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

Exercise-Based Knee and Anterior Cruciate Ligament Injury Prevention

Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability and Health From the Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy

J Orthop Sports Phys Ther. 2023;53(1): CPG1–CPG34. doi:10.2519/jospt.2023.0301

REVIEWERS: Caroline (Lewis) Brunst, PT, DPT, AT • Joseph J. Godges, DPT, MA
Sandra Kaplan, PT, DPT, PhD, FAPTA • Paul Beattie, PT, PhD

For author, coordinator, contributor, and reviewer affiliations, see end of text. Address correspondence to: Clinical Practice Guidelines Managing Editor, APTA Orthopedics, 2920 East Avenue South, Suite 200, La Crosse, WI 54601. E-mail: cpg@orthopt.org

Summary of Recommendations

SCIENTIFIC LITERATURE FOR EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

A Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and anterior cruciate ligament (ACL) injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,[5] Goodall et al,[7] Junge et al,[15] LaBella et al,[18] Malliou et al,[20] Olsen et al,[25] Pasanen et al,[27] Petersen et al,[28] and Wedderkopp et al.[37] Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, Prevent Injury and Enhance Performance (PEP), and Sportsmetrics™, and those used by Caraffa et al,[4] Heidt et al,[10] LaBella et al,[18] Myklebust et al,[23] Olsen et al,[25] and Petersen et al.[28]

C Clinicians may recommend the use of an exercise-based neuromuscular training program in the late phase of ACL reconstruction rehabilitation for the secondary prevention of ACL injuries.

EFFECTIVE EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS FOR SPECIFIC SUBGROUPS OF ATHLETES

A Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs prior to practices/training sessions or games in women athletes to reduce the risk of ACL injuries, especially in athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics™, Knäkontroll, HarmoKnee, and those used by Olsen et al[25] and Petersen et al.[28]

A Soccer players, both women and men, should use exercise-based knee injury prevention programs to reduce the risk of severe knee and ACL injuries. Programs beneficial for preventing severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics™, and the program used by Caraffa et al.[5]

B Men and women team handball players, particularly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs. Programs that could be beneficial for preventing knee injuries include those used by Olsen et al[25] and Achenbach et al.[1]

COMPONENTS, DOSAGE, AND DELIVERY OF EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

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

A Exercise-based knee injury prevention programs should involve training multiple times per week, 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 the preseason and continue performing the program through the regular season.

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

IMPLEMENTING EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

A Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as being at high risk for ACL injury, to optimally mitigate injuries and reduce 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 to 25 years of age involved in sports with a high risk of ACL injury.

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.

List of Abbreviations

11+: an injury prevention program developed originally by the FIFA Medical Assessment & Research Center (F-MARC) (previously known as FIFA 11+)
ACL: anterior cruciate ligament
AE: athlete exposure
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)
FIFA 11: also known as "the 11," an injury prevention program developed originally in association with the medical committee of FIFA and the predecessor to the 11+
ICD: International Classification of Diseases
ICF: International Classification of Functioning, Disability and Health
***JOSPT*:** *Journal of Orthopaedic & Sports Physical Therapy*
KLIP: Knee Ligament Injury Prevention program
NMT: neuromuscular training
PEDro: Physiotherapy Evidence Database
PEP: Prevent Injury and Enhance Performance injury prevention program
RCT: randomized controlled trial
RR: relative risk
RTS: return to sport
SIGN: Scottish Intercollegiate Guidelines Network

Introduction

AIM OF THE GUIDELINES

The Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy 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). 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; and other training modalities, but excludes passive interventions such as bracing or programs that only involve education. *Knee injuries* were defined as any knee joint pathology including damage to the joint (patellofemoral and/or tibiofemoral), ligaments, meniscus, or patellar tendon. The recommendations can be followed and implemented by athletes, coaches, athletic trainers, physical therapists, strength and conditioning professionals, sports scientists, physicians, surgeons, and other clinicians or health and fitness professionals.

The objectives of this CPG are as follows:

- 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 subgroups 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, parents, students, interns, residents, fellows, athletic trainers, orthopaedic and sports physical therapy clinicians, academic instructors, clinical instructors, and physicians and surgeons in orthopaedics 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.

SCOPE

The aims of the revision was to provide a concise summary of the evidence published since the original guideline in 2018. Where appropriate, the revision aimed to update or revise recommendations and evidential support based on the available literature.

Methods

The Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy appointed content experts with relevant physical therapy, medical, and surgical expertise as developers and authors of the CPG for exercise-based knee injury prevention. These experts were given the task of conducting a review of the literature and 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 Academy of Orthopaedic Physical Therapy, APTA, Inc. Funding was provided by the Academy of Orthopaedic Physical Therapy and American Academy of Sports Physical Therapy, and by 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 (T.H.), the authors systematically searched PubMed, Scopus, SPORTDiscus, CINAHL, and the Cochrane databases for relevant articles. Literature searches were performed on October 23, 2020, and updated on February 18, 2022. The searches included articles published from 2017 to February 2022 to cover the period since the previous CPG.

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, available at www.orthopt.org).

Inclusion and exclusion criteria used to select relevant articles were as follows.

INCLUSION CRITERIA

- 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; and other training modalities, 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 patellar tendon.
- Articles that focused on preventing knee injuries as a whole were included, but so too were articles focused on only one type of knee injury (eg, anterior cruciate ligament [ACL] injuries or patellofemoral pain). This CPG delineates between evidence related to ACL injuries and all knee injuries.
- Mechanism of injury included both contact (injuries as a result of collision with another person or object) and noncontact (injuries that do not involve another individual or object).[7] This CPG discusses contact and noncontact injuries together, unless specifically noted in the text.
- Meta-analyses
- Systematic reviews
- Randomized controlled trials (RCTs)
- Cost-effectiveness studies
- High-level cohort studies (critical appraisal score on the Scottish Intercollegiate Guidelines Network [SIGN] checklist of 5 or greater)
- Published in a peer-reviewed journal
- Able to access full-text articles
- Published and accessible in English

EXCLUSION CRITERIA

- 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

LITERATURE APPRAISAL

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 selecting different exercises or focusing athlete feedback on joints other than the knee. Furthermore, mechanisms of prevention may also differ. Programs targeting risk factors for knee injuries (eg, programs focused on modifying knee biomechanics during jump landing) were also excluded from this CPG. There are a number of modifiable and nonmodifiable risk factors for knee injuries. However, the magnitude 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.[8] Similarly, asymmetries in jump landing have been associated with knee injuries in women[12] but not, to date, in men. As an international group of experts in prevention, familiar with the prevention literature, as well as that specific to knee injuries, the authors felt that these were appropriate restrictions.

Components of training programs were defined as different exercise approaches involved in the prevention programs. For example, a program that only involved balance exercises was considered to only have 1 component, whereas a program that involved strengthening and plyometric exercises was considered to have multiple components. Common components include flexibility, strengthening, plyometrics, balance, and agility.

One author (D.S.) screened articles for full-text availability and for publication in English and in peer-reviewed journals. Two authors (A.A. and C.D. or R.K.) then independently screened articles for inclusion based on title and abstract. The authors then discussed their findings. Any article that clearly did not meet inclusion criteria based on title and abstract was excluded at this point, and the full text of any article that the authors were unsure of or that seemed to clearly meet inclusion criteria was then reviewed. If a CPG author was the author of a study eligible for potential inclusion, that author did not participate in the inclusion/exclusion decision for that paper. Full-text reviews were performed independently by two authors (A.A. and C.D. or R.K). The authors met to review their findings, and all disagreements on inclusion/exclusion were resolved by discussion and consultation with two other authors (A.G. and D.L.). Consensus was reached on all articles (see **APPENDIX C** for the flowchart of articles and **APPENDIX D** for the citations of articles included in this guideline, available at www.orthopt.org).

All authors were involved in the quality-assessment and data-extraction process. Two authors independently assessed the quality of each article. If a CPG author was the author of an included paper, they did not participate in the quality-assessment or data-extraction process for that paper. The A MeaSurement Tool to Assess systematic Reviews (AMSTAR) tool was used to assess the quality of meta-analyses and systematic reviews.[32] The Physiotherapy Evidence Database (PEDro) scale was used to assess the quality of RCTs,[34] the SIGN checklist was used to assess the quality of cohort studies.[31] Reliability using the quality-appraisal tools was established in the majority of authors during the creating of the 2018 guidelines. Two new authors, who did not participate in the 2018 guideline, established reliability with the lead author through independently assessing and then discussing scoring of three papers. Discrepancies in quality ratings were resolved through discussion between the 2 authors, and when needed, the lead author (A.A.) made a final decision. 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[20] (see **APPENDIX E** for quality-assessment scores, available at www.orthopt.org). Recommendations were written based on the included articles and were agreed on by all authors. **APPENDICES A** to **G** are available on the CPG web page at www.orthopt.org.

This guideline was issued in 2023 based on the published literature up to January 2022. The guideline committee will review this CPG in 2027, or sooner if significant new evidence becomes available. Any updates to the guideline in the interim will be posted on the Academy of Orthopaedic Physical Therapy 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.[31] One team of four authors (A.A., C.D., R.K., D.L.) came to consensus and assigned a level of evidence based on the quality assessment of each article, the entire author group then approved the decisions (see **APPENDICES F** and **G** for the evidence table and details on procedures used for assigning levels of evidence, available at www.orthopt.org). An abbreviated version of the grading system is provided below.

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

GRADES OF EVIDENCE

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 on the next page. 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 science/bench research supports the recommendation
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 or CPG methodology reviewed the CPG draft for integrity, accuracy, and ensuring 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 Academy of Orthopaedic Physical Therapy, APTA, Inc. In addition, a panel of consumer/patient representatives and external stakeholders, such as coaches, athletes, parents, team organizers 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 Academy of Orthopaedic Physical Therapy, 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 web page of the *JOSPT* and the Academy of Orthopaedic Physical Therapy, APTA, and APTA websites. These web pages have unrestricted public access. Implementation tools and associated implementation strategies that will be made available for athletes, coaches, patients, physicians, surgeons, clinicians, educators, payers, policy makers, and researchers are listed in **TABLE 1**.

