ratio of 0.35 (95% CI 0.23, 0.53) in reducing ACL injuries compared to programs that only used training once a week, which had an odds ratio of 0.62 (95% CI 0.41, 0.94). Programs that lasted 20 minutes or less per session had an odds ratio of 0.61 (95% CI 0.41, 0.90) in reducing ACL injuries, where programs that lasted longer than 20 minutes per session had an odds ratio of 0.35 (95% CI 0.23, 0.53). Programs with a high volume during the season, 30+ minutes per week had an odds ratio of 0.32, (95% CI 0.19, 0.52) in reducing ACL injuries, compared to those with moderate (15-30 minutes per week, odds ratio 0.46, 95% CI 0.21, 1.03) and low volumes (up to 15 minutes per week, odds ratio 0.66, 95% CI 0.43, 0.99).

I

Donnell-Fink et al[8] examined men and women, comparing preseason only and preseason + in-season programs to in-season only programs and found lower risk for knee injuries (preseason/preseason + in-season incidence rate ratio 0.24, in-season only 0.75, No confidence intervals presented, P<.01). They did not find a significant result with this same comparison for ACL injuries specifically (preseason/preseason + in-season incidence rate ratio 0.32, in-season only 0.57, P=.33).[8]

In women, exercise-based knee injury prevention programs that began in the preseason and continued throughout the season were effective (odds ratio 0.54, 95% CI 0.30, 0.97) in reducing ACL injuries. [80] Programs in-season only (odds ratio 0.32, 95% CI 0.17, 0.59), had a lower odds ratio than programs in preseason and in-season. Programs in the preseason only (odds ratio 0.35, 95% CI 0.10, 1.21) were not effective in reducing ACL injuries.[80]

I

Sugimoto et al[67] performed a meta-regression examining the "synergistic effects," of components of exercise-based knee injury prevention program components that they deemed key to optimizing ACL injury prevention. They grouped age in tertiles (14-18, 18-20, 20+), dosage was dichotomized (≤ 20 minutes per session, >20 minutes per session), frequency was dichotomized (1x/week, multiple times/ week), then number of exercises was dichotomized (programs made up of only one exercise component, programs made up of multiple components, and verbal feedback to athletes on their form was dichotomized (verbal feedback given, no verbal feedback). Points were assigned to groups based on previously reported odds ratios, with higher points given to groupings that demonstrated lower odds ratios (greater ACL injury reduction). Groups with the highest points were age 14-18 years, programs > 20 minutes in duration, programs performed multiple times per week and with multiple exercise components The results indicated an odds ratio of 0.83 ($\beta 1$= -0.29, 95% CI -0.33, -0.03, P=.03), or a 17% reduction in ACL injury risk if one of these highest point groups was present.

Compliance

I

Sugimoto et al[68] performed a meta-analysis of studies involving female soccer, basketball, volleyball, and handball athletes concluding that higher rates of compliance with exercise-based injury prevention programs were associated with lower rates of ACL injury incidence among adolescent female athletes. The authors found that when compliance was dichotomized (greater than versus less than 42.5% overall compliance rate*) the incidence rate in the high compliance group was 73% lower (incidence rate ratio 0.27, 95% CI 0.07, 0.80), and when divided into tertiles (>66.6%, 33.3-66.6%, <33.3% overall compliance) the high compliance group had 82% lower ACL injury incidence (incidence rate ratio 0.18, 95% CI 0.02, 0.77) than the medium or low compliance groups. The authors reported that a potential inverse dose-response relationship exists between compliance with an exercise-based injury prevention program and the incidence of ACL injury in adolescent female athletes. *Overall compliance rate was defined as the attendance rate multiplied by the compliance rate. With attendance rate defined as the number of participants who completed the minimum amount of session criteria in the study divided by the total number of participants in the intervention group. Compliance rate was defined as the number of sessions completed in the study by the maximum number of sessions offered to the intervention group.

II

Studies of female soccer players, with data adjusted for compliance, found greater knee injury incidence reductions in athletes who were compliant with the exercise-based prevention programs.[34, 77] Kiani et al[34] using the HarmoKnee program found a 77% lower incidence of knee injuries (rate ratio 0.23, 95% CI 0.04, 0.83) and 90% lower incidence of non-contact knee injuries (rate ratio 0.10, 95% CI 0.00, 0.70). These reductions in knee injury risk decreased further when they were adjusted for compliance (removal of 3 teams who performed the intervention with < 75% compliance, leaving 45 teams in the intervention group). Athletes who were compliant with the HarmoKnee program had an 87% reduction in knee injury incidence (rate ratio 0.17, 95% CI 0.04, 0.64) and 94% decrease in non-contact knee injuries (rate ratio 0.06, 95% CI 0.01, 0.46).

II

Walden et al[77] using the Knäkontroll program in a cluster RCT found an overall 64% decrease in ACL injury incidence (rate ratio 0.36, 95% CI 0.15, 0.85) in their intervention group compared to controls, but when they examined only their compliant players (defined as players having performed the intervention once per week on average) found an 83% reduction in ACL injury rate (rate ratio 0.17, 95% CI 0.05, 0.57). They also found that compliant players had an 82% reduction in the rate of severe knee injuries (rate ratio 0.18, 95% CI 0.07, 0.45) and 47% reduction in the rate of acute knee injuries (rate ratio 0.53, 95% CI 0.30, 0.94).

Hagglund et al[25] performed a sub-analysis on the same RCT.[77] Teams and players in the intervention group (184 teams/2471 players) were stratified into tertiles of compliance (low, intermediate, and high) based on their mean number of weekly injury prevention program training sessions during the season. High player compliance (mean 89% compliance rate) resulted in an 88% reduction in ACL injury rate compared with low compliance (mean 63% compliance rate). Intermediate compliance (mean 82% compliance rate) and high compliance reduced acute knee injury by 72-90% compared to low compliance. Low compliance players had higher rates of ACL injuries than the control players.

Evidence Synthesis

There is evidence of important benefits of exercise-based knee injury prevention programs, including reduction of risk for knee and/or ACL injuries, with little risk of adverse events and minimal cost.

Recommendations

A

Exercise-based knee injury prevention programs used for women should incorporate multiple components, proximal control exercises and should incorporate a combination of strength and plyometric exercises

A

Exercise-based knee injury prevention programs should involve training multiple times per week, individual training sessions that last longer than 20 minutes, and training volumes that are longer than 30 minutes per week. .

A

Clinicians, coaches, parents, and athletes should start exercise-based knee injury prevention programs in preseason and continue them through the regular season. .

A
Clinicians, coaches, parents, and athletes must ensure high compliance with exercise-based knee injury prevention programs, particularly in female athletes.

B
Exercise-based knee injury prevention programs may not need to incorporate balance exercises, and balance should not be the sole component of a program.

Objective: Provide suggestions for implementation of exercise-based knee injury prevention programs.

<u>Evidence</u>

I
Grindstaff et al[23] performed a systematic review to determine the number of athletes needed to treat and the relative risk reduction in non-contact ACL injuries associated with exercise-based knee injury prevention programs. The sample included female soccer, basketball, or handball athletes using 5 different prevention programs that varied in their exercise components. Frequency of training ranged from 3 times per week in the preseason to 1 to 3 times per week during the season. They reported that to prevent 1 non-contact ACL injury during a sports season, 89 athletes (95% CI or number needed to benefit 66-136) would have to participate in a prevention program. The relative risk reduction for a non-contact ACL injuries was 70% (95% CI 54, 80%) in athletes involved in a prevention program.

I
An updated systematic review was published by Sugimoto et al,[70] examining 12 studies (including all 5 studies reviewed by Grindstaff et al[23]), to determine the effectiveness of exercise-based injury prevention programs designed to reduce ACL injury risk and non-contact ACL injury risk in female athletes. Sugimoto et al[70] reported that to prevent 1 ACL injury during a sports season, 120 athletes (95% CI or number needed to benefit 74, 316) would need to participate in an exercise-based knee injury prevention program. The relative risk reduction for ACL injury was 43.8% (95% CI 28.9, 55.5%) in athletes involved in the prevention programs. Over the course of 1 season, to prevent 1 non-contact ACL injury, 108 athletes (95% CI or number needed to benefit 86, 105) would have to participate in an exercise-based knee injury prevention program, with a relative risk reduction for non-contact ACL injury of 73.4% (95% CI 62.5, 81.1%) in athletes involved in the prevention programs.

I
Lewis et al[37] performed a cost analysis of 4 hypothetical strategies for implementing exercise-based ACL injury prevention programs across Australia. Using a prevention program similar to those in the literature,[18, 31, 53, 54] performed 3 times per week for 20 minutes, and supervised by coaches and medical staff, the study examined the resulting costs if implemented across Australia in 12-25 year olds involved in high risk sports, 18-25 year olds involved in high risk sports, 12-17 year olds involved in high risk sports, or all adolescents 12-17 year olds involved in any sport. High risk sports were defined as rugby, Australian rules football, netball, soccer, basketball, and skiing. The authors found that the implementation strategy involving training 12-25 year olds involved in high risk sport had the highest break even value (or the future healthcare costs avoided) at $693 per person. The strategy of training 18-25 year olds in high risk sports was the next most cost effective with a break even cost of $401, followed

by 12-17 year olds in high risk sports at $370, and all 12-17 year olds in sports at $102. The analysis also found that the strategy of training 12-25 year olds in high risk sports would prevent the highest number of ACL injuries (3764 per 100 000 treated), had the lowest numbers needed to treat (27), as well as prevented the highest number of future knee osteoarthritis cases (842/100 000) and total knee replacements (584 per 100 000). In comparison the strategy of training 18-25 year olds in high risk sports was estimated to prevent 2303 ACL injuries per 100 000 participants (numbers needed to treat 43, osteoarthritis cases prevented: 511 per 100 000 treated, total knee replacements prevented 353 per 100 000 treated), followed by the 12-17 year olds in high risk sports preventing 2021 ACL injuries prevented per 100 000 treated (numbers needed to treat 49, osteoarthritis cases prevented 457 per 100 000 treated, total knee replacements prevented 317 per 100 000 treated), and the 12-17 year olds in all sports preventing 526 ACL injuries per 100 000 treated (numbers needed to treat 190, osteoarthritis cases prevented 119 per 100 000 treated, total knee replacements prevented 83 per 100 000 treated).

II
Swart et al[71] performed a cost-effectiveness analysis on prevention and screening programs for ACL injuries in young athletes that participated in pivoting and cutting sports. They reported that an exercise-based ACL injury prevention program performed by all athletes could reduce the incidence of ACL injury from 3% per season to 1.1% per season while a screening program that targeted high-risk athletes could reduce ACL injury incidence from 3% per season to 1.8% per season. On a per-case basis, the average cost of the universal training strategy was $100 lower than no training and $25 lower than screen and training strategy.

II
Pfile et al[55] performed a numbers needed to treat analysis examining exercise-based ACL injury prevention programs lead by coaches versus programs led by what they termed a mixed leadership group, or coaches, physiotherapists, and/or athletic trainers. Programs led by a mixed leadership group had a lower numbers needed to benefit (120 athletes needed to treat to prevent 1 ACL injury, 95% CI 73, 303), but a slightly higher relative risk reduction 48.2% (95% CI 22, 65%), compared to coach led programs which had a numbers needed to benefit of 131 (95% CI 98, 196) and relative risk reduction of 58.4% (95% CI 40, 71).

Evidence Synthesis
There is no increase in risk of adverse events when all athletes perform prevention program compared to only athletes screened as high risk, no harms in performing prevention programs. Although cost may minimally increase (depending on program) as more athletes participate, these may be outweighed in long term health care costs, and the reduction in ACL injuries.

Recommendation

A
Clinicians and coaches should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as high risk for ACL injury, to optimize the numbers needed to treat while reducing cost.

A
For the greatest reduction in future medical costs, and prevention of ACL injuries, osteoarthritis, and total knee replacements, clinicians, coaches, parents, and athletes should encourage implementation of exercise-based ACL injury prevention programs in athletes 12-25 years old and involved in high ACL injury risk sports.

B
Clinicians, coaches, parents, and athletes should support implementation of exercise-based knee injury prevention programs led by either coaches or a group of coaches and medical professionals.

Gaps in Knowledge Summary

Objective: Identify exercise-based knee injury prevention programs that are effective for specific sub-groups of athletes.
Although large scale prospective or randomized control trials are costly, the benefits of identifying programs effective in reducing knee injuries in men playing various sports outweigh these financial costs.

Researchers and clinicians should further evaluate the efficacy of exercise-based knee injury prevention programs in men of various ages and sports.. *Programs that could be beneficial*: Caraffa et al

Researchers and clinicians should further evaluate the efficacy of exercise-based knee injury prevention programs in basketball and volleyball athletes.

The recommendations made in this guideline are summarized in the **Figure**.