TABLE 1 Planned Strategies and Tools to Support the Dissemination and Implementation of this Clinical Practice Guideline

Tool	Strategy
"Perspectives for Patients" and videos for clinicians, coaches, and athletes	Patient-oriented guideline summary available on www.jospt.org and www.orthopt.org (**FIGURE 1**, **TABLE 2**)
Mobile applications of guideline-based exercises for patients/clients, athletes, coaches, and health care practitioners	Marketing and distribution of app using www.orthopt.org
Clinician's quick-reference guide	Summary of guideline recommendations available on www.orthopt.org
Read for Credit℠ continuing education content[a]	Continuing education content available from JOSPT
Webinar-based educational offerings for health care practitioners	Guideline-based instruction available for practitioners on www.orthopt.org
Videos of knee injury prevention warm-up exercise sequences for field and court sport athletes	Free-access links to videos of exercise sequences available via this CPG and on www.orthopt.org and www.jospt.org
Mobile and web-based applications for health care practitioner training	Marketing and distribution of app using www.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 www.jospt.org
Interactive digital learning modules and skill-building seminars for practitioners to improve their knowledge of and skills for implementation of the CPGs for prevention and management of common musculoskeletal conditions	Digital resources available through www.orthopt.org and AOPT's vendor partners, and standardized skill-building seminar available from AOPT's CPG seminar cosponsors, worldwide

Abbreviations: AOPT, Academy of Orthopaedic Physical Therapy; CPG, clinical practice guideline.
[a]Practitioners who attain passing examination scores have the opportunity to gain listing in the directory of CPG knowledge competency, which will be widely accessible to clients, practitioners, employers, and payors.

CLASSIFICATION

The primary International Classification of Diseases, Tenth Revision (ICD-10), codes and conditions associated with exercise-based knee injury prevention are as follows: "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," "S83.6 Sprain and strain of other unspecified parts of the knee," and "M22.2 Patellofemoral disorders."

The primary ICF activities and participation codes associated with exercise-based knee injury prevention are as follows: "d410 Changing basic body positions," "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 GUIDELINE

This CPG is arranged in relation to the following CPG objectives:

- Review the evidence in the scientific literature for exercise-based knee injury prevention programs. Evidence includes systematic reviews and meta-analyses that look at prevention programs across populations.
- Identify exercise-based knee injury prevention programs that are effective for specific subgroups of athletes. Evidence includes systematic reviews, meta-analyses, and cohort studies that specifically delineate populations.
- Describe the evidence for components, dosage, and delivery of exercise-based knee injury prevention programs.
- Provide suggestions for implementation of exercise-based knee injury prevention program

For each objective, the recommendations from the 2018 guideline are presented followed by a summary of the evidence, including the levels of evidence, a synthesis of the new evidence, a discussion of gaps in the literature, and then the new 2022 guidelines. Based on this new evidence and evidence synthesis, the updated 2022 recommendations including grades are presented at the end of each objective.

Clinical Practice Guideline

A summary of the studies included in this 2022 update are found in **TABLE 2**.

OBJECTIVES

Review the evidence in the scientific literature for exercise-based knee injury prevention programs. Evidence includes systematic reviews and meta-analyses that look at prevention programs across populations (**TABLE 2**).

2018 Recommendation

A Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and ACL injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,[5] Goodall et al,[7] Junge et al,[15] LaBella et al,[18] Malliou et al,[20] Olsen et al,[25] Pasanen et al,[27] Petersen et al,[28] and Wedderkopp et al.[37] Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, Prevent Injury and Enhance Performance (PEP), and Sportsmetrics™, and those used by Caraffa et al,[4] Heidt et al,[10] LaBella et al,[18] Myklebust et al,[23] Olsen et al,[25] and Petersen et al.[28]

Evidence Update

I A meta-analysis of 8 meta-analyses examined the efficacy of ACL injury prevention.[36] All meta-analyses indicated injury prevention programs significantly reduced the risk of ACL injury. There was a 67% reduction in risk for noncontact ACL injuries among women athletes. The findings of this meta-analysis were also supported in a systematic review by Olivares-Jabalera et al.[24]

I A systematic review with meta-analysis was performed to determine how protective ACL injury prevention programs are and what the important components of a prevention program are when accounting for study quality (randomized and cluster-randomized controls and studies that included incidence rate).[13] Eight studies with a total of 13 562 participants were included and demonstrated a significant, 53% reduction in ACL injury rates in those participating in an injury prevention program. The specific components for injury prevention programs were not identified; however, all but 2 studies provided feedback on exercises and included at least 3 types of exercise.

I Two papers reported on men and women in the same RCT examining secondary ACL injury prevention. Johnson et al[14] found no significant difference in rate or side of second ACL injury ($P = .77$ and $P = .25$, respectively) between the control and intervention groups in women athletes. Additionally, no statistically significant difference was found in rate of second ACL injuries based on age categories (22.8% for <25 years old, 28.1% for <20 years old, and 30.8% for <18 years old). Although there was no difference based on type of intervention, the overall second injury rate, particularly the contralateral second injury rate was lower than the published literature.

Arundale et al[2] found 95% of men athletes who participated in ACL-SPORTS trial and passed RTS criteria after 1 year, with 78% of athletes returning to preinjury level of play. After 2 years, 100% passed RTS criteria and 95% returned to preinjury level. Overall second ACL injury rate was 0.025 injuries per athlete, also lower than the published literature.

Note: Studies regarding secondary ACL injury prevention were screened for both the 2018 CPG and 2022 update; however in 2018 none met inclusion/exclusion criteria. This was due to programs not being specifically targeted at second knee/ACL injuries, or the outcome measure of the study not being knee/ACL injuries.

Evidence Synthesis

2022: The evidence published since 2018 provides further support of the previous recommendation on the use of exercise-based knee and ACL injury prevention. In systematic reviews, meta-analyses, and meta-analyses of meta-analyses, there seems to be strong evidence for the 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.

Two studies from the same RCT provided new evidence potentially suggesting exercise-based knee injury prevention could be beneficial in secondary ACL injury prevention.

Gaps in Knowledge

Gaps in the literature still exist. Most of the exercise-based knee and ACL injury prevention programs included in this CPG are designed to be performed as dynamic warm-ups prior to training sessions/practices or games. Recently, programs not specifically focused on knee and ACL prevention have explored alternative implementation models, such as executing strengthening portions at the end of training sessions/practices.[38] Given the success of these programs with alternative structures, both in efficacy and implementation,

further research on alternative implementation models within knee and ACL prevention could be valuable.

Early research indicates potential value in "augmented NMT."[9] Biofeedback and virtual reality present developing opportunities for athlete self-evaluation; however, research into whether an athlete's focus is internal or external and the impact of cues given during prevention programs is also needed. Thus far, many prevention programs have been focused on the physical aspects of preventing injury; however, future prevention programs may also target the brain.

Further research regarding secondary prevention using exercise-based programs is needed. Additionally, greater diversity in the athlete populations studied is crucial. The majority of exercise-based knee and ACL injury prevention studies currently come from the United States, Northern Europe, and Australia, and report minimal data sample characteristics beyond age and sex. The research and clinical communities should support communities currently underrepresented in the literature, as well as those underserved or overlooked by current health care systems.

2022 Recommendations

A Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and ACL injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,[5] Goodall et al,[7] Junge et al,[15] LaBella et al,[18] Malliou et al,[20] Olsen et al,[25] Pasanen et al,[27] Petersen et al,[28] and Wedderkopp et al.[37] Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, PEP, and Sportsmetrics™, and those used by Caraffa et al,[4] Heidt et al,[10] LaBella et al,[18] Myklebust et al,[23] Olsen et al,[25] and Petersen et al.[28]

C Clinicians may recommend the use of an exercise-based neuromuscular training (NMT) program in the late phase of ACL reconstruction rehabilitation for the secondary prevention of ACL injuries.

OBJECTIVES

Identify exercise-based knee injury prevention programs that are effective for specific subgroups of athletes. Evidence includes systematic reviews, meta-analyses, and cohort studies that specifically delineate populations (**TABLE 2**).

2018 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 athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics™, Knäkontroll, HarmoKnee, and those used by Olsen et al[25] and Petersen et al.[28]

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 severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics™, and the program used by Caraffa et al.[4]

B Men and women team handball players, particularly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs. Programs that could be beneficial for preventing knee injuries include those used by Olsen et al[25] and Achenbach et al.[1]

Evidence Update

Men

No new information.

Women

I In a meta-analysis of studies looking at interventions aiming to reduce incidence of ACL injuries in women athletes, Petushek et al[29] found injury prevention programs that included NMT reduced ACL injury risk from 1 in 54 to 1 in 111 (odds ratio (OR), 0.51: 95% CI, 0.37, 0.69). Reduction in injury risk was greater for middle school– and high school–aged athletes (OR = 0.38; 95% CI, 0.24, 0.60) than for college and professional athletes (OR = 0.65; 95% CI, 0.48, 0.89).

Soccer

II Silvers-Granelli et al[33] found an overall decrease in the rate of ACL injuries in men Division I and II soccer players who participated in FIFA 11+ versus the control group (relative risk [RR] = 0.24; 95% CI: 0.07, 0.81). Examining the rate of ACL injuries in games vs practices, amongst playing positions, between field types, or only within Division I players, there were no differences in ACL injuries between the intervention and control groups. However, there was a reduction in ACL injury rate between intervention group and control groups when looking only at Division II players (RR = 0.12; 95% CI, 0.02, 0.93).

II Krutsch et al[17] aimed to quantify the incidence of severe knee injuries in elite football (soccer) over 1 season by comparing the injury incidence between the implementation of training modules and standard training

programs for the prevention of knee injuries. In a large scale cohort study of 26 teams (n = 529) in the intervention group and 36 teams (n = 601) in the control group, they reported a significant reduction in severe knee injury in the intervention group (0.38 per 1000 hours of football exposures; prevalence 9.8%) as compared to the control group (0.68 per 1000 hours of football exposures; prevalence 18.0%) ($P < .05$).

Team Handball

No new information.

Basketball

No new information.

Volleyball

No new information.

Evidence Synthesis

The new Level 1 evidence published since 2018 around the use of exercise-based prevention programs in soccer players continues to demonstrate efficacy in reducing the risk of knee and ACL injuries. This new evidence bolsters support for the 2018 recommendations, with little risk of adverse events and minimal cost.

Gaps in Knowledge

Research in sports outside soccer is needed. There was no new research in basketball or volleyball, and high-risk team sports such as Netball, Australian Rules Football, and individual sports like skiing should be both targets of funding organizations and researchers.

2022 Recommendations

A Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs prior to practices/training sessions or games in women athletes to reduce the risk of ACL injuries, especially in athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics™, Knäkontroll, HarmoKnee, and those used by Olsen et al[25] and Petersen et al.[28]

A Soccer players, both women and men, should use exercise-based knee injury prevention programs to reduce the risk of severe knee and ACL injuries. Programs beneficial for preventing severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics™, and the program used by Caraffa et al.[4]

B Men and women team handball players, particularly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs. Programs that could be beneficial for preventing knee injuries include those used by Olsen et al[25] and Achenbach et al.[1]

OBJECTIVES

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

2018 Recommendations

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

A Exercise-based knee injury prevention programs should involve training multiple times per week, 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 the preseason and continue performing the program throughout the regular season.

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

Evidence Update

Components

II A prospective interventional study demonstrated that participation in hip-focused NMT reduced noncontact ACL injuries in collegiate women's basketball.[27] Participants received 3 educational sessions on ACL injury-related biomechanics and then completed the intervention program 3 times a week (average of 20-minute sessions) and exercises were progressed 3 times throughout the season. Exercises included hip strengthening exercises, balance exercises, and basketball-specific jump-landing exercises. The RR for noncontact ACL injury in the intervention period versus the observation period was 0.37 and the number needed to treat for noncontact ACL injury was 41.3. Compliance rate throughout the intervention period was 89%. The authors concluded that the reduction in ACL injuries was secondary to a program with multiple components, a focus on the hip, and compliance with the intervention.

Dosage and Delivery

No new information.

Compliance

No new information.

Evidence Synthesis

There was very little new research in the area of components, dosage and delivery, as well as compliance that met the inclusion criteria of this CPG published since 2018. Only one level II study, supporting the use of proximal control/hip strengthening components within exercise-based knee and ACL injury prevention programs was added. Therefore, the evidence continues to support the previous recommendations showing 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.

Gaps in Knowledge

More research is still needed on the dose-response relationship of exercise-based knee and ACL injury prevention programs, as well as around improving compliance and adherence.

2022 Recommendations

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

A Exercise-based knee injury prevention programs should involve training multiple times per week, 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 the preseason and continue performing the program throughout 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.

OBJECTIVES

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

2018 Recommendations

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

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 to 25 years of age and involved in sports with a high risk of ACL injury.

A 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.

Evidence Update

III A retrospective survey-based study examined availability of NMT programs in high schools,[22] and whether availability of these programs impacted ACL injury rates. Over 2/3 of respondents reported their high school athletes participated in NMT. Men's soccer teams participating in NMT had a significantly lower ACL injury rate ($P < .005$) compared to the literature when an athletic trainer was available for the team. The authors concluded that athletic trainers may help facilitate execution of training programs.

Evidence Synthesis

There was very little new evidence, meeting the inclusion criteria of this CPG, published since 2018 on implementation. The new level III evidence continues to support the previous Level I and II studies and 2018 recommendations that there is no increase in risk of adverse events when all athletes perform prevention programs compared to only athletes screened as high risk, and there is no harm in performing prevention programs. Although cost may minimally increase (depending on the program) as more athletes participate, the small increase in program costs is likely outweighed by long-term health care costs and by the reduction in ACL injuries.

Gaps in Knowledge

Research around how to engage key stakeholders in exercise-based knee and ACL injury prevention implementation is ongoing and implementation remains a crucial step to reducing the burden of knee and ACL injuries.[3] Examples of key stakeholders include national governing bodies, leagues, clubs, referees and referee associations, teams, coaches, parents, athletes, health, fitness and med-

ical professionals, media professionals and networks, and many more. More research, particularly larger-scale implementation studies (observational and RCTs) are needed to bolster the evidence.

2022 Recommendations

A Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as being at high risk for ACL injury, to optimally mitigate injuries and reduce 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 to 25 years of age who are involved in sports with a high risk of ACL injury.

A 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.

The recommendations made in this guideline are summarized in **FIGURE 1**. Supplementary videos, originally published in 2018 and located at https://www.jospt.org/doi/suppl/10.2519/jospt.2018.0303, also remain a clinical reference for clinicians based on the findings of both the 2018 and 2022 CPGs.

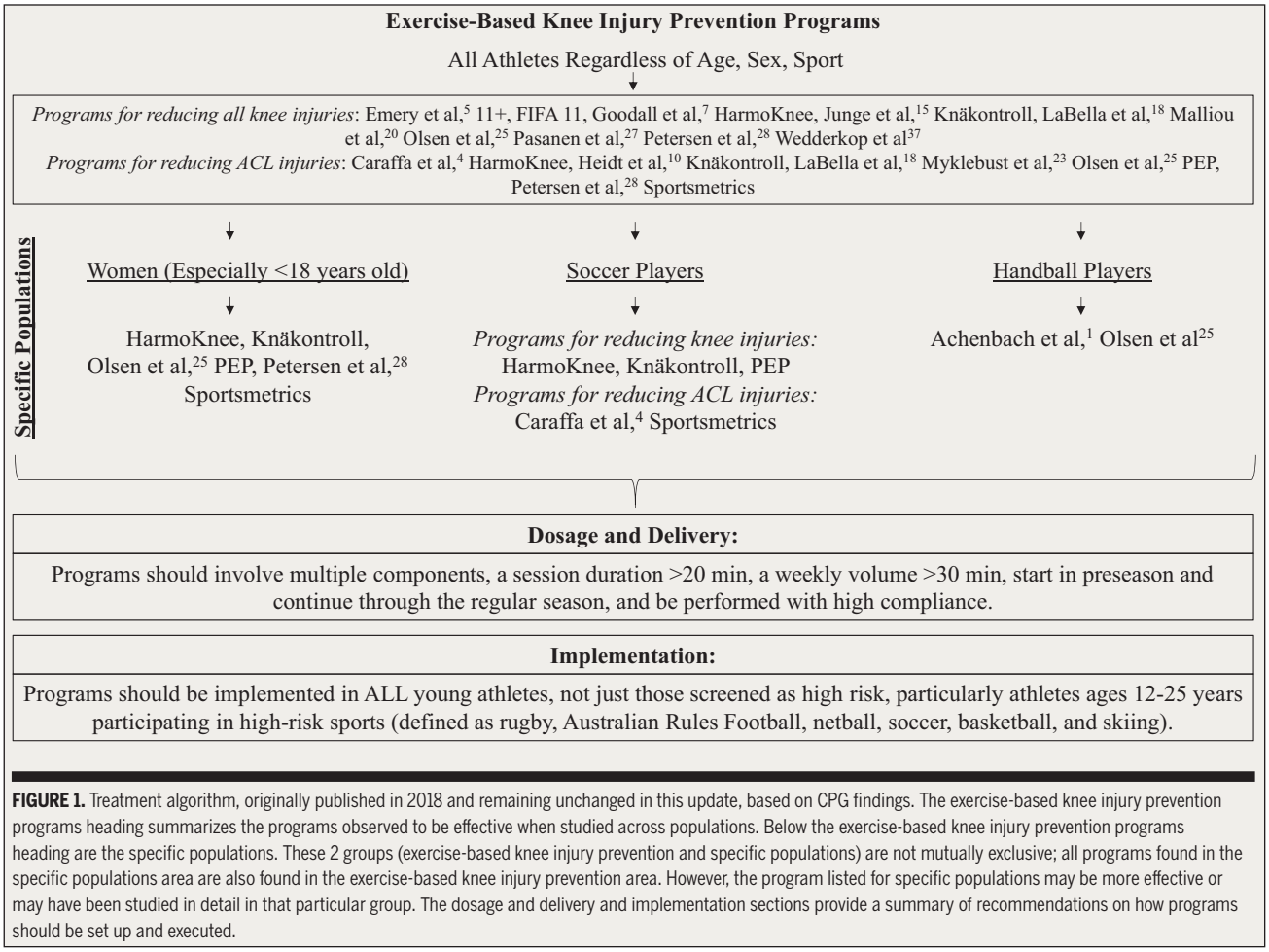


FIGURE 1. Treatment algorithm, originally published in 2018 and remaining unchanged in this update, based on CPG findings. The exercise-based knee injury prevention programs heading summarizes the programs observed to be effective when studied across populations. Below the exercise-based knee injury prevention programs heading are the specific populations. These 2 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 may 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 2 Evidence Table

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Arundale et al[2]	Randomized control study	1	(1) Three to nine months after unilateral ACL reconstruction (2) Eighty percent quadriceps strength limb symmetry (quadriceps index) (3) Minimal effusion, no pain, full range of motion, and successful completion of a running progression	Athletes were excluded if they (1) had a concomitant >1 cm^2 full-thickness chondral defect (assessed via arthroscopy or MRI) or grade 3 ligamentous injury (eg, MCL or LCL), (2) had previous ACL reconstruction or a history of major lower extremity injury or surgery to either limb, or (3) had already returned to sport.	N = 40 n = 20 (intervention) n = 20 (control) Level I/II men athletes Age: 15-54 years Mean height: 1.79 ± 0.07 m Mean weight: 85.39 ± 9.32 (kg) Mechanism of injury: 18 contact and 22 noncontact Graft type: allograft = 13, hamstring autograft = 19, and bone-patellar tendon-bone ligament autograft = 8	**Primary:** Number of athletes who returned to sport **Secondary:** Number of athletes who returned to preinjury level of sport and number of second ACL injuries	**Primary:** 1 year after ACL-R, 95% returned to sport; 2 years after ACL-R, 100% returned to sport **Secondary:** 1 year after ACL-R, 78% returned to preinjury level; 2 years after ACL-R, 95% returned to preinjury level. 1 year after ACL-R, 0 athletes had a second ACL injury; 2 years after ACL-R, 1 athlete had a second ACL injury
Johnson et al[14]	Randomized control study	1	(1) Age: 13-55 years (2) Planned to return to cutting/pivoting/jumping sport for more than 50 hours per year (3) No previous ACL injury (4) No history of major lower extremity injury/surgery	(1) Not a level 1 or 2 athlete (2) Previous ACL/lower extremity injury (3) Greater than 9 months from ACL-R (4) Continued impairments (5) Concomitant injuries	N = 39 n = 19 (intervention) n = 20 (control) Level I/II women athletes Height: 1.65 ± 0.08 m Graft type: patella tendon = 16, hamstring autograft = 18, allograft = 5	**Primary:** Rate of second ACL injury in women athletes after ACL-R **Secondary:** Rate of ipsilateral second ACL injury	**Primary:** 23% reinjury rate **Secondary:** 10% ipsilateral second injury rate

Table continues on next page.

TABLE 2 Evidence Table (continued)

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Huang et al[13]	Meta-analysis	1	(1) The intervention aimed to prevent ACL injury. (2) The study recorded the incidence rate (IR) or other outcome data such as injury counts and AEs (ie, time at risk) that made it possible to calculate ACL IR for both the intervention and control groups reported. (3) The study used a prospective randomized controlled trial (RCT) or cluster-RCT design.	(1) Review articles (2) Editorials (3) Non–full text articles such as lectures, commentaries, abstracts, case studies, or surgical techniques (4) Articles that were not peer reviewed or not written in English	8 studies n = 13 562 Men and women with age ranges from 12 to 25.9 years playing soccer, handball, basketball, or volleyball	**Primary:** ACL injury IR **Secondary:** IR based on if an injury prevention program met NATA position statement recommendations	**Primary:** IR = 0.47; 95% CI, 0.30-0.73; *P* = .001. The rate of ACL injury was 53% less in athletes who received IPPs compared with the athletes who did not receive IPPs. **Secondary:** All but 2 studies met the minimum best practice recommendations of having at least 3 exercise components and provided feedback on proper exercise technique. Specific exercises and methods of delivery and training were highly variable. Subgroup analysis was not conducted given the absence of significant heterogeneity in effects across studies.
Olivares-Jabalera et al[24]	Systematic review	1	(1) Adult (16-40 years old) soccer players, both men and women, of any level who have not suffered a severe injury in previous 2 years (2) Exercise or training-based interventions lasted at least 4 weeks, performed twice a week (3) Either contact or noncontact ACL injury incidence or rate of injury (4) Test measurements evaluating any modifiable risk factor previously reported to have an influence in ACL injury (5) RCTs, nonrandomized studies, and single-arm studies	(1) Included different cohorts of athletes apart from football players (2) Included interventions performed with exogenous modalities or exercise-based interventions lasting less than 4 weeks (3) Did not explicitly report overall injury incidence of ACL-type injuries (4) Had test-measured evaluating nonmodifiable risk factors (5) Were systematic reviews, meta-analysis, conference papers, book chapters, or studies published in languages other than English	N = 29 n = 6 (studies investigating exercise-based interventions on ACL injury rates) n = 23 (studies investigating exercise-based interventions on modifiable risk factors for ACL injury) Level I/II athletes Age: 16-40 years Study types: parallel RCTs = 11, cluster RCTs = 4, non-RCTs:= 8, and single-arm = 6	**Primary:** Effect of exercise-based interventions on ACL injury rate for adult football players **Secondary:** Effect of exercise-based interventions on modifiable risk factors for ACL injury for adult football players	**Primary:** PEP and 11+ could effectively reduce ACL injury incidence. **Secondary:** The secondary outcomes of this study are not reported in this CPG as they are not within the scope of this CPG.