Figure

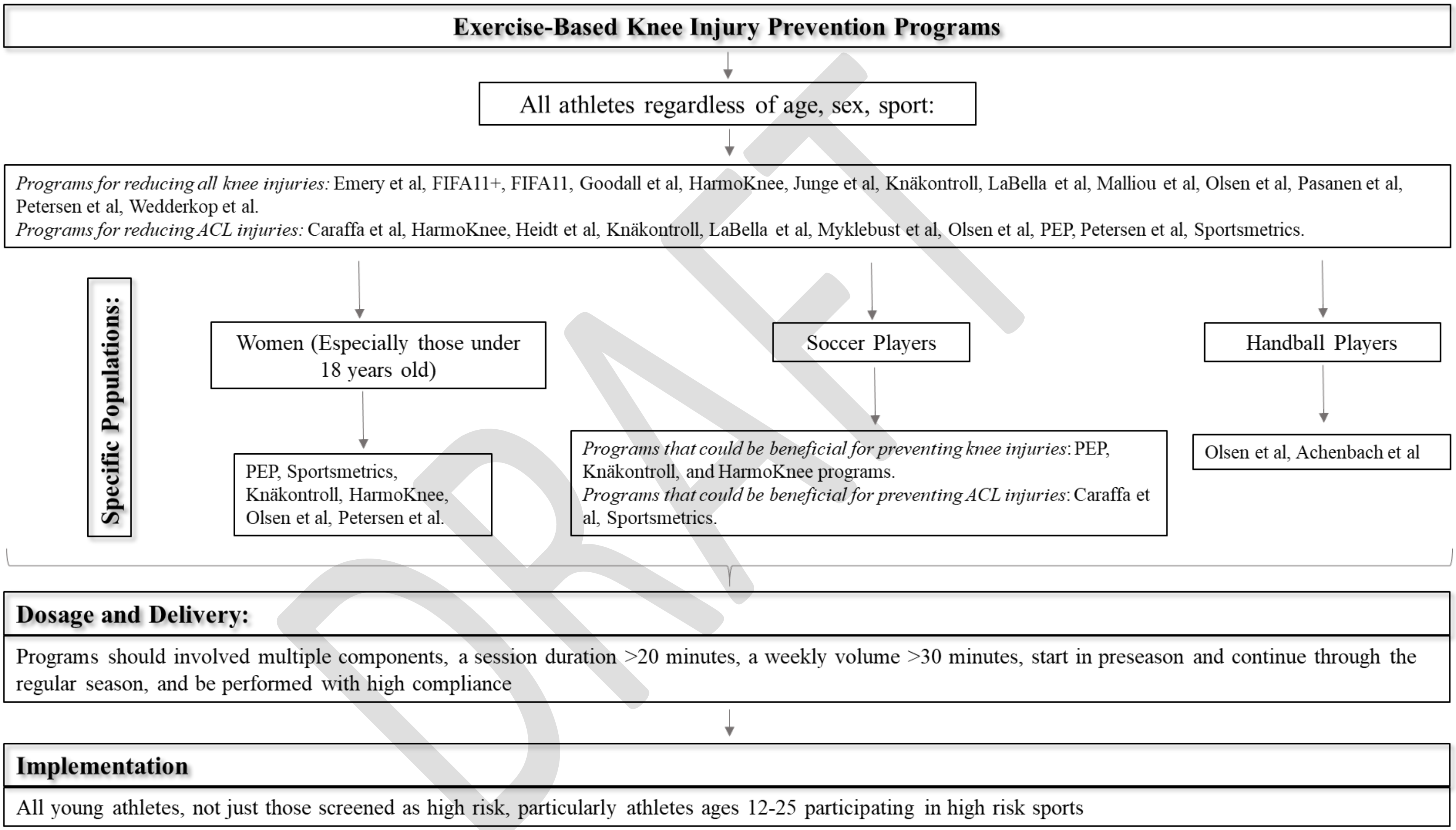
Exercise-Based Knee Injury Prevention Programs
All athletes regardless of age, sex, sport:
Programs for reducing all knee injuries: Emery et al, FIFA11+, FIFA11, Goodall et al, HarmoKnee, Junge et al, Knäkontroll, LaBella et al, Malliou et al, Olsen et al, Pasanen et al, Petersen et al, Wedderkop et al.
Programs for reducing ACL injuries: Caraffa et al, HarmoKnee, Heidt et al, Knäkontroll, LaBella et al, Myklebust et al, Olsen et al, PEP, Petersen et al, Sportsmetrics.
Specific Populations:
Women (Especially those under 18 years old)
PEP, Sportsmetrics, Knäkontroll, HarmoKnee, Olsen et al, Petersen et al.
Soccer Players
Programs that could be beneficial for preventing knee injuries: PEP, Knäkontroll, and HarmoKnee programs.
Programs that could be beneficial for preventing ACL injuries: Caraffa et al, Sportsmetrics.
Handball Players
Olsen et al, Achenbach et al
Dosage and Delivery:
Programs should involved multiple components, a session duration >20 minutes, a weekly volume >30 minutes, start in preseason and continue through the regular season, and be performed with high compliance
Implementation
All young athletes, not just those screened as high risk, particularly athletes ages 12-25 participating in high risk sports

Figure Description: The *exercise based knee injury prevention* heading summarizes the programs observed to be effective when studied across populations. Below exercise based knee injury prevention programs heading are the *specific populations*. These two groups (exercise based knee injury prevention and specific populations) are not mutually exclusive, all programs found in the specific populations area are also found in the exercise based knee injury prevention area, however the program listed for specific populations may be more effective or have been studied in detail in that particular group. The *Dosage and delivery* and *Implementation* sections provide a summary of recommendations on how programs should be set up and executed.

Table: Programs included in this guideline

Program	Study Type	Subjects	Duration	Effect	Harms
Achenbach et al	https://www.ncbi.nlm.nih.gov/pubmed/29058022				
Achenbach[1]	Block RCT	Intervention N= 168 Control N= 111 Male and female handball players ages 15-17 years old	One handball season	Significant reduction in severe (injuries that caused >28 days absence from sport) knee injuries • Control group severe knee injury incidence 0.33/1000 hours • Intervention group severe knee injury incidence 0.04/1000 hours • Odds ratio 0.11 (95% CI 0.01, 0.90), P=.02	None
Caraffa et al	http://www.ncbi.nlm.nih.gov/pubmed/8963746				
Caraffa[5]	Cohort	N=600 Semi-professional and amateur soccer players in Umbri and Marche Italy Age and sex not provided	30 days during preseason (20 min, every day)	Significant difference in injury incidence between intervention and control teams (P<.01) • Intervention teams = 0.15 ACL injuries per season • Control teams =1.15 ACL injuries per season	None
HarmoKnee	http://harmoknee.com/ http://www.ncbi.nlm.nih.gov/pubmed/20065198				
Kiani[34]	Cohort	Intervention N=777 Control N=729 Female soccer players ages 13-19	4 months (Approximately 20-25 minutes, 2x/wk during preseason, 1x/wk during the regular season)	Knee Injuries: • Intervention incidence 0.04/1000 hours • Control 0.20/1000 hours • Unadjusted rate ratio 0.23 (95% CI 0.04, 0.83) • Rate ratio adjusted for compliance 0.17 (95% CI 0.04, 0.64) Non-contact knee injuries: • Intervention 0.01/1000 hours • Control 0.15/1000 hours • Unadjusted rate ratio 0.10 (95% CI 0.00, 0.70)	None

				• Rate ratio adjusted for compliance 0.06 (95% CI 0.01, 0.46) There were no ACL injuries in the intervention group	
KLIP	http://www.ncbi.nlm.nih.gov/pubmed/15574070				
Pfieffer[54]	Cohort	Intervention N=577 Control N=862 Female high school aged soccer, basketball, or volleyball players	Throughout high school season (20 min, but the authors did not report the recommended number of times per week)	• Incidence of non-contact ACL injuries in the control group 0.078/1000 AEs and intervention group 0.167/1000 AEs • Overall there was a non-significant increase in odds of ACL injury in the intervention groups (odds ratio 2.05, 95% CI 0.21, 21.7, P>.05) • There were no non-contact ACL injuries in the volleyball control group or the soccer or volleyball intervention groups • There were more non-contact ACL injuries in the basketball intervention group 0.476/1000 AEs than the basketball control group 0.111/1000 AEs	None
Knäkontroll	App available on Apple or Android platforms: https://itunes.apple.com/se/app/knakontroll/id573826071?mt=8 https://play.google.com/store/apps/details?id=se.rf.sisu&hl=en				
Walden[77]	Stratified RCT	Intervention N=2479 Control N=2085 Female soccer players ages 13-17	Throughout soccer season (15 min, 2x/week)	64% reduction in ACL injuries in intervention group (rate ratio 0.36, 95% CI 0.15, 0.85, P=.02). When adjusted for compliance:	None

				• 83% reduction in ACL injuries (rate ratio of 0.17, 95% CI 0.05, 0.57, P<.01) • 88% reduction in severe knee injury (rate ratio 0.18, 95% CI 0.07, 0.45, P<.01) • 47% reduction in all acute knee injuries (rate ratio 0.53, 95% CI 0.30, 0.94, P=.03)	
Myklebust et al	http://www.ncbi.nlm.nih.gov/pubmed/12629423				
Myklebust[45]	Cohort	Control season N=942 1st intervention Season N=855 2nd intervention Season N=850 Female Norwegian handball league players, mean age not provided.	Through handball season including pre-season (15 minutes, 3x/week during preseason, 1x/week during regular season)	• Control season ACL injury incidence 0.14/1000 playing hours • 1st intervention season ACL injury incidence 0.13/1000 playing hours • 2nd intervention season ACL injury incidence 0.06/1000 playing hours • No significant difference in injury rate (odds ratio 0.52, 95% CI 0.15, 1.82, P=.31) • When adjusted for compliance there was a significant decrease in injury risk in the elite division (odds ratio 0.06, 95% CI 0.01, 0.54, P=.01)	None
Olsen et al	http://www.ncbi.nlm.nih.gov/pubmed/15699058				
Olsen[48]	Cluster RCT	Intervention N=958 Control N=879 Female handball players ages 16-17 years old.	Through one 8-month handball season (15-20 minutes, 15 consecutive training sessions at the start of the season, followed by 1x/week for the remainder of the season)	Significant reduction in all injuries (relative risk 0.49, 95% CI 0.39, 0.63, P<.01) • Acute knee injuries (relative risk 0.45, 95% CI 0.35-, 0.81, P<.01). • Number of athletes needed to treat to prevent 1 acute knee injury was 43 Significant reduction in knee ligament injuries (relative risk 0.2, 95% CI 0.06, 0.70, P=.01) Non-significant reduction in meniscal injuries (relative risk 0.27, 95% CI 0.06, 1.28, P=.10)	None
PEP	http://smsmf.org/smsf-programs/pep-program				

Gilchrist[18]	Cluster RCT	Control N=852 Intervention N=583 NCAA Division I Female Soccer players, Mean age 19.88 years	12 weeks through collegiate soccer season (15-20min 3x/week)	Overall no significant difference in injury rates for all knee injuries (P=.86) or ACL injuries (P=.20) The intervention group had: • Lower ACL injury rate in practices (P=.01) • Lower late season ACL injury rate (P=.03) • Lower rate of non-contact ACL injuries in those who reported a history of ACL injury (P=.05) No difference between groups in the injury rates during games (P=.62), early in the season (P=.93), or amongst those with no history of prior ACL injury (P=.43)	One player tripped during the lateral hops and had a tibia and fibular fracture. After which, the cone height used was adjusted to be shorter.
Mandelbaum[41]	Cohort	Year 1: Intervention N=1041 Control N=1905 Year 2: Intervention N=844 Control N=1931 Female soccer players, ages 14-18	Throughout soccer season (20 min, the authors did not report recommended number of times per week)	Overall incidence of ACL injuries for the intervention group was 0.09/1000 AEs and for the control group 0.49/1000 AEs over the 2-year study Relative risk 0.18 (P<.01) When broken down by year: • Year 1: 89% reduction in ACL injuries (relative risk 0.11, P<.01) • Year 2: 74% reduction in risk (relative risk 0.26, P<.01)	None
Sportsmetrics	http://sportsmetrics.org/ https://www.ncbi.nlm.nih.gov/pubmed/10569353				

Hewett[28]	Cohort	Female Intervention N=366 Female Control N=463 Male Control N=434 Female high school aged soccer, basketball, and volleyball players	6 weeks during preseason (60-90 minutes, 3x/week)	Trained females had significantly lower rate of severe knee injuries (incidence 0.12/1000 AEs) than untrained females (incidence 0.43/1000 AEs, P=.05). • Untrained females had a higher rate of severe knee injuries than males (incidence 0.09/1000 AEs, P=.03), but there was no difference in rate of severe knee injuries between trained females and males (P=.86). • The trained female group (incidence 0) had significant lower rate of non-contact knee injuries compared to the untrained female (incidence 0.35/1000 AEs, P=.01) and untrained male groups (incidence 0.05/1000 AEs P=.01).	