Table continues on next page.

TABLE 2 Evidence Table (continued)

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Webster and Hewett[36]	Meta-analysis	1	(1) A meta-analysis of RCTs or prospective cohort studies that evaluated the effectiveness of an ACL injury prevention training program (2) Reported data on the incidence of ACL injuries (3) Written in English	(1) Systematic reviews that did not pool data or perform a meta-analysis (2) Narrative reviews or those without a search algorithm or failed to describe how studies were selected for the review (3) Reviews that evaluated a general or sports injury prevention program that was not specific to ACL injury prevention (4) Reviews that included nontraining interventions such as education or an external device, that is, bracing (5) Reviews that did not report ACL injury data. Meta-analyses that only focused on components of training programs (ie, specific exercises or dosage), compliance, or only one sport were excluded.	8 meta-analyses N = 40 003 in treatment groups N = 52 704 in control groups Men and women athletes	**Primary:** Odds ratios with 95% CIs ACL injury **Secondary:** Odds ratios for ACL injuries in women and noncontact ACL injuries in women	**Primary:** ACL injuries demonstrated a 50% reduction (OR = 0.5 [0.41-0.59]; I2 = 15%) in the risk of all ACL injuries in all athletes **Secondary:** The summary meta-analysis for noncontact ACL injuries demonstrated a 67% reduction (OR = 0.33 [0.27-0.41]; I2 = 15%) in the risk of noncontact ACL injuries in women.

Table continues on next page.

TABLE 2 Evidence Table (continued)

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Evidence for Specific Subgroups of Athletes							
Krutsch et al[17]	Cohort study	2	(1) Elite men football player on a participating team (2) Played in at least one official match during the season	(1) Incomplete questionnaire (2) No playing time during the investigated season (3) Injuries prior to the start of the season.	8 studies 26 teams; n = 529 (intervention) 36 teams; n = 601 (control) Men, mean age: 22.2 ± 4.3 years (intervention), 21.9 ± 4.1 (control); mean height: 1.8 ± 4.4 m; mean weight 76.3 ± 7.5 kg	**Primary**: Severe knee injury incidence **Secondary:** ACL or PCL, MCL or LCL, cartilage or meniscus, fracture, patella dislocation, thigh injuries, ankle injuries	**Primary:** Significant reduction in severe knee injury (0.38 vs 0.68/1000 h) in the intervention group **Secondary:** No significant difference in overall injury incidence (intervention, 3.27/1000 h; control, 3.23/1000 h) No significant difference in thigh injuries, ankle injuries, or knee injuries overall MCL/LCL was significantly higher in the control group (0.3/1000 h) vs the intervention group (0.10/1000 h). Meniscus injuries were the most common severe injuries in the intervention group, but not significantly different from the control group. No difference in incidence of ACL/PCL, cartilage, fracture, or patella dislocation between the intervention and control groups.
Petushek et al[29]	Meta-analysis	1	(1) A prospective controlled trial study design (2) An NMT intervention aimed to reduce incidence of ACL injury (3) Included a comparison group (4)Recorded ACL injury incidence (5) Women	(1) No abstracts, posters, review papers, and irrelevant studies	18 studies N = 27 231 Young women athletes	**Primary:** ACL injury odds ratio **Secondary:** Heterogeneity and publication bias	**Primary:** As a whole, NMT reduced the risk for ACL injury from 1 in 54 to 1 in 111 (OR = 0.51; 95% CI, 0.37-0.69). **Secondary:** Because substantial heterogeneity was found in programming characteristics between studies (training exercises, target population, etc) and moderate statistical heterogeneity was noted, subgroup and meta-regression analyses were conducted. No significant publication bias or funnel plot asymmetry was found when standard error (Z = 0.92, *P* = .36), sample size (Z = 1.86, *P* = .06), and sample variance (Z = 1.07, *P* = .28) were used as predictors. Grouped ORs were similar between randomized trials (k = 11; OR = 0.54; 95% CI, 0.35-0.83) and nonrandomized trials (k = 9; OR = 0.46; 95% CI, 0.28-0.76).

Table continues on next page.

TABLE 2 Evidence Table (continued)

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Silvers-Granelli et al[33]	Randomized control study	1	(1) Men's college soccer player that is between the ages of 18 and 25 years in good academic standing and was medically cleared to participate in the 2012 season (2) Teams confirmed that they had not participated in an injury prevention program in the past 4 academic years.	(1) Not meeting inclusion criteria (2) Refused to participate	27 teams N = 675 (intervention group) 34 teams; N = 850 (control group) Men college soccer player between the ages of 18 and 25 years	**Primary:** Reduction in overall number of ACL injuries **Secondary:** Reduction in rate of ACL injuries based on (1) game vs practice setting, (2) player position, (3) level of play, (4) field type	**Primary:** Risk of ACL injuries reduced in intervention group (RR = 0.24; 95% CI, 0.07-0.81, *P* = .021 **Secondary:** (1) No difference between groups in injury risk during games vs practices (RR = 0.31; 95% CI, 0.09-1.11, *P* =.073); (2) no difference between groups in injury rate based on player position; (3) no difference between groups in Division I (RR = 0.3; 95% CI, 0.06-1.45; *P* = .136); however, fewer ACL injuries in Division II intervention group (RR = 0.12; 95% CI, 0.02-0.93; *P* =.042); (4) no difference between groups in ACL occurring on grass vs artificial turf (RR = 0.36; 95% CI, 0.08-1.73; *P* = .201
Evidence for Components, Dosage, and Delivery of Exercise-based Knee Injury Prevention Programs							
Murray et al[22]	Retrospective cohort study	3	Athletic directors in Minnesota high schools that participated in high school boys' football and soccer, and girls' volleyball and soccer	None reported	611 teams N = 12 799 football (men) n = 7672 volleyball (women) n = 3111 soccer (women) and 3753 soccer (men) All athletes in high school competing for their school team	**Primary:** Number of ACL injuries during sports season **Secondary:** Number of programs that performed IPP with a licensed athletic trainer	**Primary:** 167 (0.6%) **Secondary:** 13 955 (51%) NMT was associated with fewer ACL injuries for men but not women athletes.

Table continues on next page.

TABLE 2 Evidence Table (continued)

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Omi et al[26]	Cohort study	2	Must play for a women's Japanese collegiate basketball team	None stated	N = 757 n = 309 during observation period n = 448 during intervention period Women collegiate basketball players Age: 19.6 ± 1.1 years	**Primary**: IR of all ACL injuries and noncontact ACL injuries in observation vs intervention periods I and II **Secondary:** IR of all ACL injuries and noncontact ACL injuries in observation vs intervention periods I and II RR, absolute risk reduction, numbers needed to treat	**Primary:** Incidence All ACL injuries: Observation 0.25/1000 AEs Intervention Periods I + II 0.10/1000 AEs RR = 0.38 (95% CI, 0.17-0.87; *P* = .017) Incidence Noncontact ACL injuries: Observation 0.21/1000 AEs Period I + II 0.08/1000 AEs RR = 0.37 (95% CI, 0.15-0.92; *P* = .026) **Secondary:** All ACL injuries: ARR for periods I and II = .032 (95% CI, 0.027-0.037) while the NNT was 31.6 (95% CI, 27.1-37.7) All noncontact ACL injuries: ARR for periods I and II = 0.024 (95% CI, 0.020-0.029) and NNT = 41.3 (95% CI, 34.6-51.3) Period I Incidence All ACL = 0.11/1000 AEs RR = 0.43 (95% CI, 0.17-1.10; *P* = .07) ARR of 0.029 (95% CI, 0.024-0.035) and NNT of 34.0 (95% CI, 28.9-41.4) relative to observation Incidence Noncontact ACL = 0.09/1000 AEs. RR = .44 (95% CI, 0.16-1.24; *P* = .11) ARR = 0.023 (95% CI, 0.019-0.028) and NNT = 42.7 (95% CI, 35.5-53.6) relative to observation Period II Incidence All ACL = 0.08/1000 AEs RR = 0.32 (95% CI, 0.09-1.09; *P* = .053) ARR = 0.035 (95% CI, 0.030-0.040) and NNT = 28.5 (95% CI, 24.9-33.2) Incidence noncontact ACL = 0.08/1000 AEs RR = 0.39 (95% CI, 0.11-1.37; *P* = .127) ARR = 0.025 (95% CI, 0.021-0.031) and NNT = 39.4 (95% CI, 33.3-48.2) Rates of compliance with the HIP training protocol during intervention periods I and II were 88% and 91%,respectively (**TABLE 3**). The mean compliance rate during the combination of intervention periods I and II was 89%.

Abbreviations: ACL, anterior cruciate ligament; ACL-R, anterior cruciate ligament reconstruction; AE, athlete exposure; ARR, absolute risk reduction; BTB, bone-patellar tendon-bone; CI, confidence interval; CPG, clinical practice guideline; HIP, hip-focused injury prevention; IPP, injury prevention program; IR, incidence rate; LCL, lateral collateral ligament; MCL, medial collateral ligament; MRI, magnetic resonance imaging; NATA, National Athletic Trainers' Association; NMT, neuromuscular training; NNT, number needed to treat; OR, odds ratio; PCL, posterior cruciate ligament; PEP, Prevent Injury and Enhance Performance; RCT, randomized controlled trial; RR, relative risk.