Programs included in Meta-analyses/Systematic Reviews, but did not meet criteria for inclusion in CPG: The below programs were included in meta-analyses and systematic reviews that met the CPG inclusion criteria, however the individual studies of these programs did not meet the inclusion criteria.	
FIFA11+	http://fifamedicinediploma.com/lessons/prevention-fifa-11/
Emery et al[13]	https://www.ncbi.nlm.nih.gov/pubmed/20547668
Goodall et al[19]	https://www.ncbi.nlm.nih.gov/pubmed/22924758
Heidt et al[26]	https://www.ncbi.nlm.nih.gov/pubmed/11032220
Junge et al[33]	https://www.ncbi.nlm.nih.gov/pubmed/12238997
LaBella et al[36]	https://www.ncbi.nlm.nih.gov/pubmed/18832542
Malliou et al[40]	https://www.ncbi.nlm.nih.gov/pubmed/15446640
Pasanen et al[51]	https://www.ncbi.nlm.nih.gov/pubmed/18595903
Petersen et al[52]	https://www.ncbi.nlm.nih.gov/pubmed/23189409
Soderman et al[60]	https://www.ncbi.nlm.nih.gov/pubmed/11147154
Wedderkop et al[78]	https://www.ncbi.nlm.nih.gov/pubmed/9974196

AFFILIATIONS & CONTACTS

Authors:

Amelia J. H. Arundale, PT, PhD
Biomechanics and Movement Science Program
University of Delaware
Newark, DE
and
Linköping University
Department of Medical and Health Sciences
Division of Physiotherapy
Linköping, Sweden
arundale@udel.edu

Mario Bizzini, PT, PhD, MSc,
Research Associate and Orthopedic and Sports Physiotherapist
Schulthess Clinic
Zurich, Switzerland
Mario.bizzini@f-marc.com

Airelle Giordano, DPT
Assistant Professor
Department of Physical Therapy
University of Delaware
Newark, DE
aohunter@udel.edu

Tim Hewett, PhD
Director of Biomechanics and Sports Medicine Research Mayo Sports Medicine Center
Departments of Orthopedics, PM&R, and Physiology and Biomedical Engineering
The Mayo Clinic
Rochester, MN
Hewett.timothy@mayo.edu

Bert Mandelbaum, MD
Orthopedic Surgeon
Santa Monica Orthopaedic & Sports Medicine Group
Santa Monica, CA
bmandelbau@aol.com

David Logerstedt, PT, PhD
Assistant Professor
Department of Physical Therapy
University of the Sciences
Philadelphia, PA
d.logerstedt@usciences.edu

David Scalzitti, PT, PhD
Assistant Professor

Reviewers

Roy D. Altman, MD
Professor of Medicine
Division of Rheumatology and Immunology
David Geffen School of Medicine at UCLA
Los Angeles, CA
journals@royaltman.com

Paul Beattie, PT, PhD
Clinical Professor Division of Rehabilitative Sciences
Arnold School of Public Health
University of South Carolina
Columbia, SC
pbeattie@gwm.sc.edu

Dean Caswell, PT, ATC, AT/L
Clinical Director
ATI Physical Therapy Seattle Cabrini
Orthopedic Residency Committee Member ATI WA
Seattle, WA
dean.caswell@atipt.com

Marie Charpentier, PT, DPT, ATC, LAT
Coordinator of Sports and Athletic Training Residency ProgramsHouston Methodist Orthopedics and Sports Medicine
mtpotter@houstonmethodist.org

John DeWitt, DPT
Director of Physical Therapy Sports & Orthopaedic Residencies
The Ohio State University
Columbus, OH
john.dewitt@osumc.edu

James M. Elliott, PT, PhD
Professor
Northern Sydney Local Health District and Faculty of Health Sciences
The University of Sydney
Lidcombe, Sydney, AU
jim.elliott@sydney.edu.au
and
Adjunct Professor
NUPTHMS, Feinberg School of Medicine
Northwestern University
Chicago, IL

Helene M. Fearon, PT
Arizona Physical Therapy Specialists

Department of Physical Therapy
George Washington University
Washington, DC
scalzitt@gwu.edu

Holly Silvers-Granelli, PT, PhD
Physical Therapist
Velocity Physical Therapy
Santa Monica, CA
and
Biomechanics and Movement Science Program
University of Delaware
Newark, DE
hollysilverspt@gmail.com

Lynn Snyder-Mackler, PT, ScD
Alumni Distinguished Professor
Department of Physical Therapy
University of Delaware
Newark, DE
smack@udel.edu

Phoenix, AZ
hfearon123@mac.com

Amanda Ferland, DPT
Clinical Faculty
Tongji University / USC Division of Biokinesiology and Physical Therapy
Orthopaedic Physical Therapy Residency and Spine Rehabilitation Fellowship
Shanghai, China
AmandaFerland@incarehab.com

G. Kelley Fitzgerald, PT, PhD
Professor and Associate Dean of Graduate Studies
School of Health & Rehabilitation Sciences
University of Pittsburgh
Pittsburgh, PA
kfitzger@pitt.edu

Jennifer S. Howard, ATC, PhD
Assistant Professor
Athletic Training Department of Health and Exercise Science Beaver College of Health Sciences
Appalachian State University
Boone, NC
howardjs@appstate.edu

David Killoran, PhD
Patient/Consumer Representative for the ICF-based Clinical Practice Guidelines
Orthopaedic Section, APTA Inc.
La Crosse, WI
and
Professor Emeritus
Loyola Marymount University
Los Angeles, CA
david.killoran@lmu.edu

Joanna Kvist, PT, PhD
Professor
Linköping University
Department of Medical and Health Sciences
Division of Physiotherapy
Linköping, Sweden
joanna.kvist@liu.se

Robert Marx, MD, MSc
Department of Orthopaedics
Hospital for Special Surgery
New York, NY
marxr@hss.edu

Sean Stedeford
Head Women's Soccer Coach
Colorado Academy
Denver, Colorado
sean.stedeford@coloradoacademy.org

Leslie Torburn, DPT
Principal and Consultant
Silhouette Consulting, Inc.
Sacramento, CA
torburn@yahoo.com

James Zachazewski, DPT
Clinical Director
Department of Physical and Occupational Therapy
Massachusetts General Hospital
Boston, MA
jzachazewski@partners.org
and
Clinical Content Lead, Health Professions
Partners eCare
Boston, MA
and
Adjunct Assistant Clinical Professor
Program in Physical Therapy
MGH Institute of Health Professions
Charlestown, MA

ICF-based Clinical Practice Guidelines Editor

Christine M. McDonough, PT, PhD
ICF-based Clinical Practice Guidelines Editor
Orthopaedic Section, APTA Inc.
La Crosse, WI
and
Assistant Professor of Physical Therapy
School of Health and Rehabilitation Sciences
University of Pittsburgh
Pittsburg, PA
cmm295@pitt.edu

Guy G. Simoneau, PT, PhD
ICF-based Clinical Practice Guidelines Editor
Orthopaedic Section, APTA Inc.
La Crosse, WI
and
Professor
Physical Therapy Department
Marquette University

Milwaukee, WI
guy.simoneau@marquette.edu

Joseph J. Godges, DPT, MA
Adjunct Associate Professor of Clinical Physical Therapy
Division of Biokinesiology and Physical Therapy at the Ostrow School of Dentistry
University of Southern California
Los Angeles, CA
godges@usc.edu
and
ICF-based Clinical Practice Guidelines Editor
Orthopaedic Section, APTA Inc.
La Crosse, WI

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References

1. Achenbach, L., Krutsch, V., Weber, J., et al. Neuromuscular exercises prevent severe knee injury in adolescent team handball players. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017:http://dx.doi.org/10.1007/s00167-017-4758-5
2. Alentorn-Geli, E., Mendiguchia, J., Samuelsson, K., et al. Prevention of non-contact anterior cruciate ligament injuries in sports. Part ii: Systematic review of the effectiveness of prevention programmes in male athletes. *Knee Surg Sports Traumatol Arthrosc* 2014:22(1):16-25. http://dx.doi.org/10.1007/s00167-013-2739-x
3. Bencke, J., Næsborg, H., Simonsen, E. B. and Klausen, K. Motor pattern of the knee joint muscles during side-step cutting in european team handball. *Scandinavian Journal of Medicine & Science in Sports* 2000:10(2):68-77. http://dx.doi.org/10.1034/j.1600-0838.2000.010002068.x
4. Brushøj, C., Larsen, K., Albrecht-Beste, E., Nielsen, M. B., Løye, F. and Hölmich, P. Prevention of overuse injuries by a concurrent exercise program in subjects exposed to an increase in training load: A randomized controlled trial of 1020 army recruits. *American Journal of Sports Medicine* 2008:36(4):663. http://dx.doi.org/10.1177/0363546508315469
5. Caraffa, A., Cerulli, G., Projetti, M., Aisa, G. and Rizzo, A. Prevention of anterior cruciate ligament injuries in soccer. *Knee Surgery, Sports Traumatology, Arthroscopy* 1996:4(1):19.
6. Cochrane, J., Lloyd, D., Besier, T., Elliot, B., Doyle, T. and Ackland, T. Training affects knee kinematics and kinetics in cutting maneuvers in sport. *Medicine & Science in Sports & Exercise* 2010:42(8):1535-1544. http://dx.doi.org/10.1249/MSS.0b013e3181d03ba0
7. Dempsey, A., Llyod, D., Elliot, B., Steele, J., Munro, B. and Russo, K. The effect of technique change on knee loads during sidestep cutting. *Medicine & Science in Sports & Exercise* 2007:39(10):1765-1773. http://dx.doi.org/10.1249/mss.0b013e31812f56d1
8. Donnell-Fink, L. A., Klara, K., Collins, J. E., et al. Effectiveness of knee injury and anterior cruciate ligament tear prevention programs: A meta-analysis. *PLoS ONE* 2015:10(12):e0144063. http://dx.doi.org/10.1371/journal.pone.0144063
9. Donnelly, C. J., Elliott, B. C., Doyle, T. L. A., Finch, C. F., Dempsey, A. R. and Lloyd, D. G. Changes in knee joint biomechanics following balance and technique training and a season of australian football. *British Journal of Sports Medicine* 2012:http://dx.doi.org/10.1136/bjsports-2011-090829
10. Drummond, M. F. and Jefferson, T. O. Guidelines for authors and peer reviewers of economic submissions to the bmj. *Bmj* 1996:313(7052):275-283. http://dx.doi.org/10.1136/bmj.313.7052.275
11. Drummond, M. F., Sculpher, M. J., Claxton, K., Stoddart, G. L. and Torrance, G. W. *Methods for the economic evaluation of health care programmes*. Oxford university press; 2015.
12. Ekstrand, J., Gillquist, J. and Liljedahl, S.-O. Prevention of soccer injuries: Supervision by doctor and physiotherapist. *Am.J.Sports Med.* 1983:11(3):116-120. http://dx.doi.org/10.1177/036354658301100302
13. Emery, C. A. and Meeuwisse, W. H. The effectiveness of a neuromuscular prevention strategy to reduce injuries in youth soccer: A cluster-randomised controlled trial. *British Journal of Sports Medicine* 2010:44(8):555-562. http://dx.doi.org/10.1136/bjsm.2010.074377
14. Engebretsen, A. H., Myklebust, G., Holme, I., Engebretsen, L. and Bahr, R. Prevention of injuries among male soccer players: A prospective, randomized intervention study targeting players with previous injuries or reduced function. *Am.J.Sports Med.* 2008:36(6):1052-1060. http://dx.doi.org/10.1177/0363546508314432
15. Ettlinger, C. F., Johnson, R. J. and Shealy, J. E. A method to help reduce the risk of serious knee sprains incurred in alpine skiing. *Am.J.Sports Med.* 1995:23(5):531-537. http://dx.doi.org/10.1177/036354659502300503
16. Fuller, C. W., Ekstrand, J., Junge, A., et al. Consensus statement on injury definitions and data collection procedures in studies of football (soccer) injuries. *Scandinavian journal of medicine & science in sports* 2006:16(2):83-92.
17. Gagnier, J. J., Morgenstern, H. and Chess, L. Interventions designed to prevent anterior cruciate ligament injuries in adolescents and adults: A systematic review and meta-analysis. *American Journal of Sports Medicine* 2013:41(8):1952.
18. Gilchrist, J., Mandelbaum, B. R., Melancon, H., et al. A randomized controlled trial to prevent non contact anterior cruciate ligament injury in female collegiate soccer players. *American Journal of Sports Medicine* 2008:36(8):1476.