TABLE 3 Contents of Programs Frequently Referenced in the CPG

Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Harmoknee[16]	Flexibility	None	Muscle activation: approximately 2 minutes of total time, holding position and contracting the muscle for approximately 4 seconds, focusing on "finding" your muscles. Stretching is only recommended in cases of limited range of motion	• Standing calf stretch • Standing quadriceps stretch • Half-kneeling hamstring stretch • Half-kneeling hip flexor stretch • Butterfly adductor stretch • Modified figure-of-four stretch
	Running	None	As part of warm-up, 10 minutes total, separate times for each	• Jogging (4-6 minutes) • Backward jogging on toes (1 minute) • High-knee skipping (30 seconds) • Defensive pressure technique: sliding slowly, zigzag backward (30 seconds) • Alternating forward zigzag running and pressure technique: zigzag backward (2 minutes)
	Strength	None	1 minute each	• Lunges in place (alternating anterior lunges) • Nordic hamstring eccentric strengthening • Single-leg squat with toe raise
	Core stability	None	1 minute each	• Sit-ups • Plank on elbows • Bridging
	Plyometrics	Ball optional	30 seconds each	• Forward and backward double-leg jumps • Lateral single-leg jumps • Forward and backward single-leg jumps • Double-leg jump with or without a ball
PEP[21]	Flexibility	None	50 yd each, 30 × 2 repetitions each	• Calf stretch • Quadriceps stretch • Figure-of-four hamstring stretch • Inner thigh stretch • Hip flexor stretch
	Running	None	50 yd each, 2 repetitions each	• Jog from line to line of soccer field (cone to cone) • Shuttle run (side to side) • Backward running • Shuttle run with forward/backward running (40 yd) • Diagonal runs (40 yd) • Bounding run (45-50 yd)
	Strength	None	Varies by exercise	• Walking lunges, 20 yd × 2 sets • Russian hamstring, 3 sets × 10 repetitions or 30 seconds • Single toe raises, 30 repetitions each side
	Plyometrics	Cones (5-15 cm tall)	20 repetitions or 30 seconds each	• Lateral hops over cone • Forward/backward hops over cone

Table continues on next page.

TABLE 3 Contents of Programs Frequently Referenced in the CPG (continued)

Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Sportsmetrics[11]	Flexibility	None	3 sets of 30 seconds each, or 2 laps	• Gastrocnemius • Soleus • Quadriceps • Hamstrings • Hip flexors • Iliotibial band/lower back • Posterior deltoids • Latissimus dorsi • Pectorals/biceps
	Running	None	3 sets of 30 seconds each, or 2 laps	• Skipping • Side shuffle • Cool-down walk (2 minutes)
	Strength	Weight equipment/ machines	1 set of 12 repetitions for upper body, 1 set of 15 repetitions for trunk and lower body	• Back hyperextension • Leg press • Calf raise • Pullover • Bench press • Latissimus dorsi pull-down • Forearm curl
	Core stability	None	1 set of 15	Abdominal curl
	Plyometrics	None	Varies based on exercise	• Wall jumps (20 seconds, progressing to 30 seconds) • Tuck jumps (20 seconds, progressing to 30 seconds) • Broad jumps, stick (hold) landing (5-10 repetitions) • Squat jumps (10 seconds, progressing to 25 seconds) • Double-legged cone jumps (30 seconds/30 seconds side to side and back to front) • 180° jumps (20-25 seconds) • Bounding in place (20-25 seconds) • Jump, jump, jump, vertical jump (5-8 repetitions) • Bounding for distance (1-2 runs) • Scissors jump (30 seconds) • Hop, hop, stick landing (5 repetitions per leg) • Step, jump up, down, vertical (5-10 repetitions) • Mattress jumps (30 seconds/30 seconds side to side and back to front) • Single-legged jumps for distance (5 repetitions per leg) • Jump into bounding (3-4 runs)
KLIP[30]	Running	None	4 phases, each lasting 2 weeks. Time/repetitions for each exercise not specified	• Agility: "W" drill • Agility: figure-of-eights • Agility: left/right cuts
	Plyometrics	None	4 phases, each lasting 2 weeks. Time/repetitions for each exercise not specified	• Straight jumps • Tuck jumps • Standing broad jump • Bound in place • 180° jump • Single-leg lateral leaps • 45° lateral leaps • Combination jumps • Single-leg forward hops • Single-leg 45° lateral hops • Single-leg forward hops × 3

Table continues on next page.

TABLE 3 Contents of Programs Frequently Referenced in the CPG (continued)

Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Olsen et al[25]	Running	None	30 seconds and 1 repetition each	• Jogging • Backward running with sidesteps • Forward running with knee lifts and heel kicks • Sideways running with crossovers ("carioca") • Sideways running with arms lifted ("parade") • Forward running with trunk rotations • Forward running with intermittent stops • Speed run • Bounding strides • Planting and cutting
	Balance	Balance mat or wobble board	4 minutes and 2 × 90 seconds each	• Passing the ball (2-leg stance) • Squats (1- or 2-leg stance) • Passing the ball (1-leg stance) • Bouncing the ball with eyes closed • Pushing each other off balance
	Strength	None	2 minutes and 3 × 10 repetitions each	• Squats to 80° of knee flexion • Nordic hamstring eccentric strengthening
	Plyometrics	None	4 minutes and 5 × 30 seconds each	• Jump-shot landings • Forward jumps
Achenbach et al[1]	Balance	Ball optional	Not specified	Standing on 1 leg with eyes closed, try to destabilize the partner by pressing against their body
	Plyometrics	None	Not specified	• Multidirectional single-leg jumps • "Ice-skater" jumps • Jump run
	Strength	None	Not specified	Nordic hamstring eccentric strengthening
	Core stability	None	Not specified	• Plank • Side plank
Caraffa et al[4]	Balance	Rectangular wobble board, round balance board, combined round/rectangular board, BAPS board	2.5 minutes, 4 times a day for each exercise	• Phase 1: single-leg stance, with no board • Phase 2: single-leg stance on a rectangular board (on 45°) • Phase 3: single-leg stance on a round board • Phase 4: single-leg stance on a combined round and a rectangular board • Phase 5: single-leg stance on a BAPS board
	Strength	Step	Not specified (prior to balance training)	• Anterior step-up • Posterior step-up
Myklebust et al[23]	Balance	Balance mat, wobble board	Not specified	• Single-leg stance on mat with throwing • Standing on a mat with a partner, try to push your partner off • Jump onto mat while catching the ball, then turn 180° • Double-leg balance on wobble board with throwing • Double-leg squat on wobble board • Single-leg squat on wobble board • Single-leg stance on wobble board with bounding ball • Two players on wobble boards: try to push the other off
	Plyometrics	None	Not specified	• Run and plant • Double-leg jump forward/backward; the partner pushes the player (perturbation) • Jump shot (handball) from the 30- to 40-cm box with soft landing • Step off the 30- to 40-cm box with single-leg landing

Table continues on next page.

TABLE 3 Contents of Programs Frequently Referenced in the CPG (continued)

Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Knäkontroll[35]	Strength	Ball	3 sets, 8-15 repetitions. Each exercise with 4 levels of difficulty	• Level 1: double-leg squat • Level 2: double-leg squat with heel raise • Level 3: double-leg squat with a ball over head • Level 4: double-leg squat with ball held in front of the body • Level 5 (partner exercise): your partner stands next to you approximately 1 m away, facing opposite directions; hold the ball between you with one hand and the other hand on hip; apply slight pressure on the ball while performing knee squat • Level 1: forward walking lunge • Level 2: forward lunge with a ball, lateral trunk rotation • Level 3: forward lunge with a ball over head • Level 4: lateral lunge • Level 5 (partner exercise): your partner stands in front of you 5-10 m away; perform forward lunge while making throw-in with the ball • Level 1: single-leg squat • Level 2: single-leg squat with overhead ball • Level 3: single-leg squat with off leg at differing positions • Level 4: single-leg Romanian deadlift • Level 5 (partner exercise): your partner stands slightly oblique in front of you, and the ball is pressed between the lateral sides of feet of nonsupporting legs
	Core stability	None	15-30 seconds	• Level 1: prone plank on knees • Level 2: prone plank on toes • Level 3: prone plank on toes with lateral step • Level 4: side plank • Level 5 (partner exercise): plank with a partner holding your feet • Level 1: bridge, double leg • Level 2: bridge, single leg • Level 3: bridge, single leg on ball • Level 4: bridge, single leg with hop • Level 5 (partner exercise): your partner stands with flexed knees and supports the heel of one of your feet in his/her hands
	Plyometrics	None	3 sets, 5-15 repetitions	• Level 1: single-leg forward/backward hops • Level 2: double-leg lateral jumps, landing on single leg • Level 3: take a few quick steps on the same spot and do a short jump straight forward, landing on one foot • Level 4: take a few quick steps on the same spot and do a short jump, but change direction and jump to one side (90° turn); alternate sides • Level 5 (partner exercise): your partner stands in front of you approximately 5 m away; do a 2-legged jump while heading the soccer ball and land on 2 legs

Table continues on next page.

TABLE 3 Contents of Programs Frequently Referenced in the CPG (continued)

Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
11+[33]	Running	Cones	8 minutes at the beginning of warm-up, 2 minutes at the end, 2 repetitions each	Beginning of warm-up • Running straight ahead • Running hip out • Running hip in • Running circling partner • Running shoulder contact with a partner • Running quick forwards and backwards End of warm-up • Running across pitch • Bounding • Running plant and cut
	Strength	None	10 minutes (strength + plyometrics + balance combined)	• The Bench 3 × 20-30s o Level 1: static o Level 2: alternate legs o Level 3: 1 leg lift and hold • Sideways Bench 3 × 20-30 s each side o Level 1: static o Level 2: raise and lower hip o Level 3: with leg lift • Hamstrings o Level 1: beginner 3-4 o Level 2: intermediate 7-10 o Level 3: advanced 12-15 • Squats o Level 1: with toe raise 2 × 30 s o Level 2: walking lunges 2 × 30 s o Level 3: single leg squats 2 × 30 s each leg
	Plyometrics	None	10 minutes (strength + plyometrics + balance combined)	• Jumping 2 × 30s o Level 1: vertical jumps o Level 2: lateral jumps o Level 3: box jumps
	Balance	None	10 minutes (strength + plyometrics + balance combined)	• Single-leg stance 2 × 30 s o Level 1: hold the ball o Level 2: throwing the ball with your partner o Level 3: test your partner

Abbreviations: BAPS, Biomechanical Ankle Platform System; KLIP, Knee Ligament Injury Prevention; PEP, Prevent Injury and Enhance Performance.

AFFILIATIONS AND CONTACTS

AUTHORS

Amelia J.H. Arundale, PT, PhD
Physiotherapist
Red Bull Athlete Performance Center
Thalgau, Austria
and
Adjunct Professor
Department of Rehabilitation
Icahn School of Medicine at Mount Sinai Health System
New York, NY
ORCID: 0000-0002-1007-5327
aarundale@gmail.com

Mario Bizzini, PT, PhD
Research Associate
Human Performance Lab
Schulthess Clinic
Zurich, Switzerland
ORCID: 0000-0002-4161-9163
Mario.bizzini@kws.ch

Celeste Dix, PT, PhD
Physical Therapist
United States Soccer Federation
Chicago, IL
and
Research Associate
Biomechanics and Movement Science
University of Delaware Newark, NJ
ORCID: 0000-0002-8158-863X
cdix@udel.edu

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

Ryan Kelly, DPT
Physical Therapist and Pro Sports Fellow
Hospital for Special Surgery
New York, NY
kellyr@hss.edu

David Logerstedt, PT, PhD
Associate Professor
Department of Physical Therapy
Saint Joseph's University Philadelphia, PA
ORCID: 0000-0001-8977-013X
dlogerstedt@sju.edu

Bert Mandelbaum, MD
Orthopaedic Surgeon
Cedars Sinai Kerlan-Jobe Institute
Santa Monica, CA
ORCID: 0000-0002-0074-2157
bmandelbau@aol.com

David Scalzitti, PT, PhD
Associate Professor
Department of Physical Therapy
George Washington University
Washington, DC
ORCID: 0000-0002-1617-1053
scalzitt@gwu.edu

Holly Silvers-Granelli, PT, PhD
Physical Therapist
Velocity Physical Therapy
Santa Monica, CA
and
Major League Soccer Medical Assessment and Research
New York, NY
ORCID: 0000-0002-8959-9448
hollysilverspt@gmail.com

Lynn Snyder-Mackler, PT, ScD, FAPTA
Alumni Distinguished Professor
Department of Physical Therapy
University of Delaware Newark, DE
ORCID: 0000-0002-1767-7910
smack@udel.edu

REVIEWERS

Caroline (Lewis) Brunst, PT, DPT, AT
Board-Certified Clinical Specialist in Sports Physical Therapy
Board-Certified Clinical Specialist in Orthopaedic Physical Therapy
Certified Manual Therapist
Jameson Crane Sports Medicine Institute
Columbus, OH
caroline.brunst@osumc.edu

Joseph J. Godges, DPT, MA
Coordinator, CPG Knowledge Translation Academy of Orthopaedic Physical Therapy, APTA, Inc
La Crosse, WI
and
Adjunct Associate Professor of Clinical Physical Therapy
Division of Biokinesiology and Physical Therapy
Ostrow School of Dentistry
University of Southern California
Los Angeles, CA
godges@pt.usc.edu

Sandra Kaplan, PT, DPT, PhD, FAPTA
Professor
Department of Rehabilitation and Movement Services
and
Vice-Chair, Curriculum and Accreditation
Stuart D. Cook, M.D. Master Educators' Guild
Rutgers, The State of University of New Jersey
New Brunswick, NJ
kaplansa@shp.rutgers.edu

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

GUIDELINES EDITORS

Christopher Carcia, PT, PhD
ICF-Based Clinical Practice Guidelines Editor
Academy of Orthopaedic Physical Therapy, APTA, Inc
La Crosse, WI
and
Physical Therapy Program Director and Associate Professor
Department of Kinesiology
Colorado Mesa University
Grand Junction, CO
ccarcia@coloradomesa.edu

Guy G. Simoneau, PT, PhD, FAPTA
ICF-Based Clinical Practice Guidelines Editor
Academy of Orthopaedic Physical Therapy, APTA, Inc
La Crosse, WI
and
Professor
Physical Therapy Department
Marquette University
Milwaukee, WI
guy.simoneau@marquette.edu

RobRoy L. Martin, PT, PhD
ICF-Based Clinical Practice Guidelines Editor
Academy of Orthopaedic Physical Therapy, APTA, Inc
La Crosse, WI
and
Professor
Department of Physical Therapy
Rangos School of Health Science
Duquesne University
and
Staff Physical Therapist
UPMC Sports Medicine
Pittsburgh, PA
martinr280@duq.edu

ACKNOWLEDGMENTS: *The authors acknowledge the contributions of George Washington University Himmelfarb Health Sciences librarian Tom Harrod for his guidance and assistance in the design and implementation of the literature search, and Doctor of Physical Therapy students Meghan Henderson and Rachel Vazque, at George Washington University for screening articles.*

REFERENCES

1. Achenbach L, Krutsch V, Weber J, et al. Neuromuscular exercises prevent severe knee injury in adolescent team handball players. *Knee Surg Sports Traumatol Arthrosc*. 2018;26:1901-1908. https://doi.org/10.1007/s00167-017-4758-5
2. Arundale AJH, Capin JJ, Zarzycki R, Snyder-Mackler L, Smith AH. Two year ACL reinjury rate of 2.5%: outcomes report of the men in a secondary ACL injury prevention program (ACL-SPORTS). *Int J Sports Phys Ther*. 2018;13:422-431. https://doi.org/10.26603/ijspt20180422
3. Arundale AJH, Silvers-Granelli HJ, Myklebust G. ACL injury prevention: where have we come from and where are we going? *J Orthop Res*. 2022;40:43-54. https://doi.org/10.1002/jor.25058
4. Caraffa A, Cerulli G, Projetti M, Aisa G, Rizzo A. Prevention of anterior cruciate ligament injuries in soccer. A prospective controlled study of proprioceptive training. *Knee Surg Sports Traumatol Arthrosc*. 1996;4:19-21. https://doi.org/10.1007/BF01565992https://doi.org/10.1007/BF01565992
5. Emery CA, Meeuwisse WH. The effectiveness of a neuromuscular prevention strategy to reduce injuries in youth soccer: a cluster-randomised controlled trial. *Br J Sports Med*. 2010;44:555-562. https://doi.org/10.1136/bjsm.2010.074377
6. Fuller CW, Ekstrand J, Junge T, et al. Consensus statement on injury definitions and data collection procedures in studies of football (soccer) injuries. *Scand J Med Sci Sports*. 2006;16:83-92. https://doi.org/10.1111/j.1600-0838.2006.00528.x
7. Goodall RL, Pope RP, Coyle JA, Neumayer R. Balance and agility training does not always decrease lower limb injury risks: a cluster-randomised controlled trial. *Int J Inj Contr Saf Promot*. 2013;20:271-281. https://doi.org/10.1080/17457300.2012.717085
8. Griffin LY, Albohm MJ, Arendt BY, 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;34:1512-1532. https://doi.org/10.1177/0363546506286866
9. Grooms DR, Kiefer AW, Riley MA, et al. Brain-behavior mechanisms for the transfer of neuromuscular training adaptions to simulated sport: initial findings from the train the brain project. *J Sport Rehabil*. 2018;27:1-5. https://doi.org/10.1123/jsr.2017-0241
10. Heidt RS, Sweeterman LM, Carlonas RL, Traub JA, Tekulve FX. Avoidance of soccer injuries with preseason conditioning. *Am J Sports Med*. 2000;28:659-662. https://doi.org/10.1177/03635465000280050601
11. Hewett TE, Lindenfeld TN, Riccobene JV, Noyes FR. The effect of neuromuscular training on the incidence of knee injury in female athletes. A prospective study. *Am J Sports Med*. 1999;27:699-706. https://doi.org/10.1177/03635465990270060301
12. Hewett TE, Myer GD, Ford KR, 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. *Am J Sports Med*. 2005;33:492-501. https://doi.org/10.1177/0363546504269591
13. Huang YL, Jung J, Mulligan CMS, Oh J, Norcross MF. A majority of anterior cruciate ligament injuries can be prevented by injury prevention programs: a systematic review of randomized controlled trials and cluster–randomized controlled trials with meta-analysis. *Am J Sports Med*. 2020;48:1505-1515. https://doi.org/10.1177/0363546519870175
14. Johnson JL, Capin JJ, Arundale AJH, Zarzycki R, Smith AH, Snyder-Mackler L. A secondary injury prevention program may decrease contralateral anterior cruciate ligament injuries in female athletes: 2-year injury rates in the ACL-sports randomized controlled trial. *J Orthop Sports Phys Ther*. 2020;50:523-530. https://doi.org/10.2519/jospt.2020.9407
15. Junge A, Rösch D, Peterson L, Graf-Baumann T, Dvorak J. Prevention of soccer injuries: a prospective intervention study in youth amateur players. *Am J Sports Med*. 2002;30:652-659. https://doi.org/10.1177/03635465020300050401
16. Kiani A, Hellquist E, Ahlqvist K, Gedeborg R, Byberg L. Prevention of soccer-related knee injuries in teenaged girls. *Arch Intern Med*. 2010;170:43-49. https://doi.org/10.1001/archinternmed.2009.289
17. Krutsch W, Lehmann J, Jansen P, et al. Prevention of severe knee injuries in men's elite football by implementing specific training modules. *Knee Surg Sports Traumatol Arthrosc*. 2020;28:519-527. https://doi.org/10.1007/s00167-019-05706-w
18. LaBella CR, Huxford MR, Grissom J, Kim K-Y, Peng J, Christoffel KK. 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;165:1033-1040. https://doi.org/10.1001/archpediatrics.2011.168
19. Logerstedt DS, Snyder-Mackler L, Ritter RC, et al. Knee stability and movement coordination impairments: knee ligament sprain. *J Orthop Sports Phys Ther*. 2010;40:A1-A37. https://doi.org/10.2519/jospt.2010.0303
20. Malliou P, Amoutzas K, Theodosiou A, et al. Proprioceptive training for learning downhill skiing. *Percept Mot Skills*. 2004;99:149-154. https://doi.org/10.2466/pms.99.1.149-154
21. Mandelbaum BR, Silvers HJ, Watanabe DS, 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;33:1003-1010. https://doi.org/10.1177/0363546504272261
22. Murray JJ, Renier CM, Ahern JJ, Elliott BA. Neuromuscular training availability and efficacy in preventing anterior cruciate ligament injury in high school sports: a retrospective cohort study. *Clin J Sport Med*. 2017;27:524-529. https://doi.org/10.1097/JSM.0000000000000398
23. Myklebust G, Engebretsen L, Brækken IH, Skjølberg A, Olsen OE, Bahr R. Prevention of anterior cruciate ligament injuries in female team handball players: a prospective intervention study over three seasons. *Clin J Sport Med*. 2003;13:71-78. https://doi.org/10.1097/00042752-200303000-00002
24. Olivares-Jabalera J, Fílter-Ruger A, Dos'Santos T, et al. Exercise-based training strategies to reduce the incidence or mitigate the risk factors of anterior cruciate ligament injury in adult football (soccer) players: a systematic review. *Int J Environ Res Public Health*. 2021;18:13351. https://doi.org/10.3390/ijerph182413351
25. Olsen O-E, Myklebust G, Engebretsen L, Holme I, Bahr R. Exercises to prevent lower limb injuries in youth sports: cluster randomised controlled trial. *BMJ*. 2005;330:449. https://doi.org/10.1136/bmj.38330.632801.8F
26. Omi Y, Sugimoto D, Kuriyama S, et al. Effect of hip-focused injury prevention training for anterior cruciate ligament injury reduction in female basketball players: a 12-year prospective intervention study. *Am J Sports Med*. 2018;46:852-861. https://doi.org/10.1177/0363546517749474
27. 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;42:502-505. https://doi.org/10.1136/bmj.a295
28. 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. *Arch Orthop Trauma Surg*. 2005;125:614-621. https://doi.org/10.1007/s00402-005-0793-7
29. Petushek EJ, Sugimoto D, Stoolmiller M, Smith G, Myer GD. Evidence-based best-practice guidelines for preventing anterior cruciate ligament injuries in young female athletes: a systematic review and meta-analysis. *Am J Sports Med*. 2019;47:1744-1753. https://doi.org/10.1177/0363546518782460
30. Pfeiffer R, Shea K, Roberts D, Grandstrand S, Bond L. 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;88:1769-1774. https://doi.org/10.2106/JBJS.E.00616