19. Goodall, R. L., Pope, R. P., Coyle, J. A. and Neumayer, R. Balance and agility training does not always decrease lower limb injury risks: A cluster-randomised controlled trial. *International Journal of Injury Control and Safety Promotion* 2013:20(3):271-281. http://dx.doi.org/10.1080/17457300.2012.717085
20. Griffin, L. Y., Albohm, M. J., Arendt, E. A., et al. Understanding and preventing noncontact anterior cruciate ligament injuries: A review of the hunt valley ii meeting, january 2005. *Am.J.Sports Med.* 2006:34(9):1512.
21. Grimm, N. L., Jacobs, J. C., Jr., Kim, J., Denney, B. S. and Shea, K. G. Anterior cruciate ligament and knee injury prevention programs for soccer players: A systematic review and meta-analysis. *Am.J.Sports Med.* 2015:43(8):2049-2056. http://dx.doi.org/10.1177/0363546514556737
22. Grimm, N. L., Shea, K. G., Leaver, R. W., Aoki, S. K. and Carey, J. L. Efficacy and degree of bias in knee injury prevention studies: A systematic review of rcts sports. *Clin.Orthop.* 2013:471(1):308.
23. Grindstaff, T. L., Hammill, R. R., Tuzson, A. E. and Hertel, J. Neuromuscular control training programs and noncontact anterior cruciate ligament injury rates in female athletes: A numbers-needed-to-treat analysis. *Journal of Athletic Training (National Athletic Trainers' Association)* 2006:41(4):450.
24. Grooms, D. R., Palmer, T., Onate, J. A., Myer, G. D. and Grindstaff, T. Soccer-specific warm-up and lower extremity injury rates in collegiate male soccer players. *Journal of Athletic Training* 2013:48(6):782-789. http://dx.doi.org/10.4085/1062-6050-48.4.08
25. Hagglund, M., Atroshi, I., Wagner, P. and Walden, M. Superior compliance with a neuromuscular training programme is associated with fewer acl injuries and fewer acute knee injuries in female adolescent football players: Secondary analysis of an rct. *British journal of sports medicine* 2013:47(15):974. http://dx.doi.org/10.1136/bjsports-2013-092644 [doi]
26. Heidt, R. S., Sweeterman, L. M., Carlonas, R. L., Traub, J. A. and Tekulve, F. X. Avoidance of soccer injuries with preseason conditioning. *Am.J.Sports Med.* 2000:28(5):659-662.
27. Hewett, T. E., Ford, K. R. and Myer, G. D. Anterior cruciate ligament injuries in female athletes part 2, a meta-analysis of neuromuscular interventions aimed at injury prevention. *American Journal of Sports Medicine* 2006:34(3):490.
28. Hewett, T. E., Lindenfeld, T. N., Riccobene, J. V. and Noyes, F. R. The effect of neuromuscular training on the incidence of knee injury in female athletes. A prospective study. *Am.J.Sports Med.* 1999:27(6):699.
29. Hewett, T. E., Myer, G. D. and Ford, K. R. Reducing knee and anterior cruciate ligament injuries among female athletes: A systematic review of neuromuscular training interventions. *J.Knee Surg.* 2005:18(1):82.
30. Hewett, T. E., Myer, G. D., Ford, K. R., et al. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: A prospective study. *American Journal of Sports Medicine* 2005:33(4):492-501.
31. Hewett, T. E., Stroupe, A. L., Nance, T. A. and Noyes, F. R. Plyometric training in female athletes: Decreased impact forces and increased hamstring torques. *Am.J.Sports Med.* 1996:24(6):765-773. http://dx.doi.org/10.1177/036354659602400611
32. Jamison, S., McNeilan, R., Young, G., Givens, D., Best, T. and Chaudhari, A. M. W. Randomized controlled trial of the effects of a trunk stabilization program on trunk control and knee loading. *Medicine & Science in Sports & Exercise* 2012:44(10):1924-1934. http://dx.doi.org/10.1249/MSS.0b013e31825a2f61
33. Junge, A., Rösch, D., Peterson, L., Graf-Baumann, T. and Dvorak, J. Prevention of soccer injuries: A prospective intervention study in youth amateur players. *Am.J.Sports Med.* 2002:30(5):652-659.
34. Kiani, A., Hellquist, E., Ahlqvist, K., Gedeborg, R., Michaelsson, K. and Byberg, L. Prevention of soccer-related knee injuries in teenaged girls. *Arch Intern Med* 2010:170(1):43-49. http://dx.doi.org/10.1001/archinternmed.2009.289
35. LaBella, C. R., Huxford, M. R., Grissom, J., Kim, K. Y., Peng, J. and Christoffel, K. K. Effect of neuromuscular warm-up on injuries in female soccer and basketball athletes in urban public high schools: Cluster randomized controlled trial. *Arch.Pediatr.Adolesc.Med.* 2011:165(11):1033. http://dx.doi.org/10.1001/archpediatrics.2011.168 [doi]
36. LaBella, C. R., Huxford, M. R., Smith, T. L. and Cartland, J. Preseason neuromuscular exercise program reduces sports-related knee pain in female adolescent athletes. *Clin.Pediatr.(Phila)* 2009:48(3):327. http://dx.doi.org/10.1177/0009922808323903
37. Lewis, D. A., Kirkbride, B., Vertullo, C. J., Gordon, L. and Comans, T. A. Comparison of four alternative national universal anterior cruciate ligament injury prevention programme implementation strategies to reduce

secondary future medical costs. *British Journal of Sports Medicine* 2016:http://dx.doi.org/10.1136/bjsports-2016-096667
38. Logerstedt, D. S., Snyder-Mackler, L., Ritter, R. C., Axe, M. J. and Godges, J. J. Knee stability and movement coordination impairments: Knee ligament sprain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the american physical therapy association. *Journal of Orthopaedic & Sports Physical Therapy* 2010:40(4):A1-A37.
39. Longo, U. G., Loppini, M., Berton, A., Marinozzi, A., Maffulli, N. and Denaro, V. The fifa 11+ program is effective in preventing injuries in elite male basketball players: A cluster randomized controlled trial. *Am.J.Sports Med.* 2012:40(5):996-1005. http://dx.doi.org/10.1177/0363546512438761
40. Malliou, P., Amoutzas, K., Theodosiou, A., et al. Proprioceptive training for learning downhill skiing. *Perceptual and Motor Skills* 2004:99(1):149-154. http://dx.doi.org/10.2466/pms.99.1.149-154
41. Mandelbaum, B. R., Silvers, H. J., Watanabe, D. S., et al. Effectiveness of a neuromuscular and proprioceptive training program in preventing anterior cruciate ligament injuries in female athletes: 2-year follow-up. *American Journal of Sports Medicine* 2005:33(7):1003.
42. Michaelidis, M. and Koumantakis, G. A. Effects of knee injury primary prevention programs on anterior cruciate ligament injury rates in female athletes in different sports: A systematic review. *Physical Therapy in Sport* 2014:15(3):200.
43. Myer, G. D., Ford, K. R., Brent, J. L. and Hewett, T. E. Differential neuromuscular training effects on acl injury risk factors in"high-risk" versus "low-risk" athletes. *BMC Musculoskelet.Disord.* 2007:8(39. http://dx.doi.org/1471-2474-8-39 [pii]
44. Myer, G. D., Sugimoto, D., Thomas, S. and Hewett, T. E. The influence of age on the effectiveness of neuromuscular training to reduce anterior cruciate ligament injury in female athletes: A meta-analysis. *Am.J.Sports Med.* 2013:41(1):203. http://dx.doi.org/10.1177/0363546512460637 [doi]
45. Myklebust, G., Engebretsen, L., Braekken, I., Skjolberg, A., Olsen, O. and Bahr, R. Prevention of anterior cruciate ligament injuries in female team handball players: A prospective intervention study over three seasons. *Scandinavian Journal of Medicine & Science in Sports* 2003:13(4):272.
46. Noyes, F. R. and Barber-Westin, S. D. Neuromuscular retraining intervention programs: Do they reduce noncontact anterior cruciate ligament injury rates in adolescent female athletes? *Arthroscopy* 2014:30(2):245. http://dx.doi.org/10.1016/j.arthro.2013.10.009 [doi]
47. Noyes, F. R. and Barber Westin, S. D. Anterior cruciate ligament injury prevention training in female athletes: A systematic review of injury reduction and results of athletic performance tests. *Sports Health: A Multidisciplinary Approach* 2012:4(1):36.
48. Olsen, O.-E., Myklebust, G., Engebretsen, L., Holme, I. and Bahr, R. Exercises to prevent lower limb injuries in youth sports: Cluster randomised controlled trial. *Bmj* 2005:330(7489):449. http://dx.doi.org/10.1136/bmj.38330.632801.8F
49. Organization, W. H. *International classification of functioning, disability, and health*. Geneva, Switzerland; 2010.
50. Padua, D. A. and Marshall, S. W. Evidence supporting acl-injury-prevention exercise programs: A review of the literature. *Athletic Therapy Today* 2006:11(2):11.
51. Pasanen, K., Parkkari, J., Pasanen, M., et al. Neuromuscular training and the risk of leg injuries in female floorball players: Cluster randomised controlled study. *Bmj* 2008:337(http://dx.doi.org/10.1136/bmj.a295
52. Petersen, W., Braun, C., Bock, W., et al. A controlled prospective case control study of a prevention training program in female team handball players: The german experience. *Archives of Orthopaedic and Trauma Surgery* 2005:125(9):614. http://dx.doi.org/10.1007/s00402-005-0793-7
53. Petersen, W., Zantop, T., Steensen, M., Hypa, A., Wessolowski, T. and Hassenpflug, J. Prevention of lower extremity injuries in handball: Initial results of the handball injuries prevention programme. *Sportverletzung Sportschaden: Organ der Gesellschaft fur Orthopadisch-Traumatologische Sportmedizin* 2002:16(3):122-126.
54. Pfeiffer, R. P., Shea, K. G., Roberts, D. and Grandstrand, S. Lack of effect of a knee ligament injury prevention program on the incidence of noncontact anterior cruciate ligament injury. *J Bone Joint Surg (Am)* 2006:88A(8):1769.

55. Pfile, K. R. and Curioz, B. Coach-led prevention programs are effective in reducing anterior cruciate ligament injury risk in female athletes: A number-needed-to-treat analysis. *Scandinavian Journal of Medicine and Science in Sports* 2017:http://dx.doi.org/10.1111/sms.12828
56. Phillips, B., Ball, C., Sackett, D., et al. Levels of evidence. 2009; http://www.cebm.net/index.aspx?o=4590. Accessed August 4, 2009.
57. Sadoghi, P., von Keudell, A. and Vavken, P. Effectiveness of anterior cruciate ligament injury prevention training programs. *J Bone Joint Surg (Am)* 2012:94(9):769.
58. Shea, B. J., Grimshaw, J. M., Wells, G. A., et al. Development of amstar: A measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology* 2007:7(1):1-7. http://dx.doi.org/10.1186/1471-2288-7-10
59. Sleith, C. Methodology checklist 3: Cohort studies. *Checklist 3--Cohort Studies* 2012; Checklist for assessing the quality of cohort studies. Available at: http://www.sign.ac.uk/methodology/checklists.html. Accessed August 3, 2013, 2013.
60. Soderman, K., Werner, S., Pietila, T., Engstrom, B. and Alfredson, H. Balance board training: Prevention of traumatic injuries of the lower extremities in female soccer players? A prospective randomized intervention study. *Knee Surg Sports Traumatol Arthrosc* 2000:8(6):356-363.
61. Soligard, T., Myklebust, G., Steffen, K., et al. Comprehensive warm-up programme to prevent injuries in young female footballers: Cluster randomised controlled trial. *Bmj* 2008:337(a2469. http://dx.doi.org/10.1136/bmj.a2469
62. Soligard, T., Nilstad, A., Steffen, K., et al. Compliance with a comprehensive warm-up programme to prevent injuries in youth football. *British Journal of Sports Medicine* 2010:44(11):787-793. http://dx.doi.org/10.1136/bjsm.2009.070672
63. Steffen, K., Myklebust, G., Olsen, O. E., Holme, I. and Bahr, R. Preventing injuries in female youth football – a cluster-randomized controlled trial. *Scandinavian Journal of Medicine & Science in Sports* 2008:18(5):605-614. http://dx.doi.org/10.1111/j.1600-0838.2007.00703.x
64. Stevenson, J. H., Beattie, C. S., Schwartz, J. B. and Busconi, B. D. Assessing the effectiveness of neuromuscular training programs in reducing the incidence of anterior cruciate ligament injuries in female athletes: A systematic review. *American Journal of Sports Medicine* 2015:43(2):482.
65. Stojanovic, M. D. and Ostojic, S. M. Preventing acl injuries in team-sport athletes: A systematic review of training interventions. *Research in Sports Medicine* 2012:20(3):223.
66. Sugimoto, D., Myer, G., Barber Foss, K. and Hewett, T. Dosage effects of neuromuscular training intervention to reduce anterior cruciate ligament injuries in female athletes: Meta- and sub-group analyses. *Sports Medicine* 2014:44(4):551.
67. Sugimoto, D., Myer, G. D., Barber Foss, K. D., Pepin, M. J., Micheli, L. J. and Hewett, T. E. Critical components of neuromuscular training to reduce acl injury risk in female athletes: Meta-regression analysis. *British journal of sports medicine* 2016:50(20):1259-1266. http://dx.doi.org/10.1136/bjsports-2015-095596
68. Sugimoto, D., Myer, G. D., Bush, H. M., Klugman, M. F., McKeon, J. M. M. and Hewett, T. E. Compliance with neuromuscular training and anterior cruciate ligament injury risk reduction in female athletes: A meta-analysis. *Journal of Athletic Training (Allen Press)* 2012:47(6):714.
69. Sugimoto, D., Myer, G. D., Foss, K. D. B. and Hewett, T. E. Specific exercise effects of preventive neuromuscular training intervention on anterior cruciate ligament injury risk reduction in young females: Meta-analysis and subgroup analysis. *British journal of sports medicine* 2015:49(5):282.
70. Sugimoto, D., Myer, G. D., McKeon, J. M. and Hewett, T. E. Evaluation of the effectiveness of neuromuscular training to reduce anterior cruciate ligament injury in female athletes: A critical review of relative risk reduction and numbers-needed-to-treat analyses. *British journal of sports medicine* 2012:46(14):979.
71. Swart, E., Redler, L., Fabricant, P. D., Mandelbaum, B. R., Ahmad, C. S. and Wang, Y. C. Prevention and screening programs for anterior cruciate ligament injuries in young athletes: A cost-effectiveness analysis. *J Bone Joint Surg (Am)* 2014:96(9):705. http://dx.doi.org/10.2106/jbjs.m.00560
72. Taylor, J. B., Waxman, J. P., Richter, S. J. and Shultz, S. J. Evaluation of the effectiveness of anterior cruciate ligament injury prevention programme training components: A systematic review and meta-analysis *British journal of sports medicine* 2013:49(79-87. http://dx.doi.org/10.1136/bjsports-2013-092358

73. van Beijsterveldt, A. M., Krist, M. R., Schmikli, S. L., et al. Effectiveness and cost-effectiveness of an injury prevention programme for adult male amateur soccer players: Design of a cluster-randomised controlled trial. *Inj.Prev.* 2011:17(1):e2. http://dx.doi.org/10.1136/ip.2010.027979
74. van Beijsterveldt, A. M., van de Port, I. G., Krist, M. R., et al. Effectiveness of an injury prevention programme for adult male amateur soccer players: A cluster-randomised controlled trial. *British journal of sports medicine* 2012:46(16):1114. http://dx.doi.org/10.1136/bjsports-2012-091277
75. Verhagen, A. P., de Vet, H. C. W., de Bie, R. A., et al. The delphi list: A criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by delphi consensus. *Journal of Clinical Epidemiology* 1998:51(12):1235-1241. http://dx.doi.org/http://dx.doi.org/10.1016/S0895-4356(98)00131-0
76. Vescovi, J. D. and VanHeest, J. L. Effects of an anterior cruciate ligament injury prevention program on performance in adolescent female soccer players. *Scandinavian Journal of Medicine & Science in Sports* 2010:20(3):394. http://dx.doi.org/10.1111/j.1600-0838.2009.00963.x [doi]
77. Walden, M., Atroshi, I., Magnusson, H., Wagner, P. and Hgglund, M. Prevention of acute knee injuries in adolescent female football players: Cluster randomised controlled trial. *Bmj Br Med J (Overseas & Retired Doctors Ed)* 2012:344(7858):16. http://dx.doi.org/10.1136/bmj.e3042
78. Wedderkopp, N., Kaltoft, M., Lundgaard, B., Rosendahl, M. and Froberg, K. Prevention of injuries in young female players in european team handball. A prospective intervention study. *Scandinavian journal of medicine & science in sports* 1999:9(1):41-47.
79. Wen-Dien, C., Ping-Tung, L. and Turner, T. Neuromuscular training for prevention of anterior cruciate ligament injury in female athletes. *International Journal of Athletic Therapy & Training* 2014:19(6):17.
80. Yoo, J. H., Lim, B. O., Ha, M., et al. A meta-analysis of the effect of neuromuscular training on the prevention of the anterior cruciate ligament injury in female athletes. *Knee Surgery, Sports Traumatology, Arthroscopy* 2010:18(6):824.