31. Phillips B, Ball C, Sackett D, et al. Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009). Available at: https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009. Accessed August 4, 2009.
32. Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol*. 2007;7:10. https://doi.org/10.1186/1471-2288-7-10
33. Silvers-Granelli HJ, Bizzini M, Arundale A, Mandelbaum BR, Snyder-Mackler L. Does the FIFA 11+ injury prevention program reduce the incidence of ACL injury in male soccer players? *Clin Orthop Relat Res*. 2017;475:2447-2455. https://doi.org/10.1007/s11999-017-5342-5
34. Verhagen AP, de Vet HCW, de Bie RA, et al. The Delphi list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol*. 1998;51:1235-1241. https://doi.org/10.1016/S0895-4356(98)00131-0
35. Waldén M, Atroshi I, Magnusson H, Wagner P, Hägglund M. Prevention of acute knee injuries in adolescent female football players: cluster randomised controlled trial. *BMJ*. 2012;344. https://doi.org/10.1136/bmj.e3042
36. Webster KE, Hewett TE. Meta-analysis of meta-analyses of anterior cruciate ligament injury reduction training programs. *J Orthop Res*. 2018;36:2696-2708. https://doi.org/10.1002/jor.24043
37. Wedderkopp N, Kaltoft M, Lundgaard B, Rosendahl M, Froberg K. Prevention of injuries in young female players in European team handball. A prospective intervention study. *Scand J Med Sci Sports*. 1999;9:41-47. https://doi.org/10.1111/j.1600-0838.1999.tb00205.x
38. Whalan M, Lovell R, McCunn R, Sampson JA. The incidence and burden of time loss injury in Australian men's sub-elite football (soccer): a single season prospective cohort study. *J Sci Med Sport*. 2019;22:42-47. https://doi.org/10.1016/j.jsams.2018.05.024

APPENDIX A

SEARCH STRATEGY FOR ALL DATABASES SEARCHED

PubMed

Search Strategy	Search Limits
(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

Search Strategy	Search Limits
(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

Search Strategy	Search Limits
((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

Search Strategy	Search Limits
((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

Search Strategy	Search Limits
((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

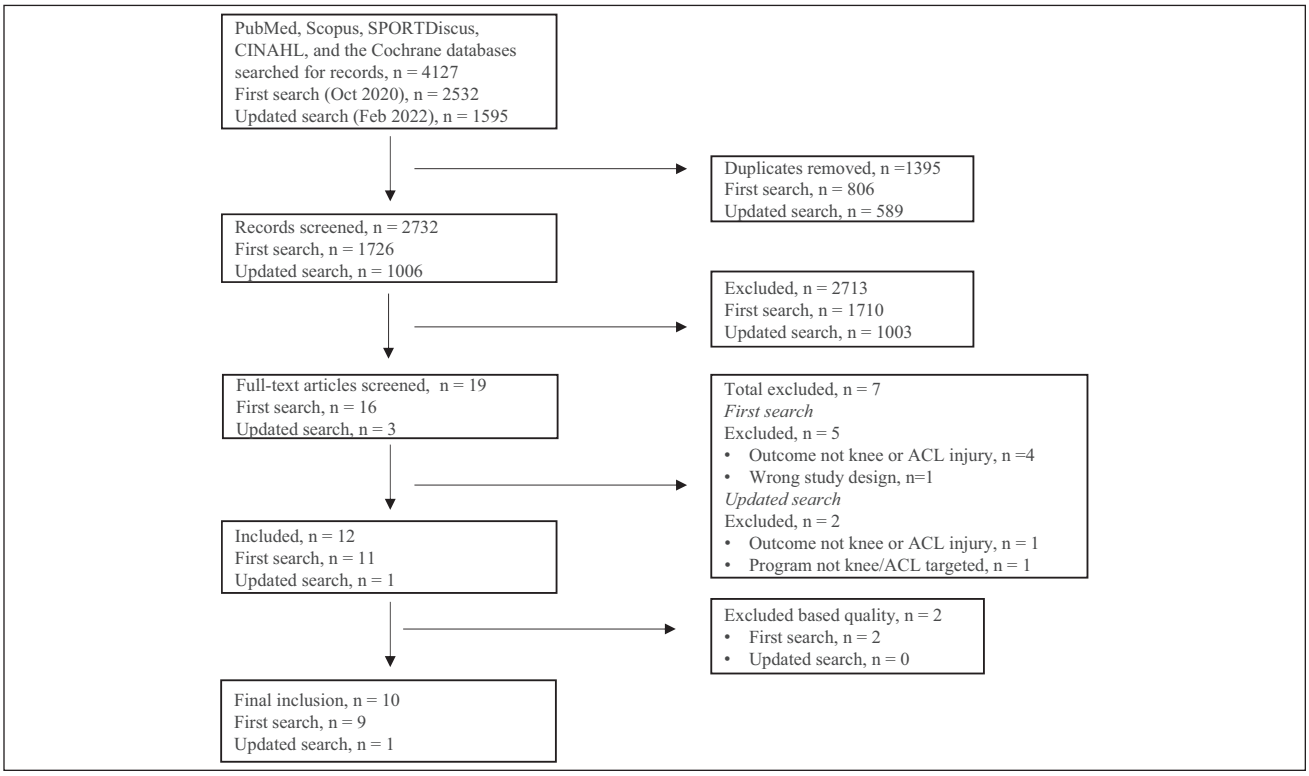
APPENDIX B

SEARCH DATES AND RESULTS

Database	Search 10/23/2020	Search 2/18/2022
PubMed	342	208
Scopus	1297	904
SportsDiscus	238	141
CINAHL	227	129
Cochrane Library	328	213
Cochrane reviews	68	36
Cochrane protocols	13	9
Trials	246	167
Clinical answers	1	1
Total	2532	1595
Total with duplicates removed	1742	1221

APPENDIX C

FLOWCHART OF LITERATURE REVIEW PROCESS



Abbreviation: ACL, anterior cruciate ligament.

APPENDIX D

INCLUDED ARTICLES

2022

Arundale AJH, Capin JJ, Zarzycki R, Snyder-Mackler L, Smith AH. Two year ACL reinjury rate of 2.5%: outcomes report of the men in a secondary ACL injury prevention program (ACL-Sports). *Int J Sports Phys Ther*. 2018;13:422-431. https://doi.org/10.26603/ijspt20180422

Huang YL, Jung J, Mulligan CMS, Oh J, Norcross MF. A majority of anterior cruciate ligament injuries can be prevented by injury prevention programs: a systematic review of randomized controlled trials and cluster–randomized controlled trials with meta-analysis. *Am J Sports Med*. 2020;48:1505-1515. https://doi.org/10.1177/0363546519870175

Johnson JL, Capin JJ, Arundale AJH, Zarzycki R, Smith AH, Snyder-Mackler L. A secondary injury prevention program may decrease contralateral anterior cruciate ligament injuries in female athletes: 2-year injury rates in the ACL-SPORTS randomized controlled trial. *J Orthop Sports Phys Ther*. 2020;50:523-530. https://doi.org/10.2519/jospt.2020.9407

Krutsch W, Lehmann J, Jansen P, et al. Prevention of severe knee injuries in men's elite football by implementing specific training modules. *Knee Surg Sports Traumatol Arthrosc*. 2020;28(2):519-527. https://doi.org/10.1007/s00167-019-05706-w

Murray JJ, Renier CM, Ahern JJ, Elliott BA. Neuromuscular training availability and efficacy in preventing anterior cruciate ligament injury in high school sports: a retrospective cohort study. *Clin J Sport Med*. 2017;27:524-529. https://doi.org/10.1097/JSM.0000000000000398

Olivares-Jabalera J, Fílter-Ruger A, Dos'Santos T, et al. Exercise-based training strategies to reduce the incidence or mitigate the risk factors of anterior cruciate ligament injury in adult football (soccer) players: a systematic review. *Int J Environ Res Public Health*. 2021;18:13351. https://doi.org/10.3390/ijerph182413351

Omi Y, Sugimoto D, Kuriyama S, et al. Effect of hip-focused injury prevention training for anterior cruciate ligament injury reduction in female basketball players: a 12-year prospective intervention study. *Am J Sports Med*. 2018;46:852-861. https://doi.org/10.1177/0363546517749474

Petushek EJ, Sugimoto D, Stoolmiller M, Smith G, Myer GD. Evidence-based best-practice guidelines for preventing anterior cruciate ligament injuries in young female athletes: a systematic review and meta-analysis. *Am J Sports Med*. 2019;47:1744-1753

Silvers-Granelli HJ, Bizzini M, Arundale A, Mandelbaum BR, Snyder-Mackler L. Does the FIFA 11+ injury prevention program reduce the incidence of ACL injury in male soccer players? *Clin Orthop Relat Res*. 2017;475:2447-2455. https://doi.org/10.1007/s11999-017-5342-5

Webster KE, Hewett TE. Meta-analysis of meta-analyses of anterior cruciate ligament injury reduction training programs. *J Orthop Res*. 2018;36:2696-2708. https://doi.org/10.1002/jor.24043

2018

Achenbach L, Krutsch V, Weber J, et al. Neuromuscular exercises prevent severe knee injury in adolescent team handball players. *Knee Surg Sports Traumatol Arthrosc*. 2018;26:1901-1908. https://doi.org/10.1007/s00167-017-4758-5

Alentorn-Geli E, Mendiguchía 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;22:16-25. https://doi.org/10.1007/s00167-013-2739-x

Caraffa A, Cerulli G, Projetti M, Aisa G, Rizzo A. Prevention of anterior cruciate ligament injuries in soccer. A prospective controlled study of proprioceptive training. *Knee Surg Sports Traumatol Arthrosc*. 1996;4:19-21. https://doi.org/10.1007/BF01565992

Donnell-Fink LA, Klara K, Collins JE, et al. Effectiveness of knee injury and anterior cruciate ligament tear prevention programs: a meta-analysis. *PLoS One*. 2015;10:e0144063. https://doi.org/10.1371/journal.pone.0144063

Gagnier JJ, Morgenstern H, 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;41:1952-1962. https://doi.org/10.1177/0363546512458227

Gilchrist J, Mandelbaum BR, Melancon H, et al. A randomized controlled trial to prevent noncontact anterior cruciate ligament injury in female collegiate soccer players. *Am J Sports Med*. 2008;36:1476-1483. https://doi.org/10.1177/0363546508318188

Grimm NL, Jacobs JC Jr, Kim J, Denney BS, Shea KG. Anterior cruciate ligament and knee injury prevention programs for soccer players: a systematic review and meta-analysis. *Am J Sports Med*. 2015;43:2049-2056. https://doi.org/10.1177/0363546514556737

Grimm NL, Shea KG, Leaver RW, Aoki SK, Carey JL. Efficacy and degree of bias in knee injury prevention studies: a systematic review of RCTs. *Clin Orthop Relat Res*. 2013;471:308-316. https://doi.org/10.1007/s11999-012-2565-3

Grindstaff TL, Hammill RR, Tuzson AE, 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;41:450-456.

Hägglund M, Atroshi I, Wagner P, Waldén 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;47:974-979. https://doi.org/10.1136/bjsports-2013-092644

Hewett TE, Lindenfeld TN, Riccobene JV, Noyes FR. The effect of neuromuscular training on the incidence of knee injury in female athletes. A prospective study. *Am J Sports Med*. 1999;27:699-706. https://doi.org/10.1177/03635465990270060301

APPENDIX D (CONTINUED)

Kiani A, Hellquist E, Ahlqvist K, Gedeborg R, Michaëlsson K, Byberg L. Prevention of soccer-related knee injuries in teenaged girls. *Arch Intern Med*. 2010;170:43-49. https://doi.org/10.1001/archinternmed.2009.289

Lewis DA, Kirkbride B, Vertullo CJ, Gordon L, Comans TA. Comparison of four alternative national universal anterior cruciate ligament injury prevention programme implementation strategies to reduce secondary future medical costs. *Br J Sports Med*. 2018;52:277-282. https://doi.org/10.1136/bjsports-2016-096667

Mandelbaum BR, Silvers HJ, Watanabe DS, 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;33:1003-1010. https://doi.org/10.1177/0363546504272261

Michaelidis M, Koumantakis GA. 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;15:200-210. https://doi.org/10.1016/j.ptsp.2013.12.002

Myer GD, Ford KR, Brent JL, Hewett TE. Differential neuromuscular training effects on ACL injury risk factors in "high-risk" versus "low-risk" athletes. *BMC Musculoskelet Disord*. 2007;8:39. https://doi.org/10.1186/1471-2474-8-39

Myer GD, Sugimoto D, Thomas S, Hewett TE. 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;41:203-215. https://doi.org/10.1177/0363546512460637

Myklebust G, Engebretsen L, Braekken IH, Skjølberg A, Olsen OE, Bahr R. Prevention of anterior cruciate ligament injuries in female team handball players: a prospective intervention study over three seasons. *Clin J Sport Med*. 2003;13:71-78. https://doi.org/10.1097/00042752-200303000-00002

Olsen OE, Myklebust G, Engebretsen L, Holme I, Bahr R. Exercises to prevent lower limb injuries in youth sports: cluster randomised controlled trial. *BMJ*. 2005;330:449. https://doi.org/10.1136/bmj.38330.632801.8F

Pfeiffer RP, Shea KG, Roberts D, Grandstrand S, Bond L. 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;88:1769-1774. https://doi.org/10.2106/JBJS.E.00616

Pfile KR, 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;27:1950-1958. https://doi.org/10.1111/sms.12828

Sadoghi P, von Keudell A, Vavken P. Effectiveness of anterior cruciate ligament injury prevention training programs. *J Bone Joint Surg Am*. 2012;94:769-776. https://doi.org/10.2106/JBJS.K.00467

Stevenson JH, Beattie CS, Schwartz JB, Busconi BD. 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;43:482-490. https://doi.org/10.1177/0363546514523388

Sugimoto D, Myer GD, Barber Foss KD, Hewett TE. Dosage effects of neuromuscular training intervention to reduce anterior cruciate ligament injuries in female athletes: meta- and sub-group analyses. *Sports Med*. 2014;44:551-562. https://doi.org/10.1007/s40279-013-0135-9

Sugimoto D, Myer GD, Barber Foss KD, Hewett TE. 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;49:282-289. https://doi.org/10.1136/bjsports-2014-093461

Sugimoto D, Myer GD, Barber Foss KD, Pepin MJ, Micheli LJ, Hewett TE. Critical components of neuromuscular training to reduce ACL injury risk in female athletes: meta-regression analysis. *Br J Sports Med*. 2016;50:1259-1266. https://doi.org/10.1136/bjsports-2015-095596

Sugimoto D, Myer GD, Bush HM, Klugman MF, Medina McKeon JM, Hewett TE. Compliance with neuromuscular training and anterior cruciate ligament injury risk reduction in female athletes: a meta-analysis. *J Athl Train*. 2012;47:714-723. https://doi.org/10.4085/1062-6050-47.6.10

Sugimoto D, Myer GD, McKeon JM, Hewett TE. 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;46:979-988. https://doi.org/10.1136/bjsports-2011-090895

Swart E, Redler L, Fabricant PD, Mandelbaum BR, Ahmad CS, Wang YC. Prevention and screening programs for anterior cruciate ligament injuries in young athletes: a cost-effectiveness analysis. *J Bone Joint Surg Am*. 2014;96:705-711. https://doi.org/10.2106/JBJS.M.00560

Taylor JB, Waxman JP, Richter SJ, Shultz SJ. Evaluation of the effectiveness of anterior cruciate ligament injury prevention programme training components: a systematic review and meta-analysis. *Br J Sports Med*. 2015;49:79-87. https://doi.org/10.1136/bjsports-2013-092358

van Beijsterveldt AM, Krist MR, Schmikli SL, 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:e2. https://doi.org/10.1136/ip.2010.027979

Waldén M, Atroshi I, Magnusson H, Wagner P, Hägglund M. Prevention of acute knee injuries in adolescent female football players: cluster randomised controlled trial. *BMJ*. 2012;344:e3042. https://doi.org/10.1136/bmj.e3042

Yoo JH, Lim BO, 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;18:824-830. https://doi.org/10.1007/s00167-009-0901-2

APPENDIX E

QUALITY-ASSESSMENT SCORES

Systematic Reviews and Meta-analyses: AMSTAR Checklist[a,b]

Study	1	2	3	4	5	6	7	8	9	10	11	Quality[b]
Huang et al[13]	X	X	X			X	X	X	X	X	X	9
Olivares-Jabalera et al[24]	X		X			X	X				X	5
Petushek et al[29]	X	X	X			X	X	X	X	X	X	9
Webster and Hewett[36]		X		X	X	X		X				5

Abbreviation: AMSTAR, A MeaSurement Tool to Assess systematic Reviews.
[a]*Yes/no. Items: 1, Was an a priori design provided? 2, Was there duplicate study selection and data extraction? 3, Was a comprehensive literature search performed? 4, Was the status of publication (ie, gray literature) used as an inclusion criterion? 5, Was a list of studies (included and excluded) provided? 6, Were the characteristics of the included studies provided? 7, Was the scientific quality of the included studies assessed and documented? 8, Was the scientific quality of the included studies used appropriately in formulating conclusions? 9, Were the methods used to combine the findings of studies appropriate? 10, Was the likelihood of publication bias assessed? 11, Was the conflict of interest included?*
[b]*What is your overall assessment of the methodological quality of this review? Quality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.*

Randomized Controlled Trials: Physiotherapy Evidence Database Scale (PEDro)[a]

Study	1	2	3	4	5	6	7	8	9	10	11	Quality[b]
Arundale et al[2]	X	X	X	X			X	X	X	X	X	9
Johnson et al[14]	X	X	X	X			X	X	X	X	X	9
Silvers-Granelli et al[33]	X	X		X				X	X	X	X	7

[a]*Items: 1, Eligibility criteria were specified; 2, Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received); 3, Allocation was concealed; 4, The groups were similar at baseline regarding the most important prognostic indicators; 5, There was blinding of all subjects; 6, There was blinding of all therapists who administered the therapy; 7, There was blinding of all assessors who measured at least 1 key outcome; 8, Measures of at least 1 key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9, 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 1 key outcome were analyzed by "intention to treat"; 10, The results of between-group statistical comparisons were reported for at least 1 key outcome; 11, The study provides both point measures and measures of variability for at least 1 key outcome.*
[b]*Quality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.*

Cohort Studies: Scottish Intercollegiate Guidelines Network Checklist (SIGN)[a]

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality[b]
Krutsch et al[17]	X	X	X		X		X								5
Murray et al[22]	X	X			N/A	N/A	X	N/A	X				X	X	6

[a]*Items: 1, The study addresses an appropriate and clearly focused question; 2, The 2 groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation; 3, The study indicates how many of the people asked to take part did so, in each of the groups being studied; 4, The likelihood that some eligible subjects might have the outcome at the time of enrollment is assessed and taken into account in the analysis; 5, What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed? 6, Comparison is made between full participants and those lost to follow-up, by exposure status; 7, The outcomes are clearly defined; 8, The assessment of outcome is made blind to exposure status (if the study is retrospective, this may not be applicable); 9, Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome; 10, The method of assessment of exposure is reliable; 11, Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable; 12, Exposure level or prognostic factor is assessed more than once; 13, The main potential confounders are identified and taken into account in the design and analysis; 14, Have confidence intervals been provided?*
[b]*How well was the study done to minimize the risk of bias or confounding? Quality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.*

APPENDIX F

LEVELS OF EVIDENCE TABLE[A]

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[b]	Systematic review of prospective cohort studies High-quality prospective cohort study[c]	Systematic review of high-quality diagnostic studies High-quality diagnostic study[d] with validation	Systematic review, high-quality cross-sectional studies High-quality cross-sectional study[e]	Systematic review of prospective cohort studies High-quality prospective cohort study
II	Systematic review of high-quality cohort studies High-quality cohort study[c] Outcomes study or ecological study Lower-quality RCT[f]	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.

[a]*Adapted from the work of Phillips et al.*[4] *See also* ***APPENDIX G.***

[b]*High quality includes RCTs with greater than 80% follow-up, blinding, and appropriate randomization procedures.*

[c]*High-quality cohort study includes greater than 80% follow-up.*

[d]*High-quality diagnostic study includes consistently applied reference standard and blinding.*

[e]*High-quality prevalence study is a cross-sectional study that uses a local and current random sample or censuses.*

[f]*Weaker diagnostic criteria and reference standards, improper randomization, no blinding, and less than 80% follow-up 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 (eg, 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): the study remains at the assigned level of evidence (eg, if the randomized clinical trial is rated high quality, its final assignment is level I). High quality should include the following:
  - a randomized clinical trial with greater than 80% follow-up, blinding, and appropriate randomization procedures
  - a cohort study with greater than 80% follow-up
  - a diagnostic study with consistently applied reference standard and blinding
  - a prevalence study, which 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 the 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).