APPENDIX A Search strategy for all databases searched

Search Strategy	**Search Limits**
PubMed	
(Sports [MeSH] OR Athletes [MeSH] OR Exercise [MeSH] OR Athletic Injuries [MeSH]) AND ((Knee Injuries [MeSH]) OR ((Wounds and Injuries [MeSH] OR injur* [TW]) AND (ACL [TW] OR Anterior Cruciate Ligament* [TW] OR Anterior Cruciate Ligament [MeSH]))) AND (Risk Reduction Behavior [MeSH] OR Prevent* [TW] OR Predict* [TW])	English only, then Clinical Trial, Clinical Trial Phase I, Clinical Trial Phase II, Clinical Trial Phase III, Clinical Trial Phase IV, Comparative Study, Controlled Clinical Trial, Evaluation Studies, Guideline, Introductory Journal Article, Journal Article, Meta-Analysis, Multicenter Study, Observational Study, Practice Guideline, Pragmatic Clinical Trial, Randomized Control Trial, Systematic Reviews, Twin Study
Scopus	
(TITLE-ABS-KEY (Sport*) OR TITLE-ABS-KEY (Athlet*) OR TITLE-ABS-KEY (Exercise) OR TITLE-ABS-KEY (Athletic Injur*)) AND ((TITLE-ABS-KEY (Knee Injur*)) OR ((TITLE-ABS-KEY(Wound*) OR TITLE-ABS-KEY (Injur*)) AND (TITLE-ABS-KEY (Anterior Cruciate Ligament) OR TITLE-ABS-KEY (ACL)))) AND (TITLE-ABS-KEY (Risk Reduction) OR TITLE-ABS-KEY (Prevent*) OR TITLE-ABS-KEY (Predict*))	English only, limit to Article, Review, and Article in Press
SportDiscus	
((TI (Sport*) OR AB (Sport*) OR (DE "Sports")) OR (TI (Athlet*) OR AB (Athlet*) OR (DE "ATHLETICS")) OR (TI (Exercise) OR AB (Exercise) OR (DE "EXERCISE")) OR (TI (Athletic Injur*) OR AB (Athletic Injur*))) AND ((TI (Knee Injur*) OR AB (Knee Injur*)) OR ((((TI (Wound*) OR AB (Wound*)) OR (TI (Injur*) OR AB (Injur*))) OR (DE "WOUNDS & injuries")) AND ((TI (Anterior Cruciate Ligament) OR AB (Anterior Cruciate Ligament) OR (DE "ANTERIOR cruciate ligament")) OR (TI (ACL) OR AB (ACL))))) AND ((TI (Risk Reduction) OR AB (Risk Reduction)) OR (TI (Prevent*) OR AB (Prevent*) OR (DE "PREVENTION")) OR (TI (Predict*) OR AB (Predict*)))	English, English Abstract Only, Peer-Reviewed, Academic Journal
CINAHL	
((TI (Sport*) OR AB (Sport*) OR (MH "Sports+")) OR (TI (Athlet*) OR AB (Athlet*)) OR (TI (Exercise) OR AB (Exercise) OR (MH "Exercise+")) OR (TI (Athletic Injur*) OR AB (Athletic Injur*) OR (MH "Athletic Injuries+"))) AND ((TI (Knee Injur*) OR AB (Knee Injur*) OR (MH "Knee Injuries+")) OR ((TI (Wound*) OR AB (Wound*) OR TI (Injur*) OR AB (Injur*) OR (MH "Wounds and Injuries+")) AND (TI (Anterior Cruciate Ligament) OR AB (Anterior Cruciate Ligament) OR TI (ACL) OR AB (ACL) OR (MH "Anterior Cruciate Ligament+")))) AND ((TI (Risk Reduction) OR AB (Risk Reduction)) OR (TI (Prevent*) OR AB (Prevent*)) OR (TI (Predict*) OR AB (Predict*)))	English Language checkbox, Adolescent, Adult, Middle-Aged, Aged 65+. Aged 80+, Clinical Trial, Corrected Article, Journal Article, Practice Guidelines, Research, Systematic Review
Cochrane	
((Sport*) OR (Athlet*) OR (Exercise) OR (Athletic Injur*)) AND (((Knee Injur*)) OR (((Wound*) OR (Injur*)) AND ((Anterior Cruciate Ligament) OR (ACL)))) AND ((Risk Reduction) OR (Prevent*) OR (Predict*))	Cochrane Reviews - ALL, Other Reviews, Trials, Technology Assessments, Economic Evaluations

APPENDIX B Search dates and results

Initial Search

Database	**Date Conducted**	**Results, n**
PubMed	3/31/2015	812
SCOPUS	3/31/2015	2083
SportDiscus	3/31/2015	511
CINAHL	3/31/2015	275
Cochrane Library	3/31/2015	145
Cochrane reviews		6
Other reviews		12
Trials		126
Technology assessments		0
Economic evaluations		1
Total		3826
Total with duplicates removed		2623

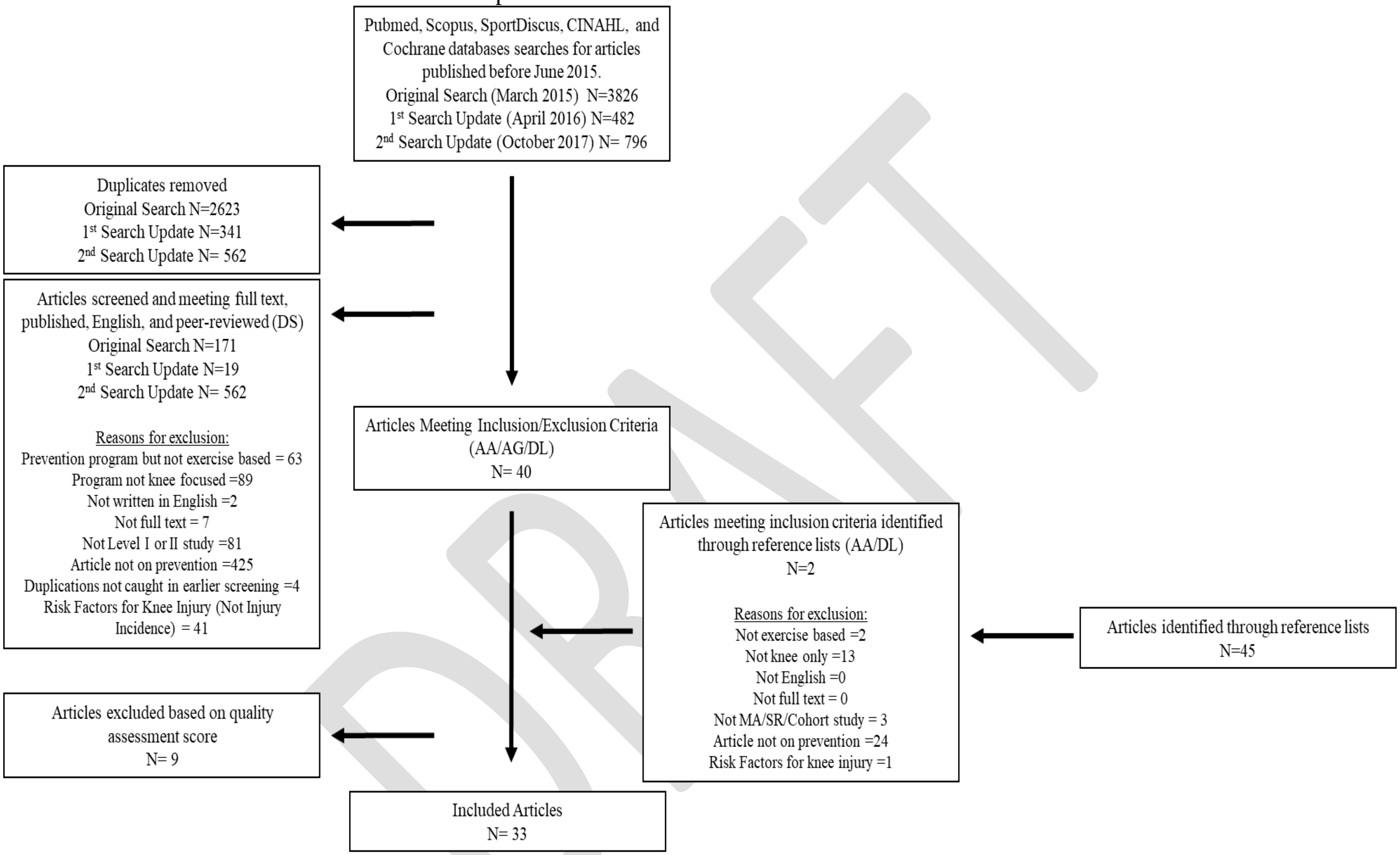
Search Update (2016)

Database	**Date Conducted**	**Results, n**
PubMed	4/1/2016	57
SCOPUS	4/1/2016	297
SportDiscus	4/1/2016	96
CINAHL	4/1/2016	18
Cochrane Library	4/1/2016	14
Cochrane reviews		2
Other reviews		0
Trials		12
Technology assessments		0
Economic evaluations		0
Total		482
Total with duplicates removed		341

Search Update 2017

Database	**Date Conducted**	**Results, n**
PubMed	10/19/2017	129
SCOPUS	10/19/2017	508
SportDiscus	10/19/2017	94
CINAHL	10/19/2017	21
Cochrane Library	10/19/2017	44
Cochrane reviews		1
Other reviews		0
Trials		43
Technology assessments		0
Economic evaluations		0
Total		796
Total with duplicates removed		562

APPENDIX C: Flowchart of literature review process



APPENDIX D Included Articles

Achenbach, L., Krutsch, V., Weber, J., et al. Neuromuscular exercises prevent severe knee injury in adolescent team handball players. Knee Surg Sports Traumatol Arthrosc 2017:http://dx.doi.org/10.1007/s00167-017-4758-5

Alentorn-Geli, E., Mendiguchia, J., Samuelsson, K., et al. Prevention of non-contact anterior cruciate ligament injuries in sports. Part ii: Systematic review of the effectiveness of prevention programmes in male athletes. Knee Surg Sports Traumatol Arthrosc 2014:22(1):16-25. http://dx.doi.org/10.1007/s00167-013-2739-x

Caraffa, A., Cerulli, G., Projetti, M., Aisa, G. and Rizzo, A. Prevention of anterior cruciate ligament injuries in soccer. Knee Surg Sports Traumatol Arthrosc 1996:4(1):19.

Donnell-Fink, L. A., Klara, K., Collins, J. E., et al. Effectiveness of knee injury and anterior cruciate ligament tear prevention programs: A meta-analysis. PLoS ONE 2015:10(12):e0144063. http://dx.doi.org/10.1371/journal.pone.0144063

Gagnier, J. J., Morgenstern, H. and Chess, L. Interventions designed to prevent anterior cruciate ligament injuries in adolescents and adults: A systematic review and meta-analysis. Am J Sports Med 2013:41(8):1952.

Gilchrist, J., Mandelbaum, B. R., Melancon, H., et al. A randomized controlled trial to prevent non contact anterior cruciate ligament injury in female collegiate soccer players. Am J Sports Med 2008:36(8):1476.

Grimm, N. L., Jacobs, J. C., Jr., Kim, J., Denney, B. S. and Shea, K. G. Anterior cruciate ligament and knee injury prevention programs for soccer players: A systematic review and meta-analysis. Am J Sports Med 2015:43(8):2049-2056. http://dx.doi.org/10.1177/0363546514556737

Grimm, N. L., Shea, K. G., Leaver, R. W., Aoki, S. K. and Carey, J. L. Efficacy and degree of bias in knee injury prevention studies: A systematic review of rcts sports. Clin Orthop Rel Res 2013:471(1):308.

Grindstaff, T. L., Hammill, R. R., Tuzson, A. E. and Hertel, J. Neuromuscular control training programs and noncontact anterior cruciate ligament injury rates in female athletes: A numbers-needed-to-treat analysis. J Athl Train 2006:41(4):450.

Hagglund, M., Atroshi, I., Wagner, P. and Walden, M. Superior compliance with a neuromuscular training programme is associated with fewer acl injuries and fewer acute knee injuries in female adolescent football players: Secondary analysis of an rct. Br J Sports Med 2013:47(15):974. http://dx.doi.org/10.1136/bjsports-2013-092644 [doi]

Hewett, T. E., Lindenfeld, T. N., Riccobene, J. V. and Noyes, F. R. The effect of neuromuscular training on the incidence of knee injury in female athletes. A prospective study. Am J Sports Med 1999:27(6):699.

Kiani, A., Hellquist, E., Ahlqvist, K., Gedeborg, R., Michaelsson, K. and Byberg, L. Prevention of soccer-related knee injuries in teenaged girls. Arch Intern Med 2010:170(1):43-49. http://dx.doi.org/10.1001/archinternmed.2009.289

Lewis, D. A., Kirkbride, B., Vertullo, C. J., Gordon, L. and Comans, T. A. Comparison of four alternative national universal anterior cruciate ligament injury prevention programme implementation strategies to reduce secondary future medical costs. Br J Sports Med 2016:http://dx.doi.org/10.1136/bjsports-2016-096667

Mandelbaum, B. R., Silvers, H. J., Watanabe, D. S., et al. Effectiveness of a neuromuscular and proprioceptive training program in preventing anterior cruciate ligament injuries in female athletes: 2-year follow-up. Am J Sports Med 2005:33(7):1003.

Michaelidis, M. and Koumantakis, G. A. Effects of knee injury primary prevention programs on anterior cruciate ligament injury rates in female athletes in different sports: A systematic review. Phys Ther Sport 2014:15(3):200.

Myer, G. D., Ford, K. R., Brent, J. L. and Hewett, T. E. Differential neuromuscular training effects on acl injury risk factors in"high-risk" versus "low-risk" athletes. BMC Musculoskelet Disord 2007:8(39. http://dx.doi.org/1471-2474-8-39 [pii]

Myer, G. D., Sugimoto, D., Thomas, S. and Hewett, T. E. The influence of age on the effectiveness of neuromuscular training to reduce anterior cruciate ligament injury in female athletes: A meta-analysis. Am J Sports Med 2013:41(1):203. http://dx.doi.org/10.1177/0363546512460637 [doi]

Myklebust, G., Engebretsen, L., Braekken, I., Skjolberg, A., Olsen, O. and Bahr, R. Prevention of anterior cruciate ligament injuries in female team handball players: A prospective intervention study over three seasons. Scand J Med Sci Sports 2003:13(4):272.

Olsen, O.-E., Myklebust, G., Engebretsen, L., Holme, I. and Bahr, R. Exercises to prevent lower limb injuries in youth sports: Cluster randomised controlled trial. BMJ 2005:330(7489):449. http://dx.doi.org/10.1136/bmj.38330.632801.8F

Pfeiffer, R. P., Shea, K. G., Roberts, D. and Grandstrand, S. Lack of effect of a knee ligament injury prevention program on the incidence of noncontact anterior cruciate ligament injury. J Bone Joint Surg 2006:88A(8):1769.

Pfile, K. R. and Curioz, B. Coach-led prevention programs are effective in reducing anterior cruciate ligament injury risk in female athletes: A number-needed-to-treat analysis. Scand J Med Sci Sports 2017:http://dx.doi.org/10.1111/sms.12828

Sadoghi, P., von Keudell, A. and Vavken, P. Effectiveness of anterior cruciate ligament injury prevention training programs. J Bone Joint Surg 2012:94(9):769.

Stevenson, J. H., Beattie, C. S., Schwartz, J. B. and Busconi, B. D. Assessing the effectiveness of neuromuscular training programs in reducing the incidence of anterior cruciate ligament injuries in female athletes: A systematic review. Am J Sports Med 2015:43(2):482.

Sugimoto, D., Myer, G., Barber Foss, K. and Hewett, T. Dosage effects of neuromuscular training intervention to reduce anterior cruciate ligament injuries in female athletes: Meta- and sub-group analyses. Sports Med 2014:44(4):551.

Sugimoto, D., Myer, G. D., Barber Foss, K. D., Pepin, M. J., Micheli, L. J. and Hewett, T. E. Critical components of neuromuscular training to reduce acl injury risk in female athletes: Meta-regression analysis. Br J Sports Med 2016:50(20):1259-1266. http://dx.doi.org/10.1136/bjsports-2015-095596

Sugimoto, D., Myer, G. D., Bush, H. M., Klugman, M. F., McKeon, J. M. M. and Hewett, T. E. Compliance with neuromuscular training and anterior cruciate ligament injury risk reduction in female athletes: A meta-analysis. J Athl Train 2012:47(6):714.

Sugimoto, D., Myer, G. D., Foss, K. D. B. and Hewett, T. E. Specific exercise effects of preventive neuromuscular training intervention on anterior cruciate ligament injury risk reduction in young females: Meta-analysis and subgroup analysis. Br J Sports Med 2015:49(5):282.

Sugimoto, D., Myer, G. D., McKeon, J. M. and Hewett, T. E. Evaluation of the effectiveness of neuromuscular training to reduce anterior cruciate ligament injury in female athletes: A critical review of relative risk reduction and numbers-needed-to-treat analyses. Br J Sports Med 2012:46(14):979.

Swart, E., Redler, L., Fabricant, P. D., Mandelbaum, B. R., Ahmad, C. S. and Wang, Y. C. Prevention and screening programs for anterior cruciate ligament injuries in young athletes: A cost-effectiveness analysis. J Bone Joint Surg 2014:96(9):705. http://dx.doi.org/10.2106/jbjs.m.00560

Taylor, J. B., Waxman, J. P., Richter, S. J. and Shultz, S. J. Evaluation of the effectiveness of anterior cruciate ligament injury prevention programme training components: A systematic review and meta-analysis Br J Sports Med 2013:49(79-87. http://dx.doi.org/10.1136/bjsports-2013-092358

van Beijsterveldt, A. M., Krist, M. R., Schmikli, S. L., et al. Effectiveness and cost-effectiveness of an injury prevention programme for adult male amateur soccer players: Design of a cluster-randomised controlled trial. Inj Prev 2011:17(1):e2. http://dx.doi.org/10.1136/ip.2010.027979

Walden, M., Atroshi, I., Magnusson, H., Wagner, P. and Hgglund, M. Prevention of acute knee injuries in adolescent female football players: Cluster randomised controlled trial. BMJ: Br Med J 2012:344(7858):16. http://dx.doi.org/10.1136/bmj.e3042

Yoo, J. H., Lim, B. O., Ha, M., et al. A meta-analysis of the effect of neuromuscular training on the prevention of the anterior cruciate ligament injury in female athletes. Knee Surg Sports Traumatol Arthrosc 2010:18(6):824.

APPENDIX E Quality assessment scores

Systematic Reviews and Meta-analyses: AMSTAR Checklist

Checklist Items	Alentorn-Geli[2]	Donnell-Fink[8]	Gagnier[17]	Grimm[21]	Grimm[22]	Grindstaff[23]	Hewett[29]	Hewett[27]	Michaelidis[42]	Myer[44]	Noyes[46]	Noyes[47]	Padua[50]	Pfile[55]	Sadoghi[57]	Stevenson[64]	Stojanovic[65]	Sugimoto[67]	Sugimoto[68]	Sugimoto[66]	Sugimoto[69]	Sugimoto[70]	Taylor[72]	Wen-Dien[79]	Yoo[80]
Was an a priori design provided?	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Was there duplicate study selection and data extraction?	X	X	X	X	X	X								X		X		X			X	X	X	X	
Was a comprehensive literature search performed?	X	X	X	X	X	X	X		X		X	X		X	X	X		X	X			X	X		X
Was the status of publication (grey literature) used as an inclusion criterion?										X				X				X	X	X		X			
Was a list of studies (included and excluded) provided?															X				X						
Were the characteristics of the included studies provided?	X	X	X	X	X	X		X	X	X	X			X		X		X	X	X	X	X	X		X
Was the scientific quality of the included studies assessed and documented?	X	X	X	X	X	X			X	X			X	X	X	X	X	X	X	X	X	X	X	X	
Was the scientific quality of the included studies used appropriately in formulating conclusions?			X			X							X	X			X		X	X	X	X			
Were the methods used to combine the findings of studies appropriate?		X	X	X											X			X		X	X		X		X
Was the likelihood of publication bias assessed?		X	X	X	X	X				X					X			X		X	X	X	X		X
Was the conflict of interest included?		X	X	X	X			X	X	X	X				X	X	X	X		X	X	X	X	X	

What is your overall assessment of the methodological quality of this review? (High Quality ≥ 8 Acceptable ≥5 Reject ≤4	5	8	9	8	7	7	2	3	5	6	4	2	3	7	7	6	4	9	7	8	8	9	8	4	5

Randomized Control Trials: PEDro Scale

Checklist Items	Achenbach[1]	Gilchrist[18]	Hagglund[25]	Olsen[48]	van Beijsterveldt[73]	Vescovi[76]	Walden[77]
Eligibility criteria were specified		X	X	X	X	X	X
Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	X	X		X	X	X	X
Allocation was concealed				X	X		X
The groups were similar at baseline regarding the most important prognostic indicators	X	X		X	X		X
There was blinding of all subjects							
There was blinding of all therapists who administered the therapy							
There was blinding of all assessors who measured at least one key outcome		X		X			X
Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	X	X	X	X	X		
All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat"	X	X	X		X		X
The results of between-group statistical comparisons are reported for at least one key outcome	X	X	X	X	X	X	X
The study provides both point measures and measures of variability for at least one key outcome	X	X	X	X	X	X	X
High Quality ≥8 **Acceptable ≥5** **Reject ≤4**	5	8	5	7	8	4	8

Cohort Studies: SIGN checklist

Checklist Items	Caraffa[5]	Hewett[28]	Kiani[34]	LaBella[36]	Mandelbaum[41]	Myer[43]	Myklebust[45]	Pfeiffer[54]
The study addresses an appropriate and clearly focused question.	X		X	X	X	X	X	X
The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	X	X	X	X	X		X	
The study indicates how many of the people asked to take part did so, in each of the groups being studied.	X		X		X		X	
The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	X							
What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?		X	X				X	
Comparison is made between full participants and those lost to follow up, by exposure status.	X		X					X
The outcomes are clearly defined.	X	X	X	X	X	X		X
The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable.								
Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	X	X		X	X			X
The method of assessment of exposure is reliable	X	X	X		X	X		
Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	X		X			X		
Exposure level or prognostic factor is assessed more than once			X		X	X	X	X
The main potential confounders are identified and taken into account in the design and analysis.			X				X	X
Have confidence intervals been provided?			X		X		X	
How well was the study done to minimize the risk of bias or confounding? **High Quality ≥8 Acceptable ≥5 Reject ≤4**	8	5	12	4	8	5	6	7

Economic Analysis: Drummond Checklist [10]

Questions	Checklist Items	Swart[71]	Lewis[37]
Was a well-defined question posed in answerable form?	Did the study examine both costs and effects of the service(s) or program(s)?	X	X
	Did the study involve a comparison of alternatives?	X	X
	Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	X	X
Was a comprehensive description of the competing alternatives given?	Were any relevant alternatives omitted?	X	
	Was (should) a do-nothing alternative (be) considered?	X	
Was the effectiveness of the program or services established?	Was this done through a randomized, controlled clinical trial? If so did the trial protocol reflect what would happen in regular practice?		
	Were effectiveness data collected and summarized through a systematic overview of clinical studies? If so, were the search strategies and rules for inclusion or exclusion outlined?	X	
	Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?	X	X
Were all the important and relevant costs and consequences for each alternative identified?	Was the range wide enough for the research question at hand?	X	X
	Did it cover all relevant viewpoints?	X	X
	Were the capital costs, as well as operating costs included?	X	X
Were costs and consequences measured accurately in appropriate physical units?	Were the sources of resource utilization described and justified?	X	X
	Were any of the identified items omitted from measurement? If so does this mean that they carried no weight in the subsequent analysis?		
	Were there any special circumstances that made measurement difficult? Were these circumstances handled appropriately/		
Were costs and consequences valued credibly?	Were the sources of all values clearly identified?	X	X
	Were market values employed for changes involving resources gained or depleted?		X
	Where market values were absent, or market values did not reflect actual values, were adjustments made to approximate market values?	X	
	Was the valuation of consequences appropriate for the question posed?	X	X
Were costs and consequences adjusted for differential timing?	Were costs and consequences that occur in the future 'discounted' to their present values?		X
	Was any justification given for the discounted rate used?		X
Was an incremental analysis of costs and	Were the additional costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?		X

consequences of alternatives performed			
Was allowance made for uncertainty in the estimates of cost and consequences?	If patient level data on costs or consequences were available, were appropriate statistical analyses performed?	X	X
	If a sensitivity analysis was employed, was justification provided for the ranges or distributions of values, and the form of sensitivity analysis used?	X	X
	Were the conclusions of the study sensitive to the uncertainty in the results, as quantified by the statistical and/or sensitivity analysis?	X	X
Did the presentation and discussion of study results include all issues of concern to users?	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences? If so was the index interpreted intelligently or in a mechanistic fashion?	X	X
	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?		
	Did the study discuss the generalizability of the results to other settings and patient/client groups?	X	
	Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X	X
	Did the study discuss issues of implementation, such as feasibility of adopting the 'preferred' program given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programs?	X	X
Quality Score		21	20

APPENDIX F. LEVELS OF EVIDENCE TABLE*

Level	Intervention/ Prevention	Pathoanatomic/Risk/ Clinical Course/Prognosis/ Differential Diagnosis	Diagnosis/Diagnostic Accuracy	Prevalence of Condition/Disorder	Exam/Outcomes
I	Systematic review of high-quality RCTs High-quality RCT†	Systematic review of prospective cohort studies High-quality prospective cohort study‡	Systematic review of high-quality diagnostic studies High-quality diagnostic study§ with validation	Systematic review, high-quality cross-sectional studies High-quality cross-sectional study║	Systematic review of prospective cohort studies High-quality prospective cohort study
II	Systematic review of high-quality cohort studies High-quality cohort study‡ Outcomes study or ecological study Lower-quality RCT¶	Systematic review of retrospective cohort study Lower-quality prospective cohort study High-quality retrospective cohort study Consecutive cohort Outcomes study or ecological study	Systematic review of exploratory diagnostic studies or consecutive cohort studies High-quality exploratory diagnostic studies Consecutive retrospective cohort	Systematic review of studies that allows relevant estimate Lower-quality cross-sectional study	Systematic review of lower-quality prospective cohort studies Lower-quality prospective cohort study
III	Systematic reviews of case-control studies High-quality case-control study Lower-quality cohort study	Lower-quality retrospective cohort study High-quality cross-sectional study Case-control study	Lower-quality exploratory diagnostic studies Nonconsecutive retrospective cohort	Local nonrandom study	High-quality cross-sectional study
IV	Case series	Case series	Case-control study		Lower-quality cross-sectional study
V	Expert opinion	Expert opinion	Expert opinion	Expert opinion	Expert opinion

Abbreviation: RCT, randomized clinical trial.
Adapted from Phillips et al*62 *(http://www.cebm.net/index.aspx?o=1025). See also* **APPENDIX G.
†*High quality includes RCTs with greater than 80% follow-up, blinding, and appropriate randomization procedures.*
‡*High-quality cohort study includes greater than 80% follow-up.*
§*High-quality diagnostic study includes consistently applied reference standard and blinding.*
║*High-quality prevalence study is a cross-sectional study that uses a local and current random sample or censuses*
Weaker diagnostic criteria and reference standards, improper randomization, no blinding, and less than 80% followup may add bias and threats to validity.

APPENDIX G Procedures used for assigning levels of evidence

- Level of evidence is assigned based on the study design using the Levels of Evidence table (**APPENDIX F**), assuming high quality (e.g. for intervention, randomized clinical trial starts at level I)
- Study quality is assessed using the critical appraisal tool, and the study is assigned 1 of 4 overall quality ratings based on the critical appraisal results
- Level of evidence assignment is adjusted based on the overall quality rating:
  - High quality (high confidence in the estimate/results): study remains at assigned level of evidence (e.g., if the randomized clinical trial is rated high quality, its final assignment is level
    1. High quality should include:
       - Randomized clinical trial with greater than 80% follow-up, blinding, and appropriate randomization procedures
       - Cohort study includes greater than 80% follow-up
       - Diagnostic study includes consistently applied reference standard and blinding
       - Prevalence study is a cross-sectional study that uses a local and current random sample or censuses
  - Acceptable quality (the study does not meet requirements for high quality and weaknesses limit the confidence in the accuracy of the estimate): downgrade 1 level
    - Based on critical appraisal results
  - Low quality: the study has significant limitations that substantially limit confidence in the estimate: downgrade 2 levels
    - Based on critical appraisal results
  - Unacceptable quality: serious limitations—exclude from consideration in the guideline
    - Based on critical appraisal results

APPENDIX H. Efficacy of exercise-based knee injury prevention programs

Review	**Included Articles**	**Outcomes Examined**	**Findings**

Donnell-Fink[8]	Caraffa[5]
	Emery,[13]
	Gilchrist,[18]
	Goodall,[19]
	Grooms,[24]
	Heidt,[26]
	Hewett,[28]
	Junge,[33]
	Kiani,[34]
	LaBella,[36]
	Longo,[39]
	Malliou,[40]
	Mandelbaum,[41]
	Myklebust,[45]
	Olsen,[48]
	Pasanen,[51]
	Petersen,[52]
	Pfeiffer,[54]
	Soderman,[60]
	Soligard,[62]
	Steffen,[63]
	van Beijsterveldt,[74]
	Walden,[77]
	Wedderkop,[78]
		Primary: Incidence of knee and ACL injuries
		Secondary: Subgroup analysis of knee and ACL injuries
		Tertiary: Incidence of non-contact ACL injuries
			Primary:
			• Pooled incidence reduction ratio for knee injury prevention 0.731 (95% CI 0.61, 0.87)
			• Pooled incidence reduction ratio for ACL injury prevention 0.493 (95% CI 0.285, 0.854)
			Secondary subgroups analysis:
			• Age (dichotomized by high school age or older than high school) not associated with knee or ACL injury reduction
			  o Knee injuries (high school incidence reduction ratio 0.79, older than high school incidence reduction ratio 0.58, P=.20)
			  o AC injuries (high school incidence reduction ratio 0.36, older than high school incidence reduction ratio 0.58, P=.41)
			• Programs during preseason or preseason + in-season versus in-season only programs
			  o Lower risk of knee injury in preseason/preseason+ in-season (incidence reduction ratio 0.24) than in-season only (incidence reduction ratio 0.75, P<.01)
			  o No difference for ACL injuries (preseason/preseason + in-season incidence reduction ratio 0.32, in-season only incidence reduction ratio 0.57, P=.33)
			Tertiary:
			• Pooled incidence rate ratio for non-contact ACL injuries 0.51 (95% CI 0.30, 0.88)

Gagnier[17]	Caraffa[5],
	Ettlinger[15],
	Gilchrist[18]
	Heidt[26],
	Hewett[28],
	Kiani[34],
	Mandelbaum[41],
	Myklebust[45],
	Olsen[48],
	Pasanen[51],
	Petersen[52],
		Primary: Overall ACL injury incidence
		Secondary: Subgroup analysis of ACL injury incidence
			Primary:
			• Pooled incidence rate ratio 0.49 (95% CI 0.30, 0.79, P<.01) with some effects of heterogeneity.
			Secondary subgroup analysis:
			• Pooled incidence rate ratio smaller (stronger inverse association) for:
			  o Non-randomized cohort studies (pooled incidence rate ratio 0.38, 95% CI 0.20, 0.70, P<.01)
			  o Studies in the United States (pooled incidence rate ratio 0.362, 95% CI 0.15, 0.88, P=.03)

	Pfeiffer[54], Soderman[60], Steffen[63]		o Studies of longer duration (>14 months) (pooled incidence rate ratio 0.41, 95% CI 0.20, 0.84, P=.01) o Studies with more hours of training per week (>0.75 hr) (pooled incidence rate ratio 0.38, 95% CI 0.18, 0.77, P<.01) o Studies that reported better compliance (>64%) (pooled incidence rate ratio 0.39, 95% CI 0.17, 0.89, P=.03) o Studies that reported no dropouts (pooled incidence rate ratio 0.3, 95% CI 0.15, 0.62, P<.01) o Studies that included only soccer players (pooled incidence rate ratio 0.30, 95% CI 0.16, 0.56, P<.01). • Little difference, though significant for females (pooled incidence rate ratio 0.51, 95% CI 0.28, 0.94, P=.31) • No significant difference between those interventions which included plyometric exercises compared to those that did not (no P-value presented)
Sadoghi[57]	Caraffa[5], Gilchrist[18], Heidt[26], Hewett[28], Mandelbaum[41], Petersen[53], Petersen[52], Pfeiffer[54], Soderman[60], Myklebust[45]	Risk of ACL injury	• Risk differences reported in the component studies varied considerably o Numbers needed to treat ranging from 5-187 ▪ One study actually had a lower risk in controls • Pooled risk ratio was 0.38, 95% CI 0.20, 0.72, P<.01, indicating a significant decrease in risk in the intervention groups • Stratified by sex: pooled risk ratio was women 0.48 (95% CI 0.26, 0.89, P=.02) and men 0.15 (95% CI 0.08, 0.28, P<.01) • Use of a balance board or video assistance, the duration of follow-up, or year of publication did not affect the pooled risk ratio • Conducting the intervention during preseason, compared to during the playing season reduced the risk by 19.1% but this was not significant

APPENDIX I. Efficacy of exercise-based knee injury prevention programs in men and women

Review	Included Articles	Outcomes Examined	Findings
Men			
Alentorn-Geli[2]	Bencke[3], Caraffa[5], Cochrane[6], Dempsey[7], Donnelly[9], Grooms[24], Jamison[32]	Reduction of ACL injury	• Two of 7 studies examined the effect of interventions on ACL injury rates o One found a significant reduction in ACL injury rates,[5] one had no ACL injuries in either group (but did have a 72% decrease in lower extremity injury risk)[24] • The quality of studies increased over time
Women			

Grimm[22]	Brushoj[4], Ekstrand[12], Emery and Meeuwisse[13], Engebretsen[14], Gilchrist[18], Olsen[48], Soderman[60], Soligard[61], Steffen[63], Wedderkopp[78]	Knee and ACL injury incidence	• Two of 10 studies showed a reduction in knee injuries[12, 48]
			  o Four studies reported a non-significant increase in knee injuries in the intervention group[13, 14, 18, 61]
			• Two of 3 studies examining ACL injury incidence found decreases in numbers of injury, but none found a significant reduction[18, 48, 60]
			  o One study showed a non-significant increase in ACL injuries in the intervention group[60]
			• No evidence of publication bias

Myer[44]	Gilchrist[18], Heidt[26], Hewett[28], Kiani[34], LaBella[35], Madelbaum[41], Myklebust[45], Olsen[48], Pasanen[51], Petersen[52], Pfeiffer[54], Soderman[60], Steffen[63], Walden[77]	ACL injury incidence based on age	• Overall a significantly greater knee injury reduction in female athletes in intervention groups compared to controls (odds ratio 0.54, 95% CI 0.35, 0.83)
			• Age dichotomized:
			  o Under 18 (odds ratio 0.28, 95% CI 0.18, 0.42, P<.01)
			  o Over 18 (odds ratio 0.84, 95% CI 0.56, 1.26, P=.39)
			• Age in tertiles:
			  o Age 14-18 years had an odds ratio of 0.28 (95% CI 0.18, 0.42, P<.01),
			  o Age 18-20 years odds ratio 0.48 (95% CI 0.21, 1.07, P=.07)
			  o Age >20 years odds ratio 1.01 (95% CI 0.62, 1.64, P=.97).
			• No evidence of publication bias

Stevenson[64]	Gilchrist[18], Heidt[26], Hewett[28], Kiani[34], Madelbaum[41], Myklebust[45], Pfeiffer[54], Petersen[52], Soderman[60], Steffen[63],	ACL injury incidence	• Two of 10 programs achieved a statistically significant decrease in ACL injuries.[28, 41] o One study had a significant decrease in the incidence of ACL injuries during practices, late in the season, and in non-contact ACL injuries in those with a history of prior ACL injuries[18] o Another study had a significant decrease in the ACL injury incidence in elite athletes[45] o Two studies had significant decreases in the ACL injury rate among those who were deemed compliant with the program[45, 63] o One study had all non-contact ACL injuries in the control group, but no non-contact ACL injuries in the intervention group[52] • One study had a significant increase in major knee injuries (80% of injuries in the intervention group)[60] • One study had an increase in non-contact ACL injuries in the intervention group, however it did not reach statistical significance.[54] When controlling for sport this study actually had a 4 times higher incidence of injuries in trained female basketball players than the control players. • Eight of the 10 studies included plyometric exercises[18, 26, 28, 41, 45, 52, 54, 63] o All 4 studies reporting some statistically significant decrease in ACL injuries included plyometrics, strength training, and flexibility[18, 28, 41, 45] o Only 1 of the studies which included plyometrics failed to show a decrease in ACL injuries[54] • The 1 study which only included a balance component to the training had an increase in ACL injury incidence[60]
Sugimoto[69]	Gilchrist[18], Heidt[26], Hewett[28], Kiani[34], LaBella[35], Mandelbaum[41], Myklebust[45], Olsen[48], Pasanen[51], Petersen[52], Pfeiffer[54], Soderman[60], Steffen[63], Walden[77]	ACL injury incidence	• 11 of 14 studies demonstrated fewer ACL injuries in intervention groups compared to controls[18, 26, 28, 34, 35, 41, 45, 48, 52, 63, 77] • Exercise-based knee injury prevention programs which incorporated multiple exercise components had a greater ACL injury reduction (odds ratio 0.32, 95% CI 0.22,0.46, P<.01) than those programs with only 1 exercise component (odds ratio 1.15, 95% CI 0.70-1.89, P=.59) • Balance exercises: There was no significant difference in the reduction in incidence of ACL injuries in neuromuscular training programs with balance exercises (odds ratio 0.59, 95% CI 0.42, 0.83, P<.01) compared to those with no balance (odds ratio 0.34, 95% CI 0.20, 0.56, P<.01) exercises. • Plyometric Exercises: There was no significant difference in the reduction of ACL injury risk between neuromuscular training programs with plyometric exercises (odds ratio 0.39, 95% CI 0.26, 0.57, P<.01) compared to those with no plyometric exercises (odds ratio 0.59, 95% CI 0.39, 0.89, P=.01).

			• Strength Exercises: There was a significant reduction in the number of ACL injuries in those neuromuscular training programs with strengthening exercises (odds ratio 0.32, 95% CI 0.23, 0.46, P<.01) but not in programs without strengthening (odd ratio 1.02, 95% CI 0.63-, 1.64, P=.95). • Proximal Control Exercises: Neuromuscular programs that included proximal control exercises reduced ACL injuries (odds ratio 0.33, 95% CI 0.23-, 0.47, P<.01). Programs that did not include proximal control exercises (odds ratio 0.95, 95% CI 0.60-, 1.50, P=.82) did not reduce ACL injuries.
Sugimoto[67]	Gilchrist,[18] Heidt,[26] Hewett,[28] Kiani,[34] LaBella,[35] Mandelbaum,[41] Myklebust,[45] Olsen,[48] Pasanen,[51] Petersen,[52] Pfeiffer,[54] Soderman,[60] Steffen,[63] Walden,[77]	ACL injury incidence	Critical components of exercise-based ACL injury prevention programs: • Based on the odds ratios of previous studies age (14-18), dosage (20+ minutes per training session), frequency (multiple times per week), and exercises (multiple exercise components) were deemed necessary attributes of prevention programs. • Using meta-regression the authors found there was a 17% reduction in ACL injury risk if 1 of these 4 necessary components was included in a prevention program (odds ratio 0.83, $\beta1$= -0.29, 95% CI -0.33, -0.05, P<.01). This finding was similar when using a fixed effects or random effects model. Age: • There was a statistically greater ACL injury reduction in mid-teens (14-18 years old, odds ratio 0.29, 95% CI 0.19,– 0.44, P=.01) compared to early teens (<14 years old, odds ratio 0.29, 95% CI 0.01, -7.09, P=.45), late teens (18-20 years old, odds ratio 0.48, 95% CI 0.21, -1.07, P=07) or early adults (>20 years old, odds ratio 1.01, 95% CI 0.62, -1.64, P=.97).
Taylor[72]	Gilchrist[18], Heidt[26], Hewett[28], Kiani[34], LaBella[36], Madelbaum[41], Myklebust[45], Olsen[48], Petersen[52], Pfeiffer[54], Soderman[60],	Primary: ACL injury incidence (all and non-contact) Secondary: Amount of time to complete program, season, age, presence of feedback, minutes per training session, total number of training session, AEs, player seasons (PSs), duration and variety of training exercises,	Primary: • Statistically significant reduction in ACL injuries (odds ratio 0.61, 95% CI 0.44, 0.85) and non-contact ACL injuries (odds ratio 0.35, 95% CI 0.23, 0.54) when expressed as player seasons. • Statistically significant reduction in ACL injuries (odds ratio 0.64, 95% CI 0.42, 0.99) and non-contact ACL injuries (odds ratio 0.38, 95% CI 0.22, 0.64) when expressed in AEs. Secondary: • No effect of total training time or session duration on ACL injury rate • ACL injury risk increases as duration of balance exercises increases • Injury risk decrease with greater emphasis and longer duration of prescribed static stretching • No significant difference in injury incidence between programs where feedback was given compared to those where no feedback was given

Yoo[80]	Heidt[26], Hewett[28], Mandelbaum[41], Myklebust[45], Petersen[52], Pfeiffer[54], Soderman[60],	ACL injury incidence	• Pooling all studies the authors found an odds ratio of 0.40 (95% CI 0.27, 0.60), indicating that exercise-based knee injury prevention programs were effective at reducing the risk of ACL injuries • Subgroup analysis: o Prevention programs in athletes under 18 (odds ratio 0.27, 95% CI 0.14, 0.49) were effective, but were not effective in athletes over 18 (odds ratio 0.78, 95% CI 0.23, 2.64) o Prevention programs in soccer players (odds ratio 0.32, 95% CI 0.19, 0.56) had a lower odds ratio than programs in handball players (odds ratio 0.54, 95% CI 0.30, 0.97) o Programs that began in the preseason and continued throughout the season were effective (odds ratio 0.54, 95% CI 0.30, 0.97) and had a higher odds ratio than programs that were in season only (odds ratio 0.32, 95% CI 0.17, 0.59) but programs in the preseason only (odds ratio 0.35, 95% CI 0.10, 1.21) were not effective. o Programs with plyometric (odds ratio 0.37, 95% CI 0.23, 0.55) and strengthening 0.21 (odds ratio 0.21, 95% CI 0.11, 0.43) were effective. Programs without these components (odds ratio 0.69, 95% CI 0.41, 1.15) were not. o Programs without balance training (odds ratio 0.27, 95% CI 0.14, 0.49) were effective. Programs with balance components (odds ratio 0.63, 95% CI 0.37, 1.09) were not effective • No significant heterogeneity was found or publication bias

APPENDIX J.: Efficacy of exercise-based knee injury prevention programs by sport
Note: Programs are organized by sport and only the results related to the specific sport are presented in this table- full results of each program are listed in the **Table** organized by program

Program	Study Type	Subjects	Duration	Effect	Harms
Soccer					

Caraffa[5]	Cohort	N=600 Semi-professional and amateur soccer players in Umbri and Marche Italy
		
		Age and sex not provided
			30 days during preseason (20 min, every day)	• Significant difference in injury incidence between intervention and control teams (P<.01)
				    o Intervention teams = 0.15 ACL injuries per season
				    o Control teams =1.15 ACL injuries per season
					None

Gilchrist[18]	Cluster RCT	Control N=852
		Intervention N=583
		
		NCAA Division I female soccer players, mean age 19.88 years
			12 weeks through collegiate soccer season (15-20min 3x/week)	• Overall no significant difference in injury rates for all knee injuries (P=.86) or ACL injuries (P=.20)
				• The intervention group had:
				    o Lower ACL injury rate in practices (P=.01)
				    o Lower late season ACL injury rate (P=.03)
				    o Lower rate of non-contact ACL injuries in those who reported a history of previous ACL injury (P=.05)
				• No difference between groups in the injury rates during games (P=.62), early in the season (P=.93), or amongst those with no history of prior ACL injury (P=.43)
					One player tripped during the lateral hops and had a tibia and fibular fracture. After which, the cone height used was adjusted to be shorter.

Grimm[21]	Meta-analysis (Ekstrand,[12] Emery and Meeuwisse,[13] Engebretsen,[1]	Knee and ACL injury prevention programs tested in level 1 RCTs only in soccer players	n/a	• Pooled relative risk for knee injuries (0.74, 95% CI 0.55, 0.98, P=.04) • Pooled relative risk for ACL injuries (0.66, 95% CI 0.33, 1.32, P=.24)	None

	[4] Gilchrist,[18] Soderman,[60] Soligard,[61] Steffen,[63] van Beijsterveldt,[74] Walden[77])				

Hewett[28]	Cohort	Female Intervention N=97
		Female Control N=193
		Male Control N=209
		
		High school aged soccer players
			6 weeks during preseason (60-90 minutes, 3x/week)	• Serious knee injuries in only soccer players:
				  o Trained females 0
				  o Untrained females 0.56/1000 AEs
				  o Untrained males 0.12/1000AEs
					None

Kiani[34]	Cohort	Intervention N=777 Control N=729
		
		Female soccer players ages 13-19
			4 months (Approximately 20-25 minutes, 2x/wk during preseason, 1x/wk during the regular season)	• Knee injuries:
				  o Intervention incidence 0.04/1000 hours
				  o Control 0.20/1000 hours.
				  o Unadjusted rate ratio 0.23 (95% CI 0.04, 0.83)
				  o Rate ratio adjusted for compliance 0.17 (95% CI 0.04, 0.64)
				• Non-contact knee injuries:
				  o Intervention 0.01/1000 hours
				  o Control 0.15/1000 hours
				  o Unadjusted rate ratio 0.10 (95% CI 0.00, 0.70)
				  o Rate ratio adjusted for compliance 0.06 (95% CI 0.01, 0.46)
				• There were no ACL injuries in the intervention group.
					None

Mandelbaum[41]	Cohort	Year 1: Intervention N=1041 Control N=1905.
		Year 2: Intervention N=844 Control N=1931
		
		Female soccer players, ages 14-18
			Throughout soccer season (20 min, the authors did not report recommended number of times per week)	• Overall injury incidence of ACL injuries for the intervention group 0.09/1000 AEs and for control group 0.49/1000 AEs over the 2-year study
				• Relative risk 0.18 (P<.01)
				• When broken down by year:
				  o Year 1: 89% reduction in ACL injuries (relative risk 0.11, P<.01)
				  o Year 2: 74% reduction in risk (relative risk 0.26, P<.01)
					None

Pfieffer[54]	Cohort	Intervention N=189 Control N=244 Female high school aged soccer players	Throughout high school soccer season (20 min, the authors did not report the recommended number of times per week)	• No non-contact ACL injuries in intervention group • Control group incidence of non-contact ACL injuries 0.107/1000 AEs	None
Walden[77]	Stratified RCT	Intervention N=2479 Control N=2085 Female soccer players ages 13-17	Throughout soccer season (15 min, 2x/week)	• 64% reduction in ACL injuries in intervention group (rate ratio 0.36, 95% CI 0.15, 0.85, P=.02). • When adjusted for compliance: o 83% reduction in ACL injuries (rate ratio of 0.17, 95% CI 0.05, 0.57, P<.01). o 88% reduction in severe knee injury (rate ratio 0.18, 95% CI 0.07, 0.45, P<.01) o 47% reduction in all acute knee injuries (rate ratio 0.53, 95% CI 0.30, 0.94, P=.03).	None
Handball					
Achenbach[1]	Blocked RCT	Intervention N=168 Control N=111 15-17 year old handball players, men and women	Through one handball season (15 minutes, 2-3x/week, throughout the season)	• Outcome of interest was severe knee injuries (intraarticular facture, patellar subluxation, rupture of the collateral or cruciate ligaments, meniscus tear or cartilage injury that lead to over 28 days absence from sport) 0.04/1000 hours • Control group injury incidence 0.33/1000 hours • Intervention group 0.04/1000 hours • Intervention lead to a significant decrease in severe knee injuries odds ratio 0.11 (95% CI 0.01, 0.90, P=.02)	
Myklebust[45]	Cohort	Control season N=942 1st Intervention Season N=855 2nd Intervention Season N=850 Female Norwegian handball league players, mean age not provided.	Through handball season including pre-season (15 minutes, 3x/week during preseason, 1x/week during regular season)	• Control season ACL injury incidence 0.14/1000 playing hours • 1st intervention season ACL injury incidence 0.13/1000 playing hours • 2nd intervention season ACL injury incidence 0.06/1000 playing hours • No significant difference in injury rate (odds ratio 0.52, 95% CI 0.15, 1.82, P=.31) • When adjusted for compliance there was a significant decrease in injury risk in the elite division (odds ratio 0.06, 95% CI 0.01, 0.54, P=.01)	None

Olsen[48]	Cluster RCT	Intervention N=958 Control N=879
		
		Female handball players ages 16-17 years old.
			Through one 8-month handball season (15-20 minutes, 15 consecutive training sessions at the start of the season, followed by 1x/week for the remainder of the season)	• Significant reduction in all injuries (relative risk 0.49, 95% CI 0.39, 0.63, P<.01),
				  o Lower extremity injuries (relative risk 0.51, 95% CI 0.36, 0.73, P<.10),
				  o Acute knee injuries (relative risk 0.45, 95% CI 0.35, 0.81, P<.01).
				  o Number of athletes needed to treat to prevent 1 injury was 11
				  o Number of athletes needed to treat to prevent 1 acute knee injury was 43
				• Significant reduction in knee ligament injuries (relative risk 0.2, 95% CI 0.06, 0.70, P=.01)
				• Non-significant reduction in meniscal injuries (relative risk 0.27, 95% CI 0.06, 1.28, P=.10)
					None

Basketball					

Hewett[28]	Cohort	Female Intervention N=84
		Female Control N=189
		Male Control N=225
		
		High school aged basketball players
			6 weeks during preseason (60-90 minutes, 3x/week)	• Incidence of serious knee injuries in basketball players:
				  o Trained females 0.42/1000 AEs
				  o Untrained females 0.48/1000 AEs
				  o Untrained males 0.08/1000 AEs
				  o No significant difference in the number of serious knee injuries between trained and untrained females (P=.89)
				  o There was a trend towards fewer noncontact knee injuries in trained females (P=.02)
					Non
					e

Pfieffer[54]	Cohort	Intervention N=191 Control N=319 Female high school age basketball	Throughout high school basketball season (20 min, the authors did not report the recommended number of times per week)	• Basketball control group 0.111/1000 AEs • Basketball intervention group 0.476/1000 AEs	None
Volleyball					
Hewett[28]	Cohort	Female Intervention N=185 Female Control N=81	6 weeks during preseason (60-90 minutes, 3x/week)	• No serious knee injuries in any volleyball players in this study, thus unable to make any comparison	None

		High school aged volleyball players			
Pfieffer[54]	Cohort	Intervention N=197 Control N=299 Female high school age volleyball players	Throughout high school volleyball season (20 min, the authors did not report the recommended number of times per week)	• No non-contact ACL injuries in any volleyball players in this study, thus unable to make any comparison	

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