Evidence report for management of anterior cruciate ligament rupture

Part 1 - Scoping

Prepared by EBSCO Information Services

March 18, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

Using an established, structured template that delineates key elements for scoping (i.e., the population, interventions, and key outcomes to consider), we collaboratively agreed with UKSH on the scope of the present evidence report. Scoping was completed on March 20, 2019.

Results – Criteria Selection for Critical Appraisal

Population:

Inclusion criteria

Adults with anterior cruciate ligament rupture (based on history, clinical presentation, magnetic resonance imaging, or arthroscopy)

Exclusion criteria

None

Intervention and Comparator:

ACL reconstruction surgery

Surgical repair of the ACL tendon, which is followed by a rehabilitation program

Conservative (non-surgical) treatment

Includes a broad array of options, including physiotherapy/physical therapy and/or rehabilitation programs consisting of strength and range-of-motion exercises, neuromuscular training, bracing, casting, taping, electrotherapy, muscle stimulation interventions, graded return to exercise and activities, and arthroscopy

Outcomes:

FAQ 1: What does the treatment involve?

Include a description of the treatment or procedure. Include length of hospital stay if relevant for surgical option (ambulatory vs in-hospital surgery).

Descriptive responses are acceptable, and this does not involve systematic evidence searches, critical appraisal, or evidence synthesis.

FAQ 2: Will my symptoms get better?

Outcomes of interest are patient-relevant outcomes, such as pain or function. If composite scales are reported that incorporate different domains of patient-relevant outcomes (e.g., combining subscales that assess pain and function), outcomes on the subscales may be reported if available. Surrogate outcomes (e.g., as assessed by an arthrometer) will not be considered unless no patient-relevant outcomes are available.

FAQ 3: Will I need to get surgery later?

The outcome of interest is reoperation rate in the surgical treatment group or eventual need for surgery (delayed surgery) in the conservative treatment group.

FAQ 4: When will I recover?

The outcomes of interest are return to usual activities and return to sports, which will be reported separately if possible. We will also provide descriptive summaries for recovery-related concepts such as return to work and return to driving if these outcomes are not addressed in systematic reviews of the available evidence. Sport-specific evidence (e.g., a study of football players) will not be included as this may not be generalizable and the effort to seek evidence for each sport is beyond the scope.

FAQ 5: What are the risks?

Outcomes of interest include infection, donor site morbidity, failure of graft (including re-rupture), and venous thromboembolic events.

FAQ 6: What are the side effects?

Outcomes of interest include postsurgical pain and swelling in the surgery group.

If not reported in the evidence systematically identified for other FAQs, then descriptive responses are acceptable, which will not involve systematic evidence searches, critical appraisal, or evidence synthesis.

Evidence report for management of anterior cruciate ligament rupture

Part 2 - Search and Selection

Prepared by EBSCO Information Services

March 25, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

First-round searching will consist of searching DynaMed Plus summaries pertinent to the topic. The search starts with DynaMed Plus because DynaMed Plus content is based on a thorough, systematic search and active literature surveillance system.

> Systematic literature surveillance (SLS) has been a cornerstone of creating DynaMed content since its inception. Currently, the SLS team works closely with members of McMaster University's Department of Health Research Methods, Evidence, and Impact to define and refine optimal search strategies, utilizing search terms for methodology and for clinical concepts (especially diagnosis and treatment) for each journal. These filters for PubMed searches are derived from PubMed Clinical Queries, McMaster University Hedges system, and DynaMed search filters and were found to capture >95% of relevant valid articles for use in DynaMed.[1]
> [1]Alper BS, Iorio A. Optimising search filters for active literature surveillance: a concordance study. Global Evidence Summit. Cape Town, South Africa; September 2017.
>
> The SLS team, in collaboration with McMaster University, continually evaluates and improves these filters to keep abreast of the ever-changing medical literature landscape. PubMed searches are performed daily. Each article is assessed by an external screener for clinical relevance, then reviewed by internal staff for both clinical relevance and validity. Any disagreements are settled by the Deputy Editor of the SLS team.
> In addition, the SLS team continually monitors the Journal source list against the list of journals catalogued in MEDLINE and existing DynaMed content to determine the set of journals that provide the highest yield for valid, clinically relevant content. As of November 2018, 507 Journals are systematically searched (see http://dynamed.com/home/content/content-sources). The journal selection threshold leads to routine adjustments to the number of journals selected.

Second-round searching will involve PubMed/MEDLINE® searches for intervention-specific systematic reviews that are more recent than those identified in first-round searching.

Third-round searching will involve original study tracing from systematic reviews, guidelines or other relevant sources. This may be done to identify additional evidence sources if the results from the first two rounds of searching are insufficient.

Fourth-round searching will involve searches for original evidence reports. Such searching will be limited to areas considered insufficiently addressed by earlier searches, such as focused concepts published after search dates in systematic reviews.

Additional selective searching, such as tracing citations from articles found or seeking related articles, may be done for additional concepts discovered.

Additional evidence updates may also be added continuously from feedback from any source.

FAQ Summary

Results

First-round searching – DynaMed Plus:

DynaMed Plus subsection	Relevant for FAQ(s)	Number of article citations	Number of unique references included
Management of anterior cruciate ligament injury topic, Initial management in acute phase section (March 25, 2019)	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	3	0
Management of anterior cruciate ligament injury topic, Nonoperative management (rehabilitation) section (March 25, 2019)	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	6	0
Management of anterior cruciate ligament injury topic, Surgical reconstruction and repair section, ACL reconstruction using tissue grafts subsection, Early vs. late reconstruction subsection (March 25, 2019)	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	15	3 (Frobell 2010, Frobell 2013, Monk 2016)*
Management of anterior cruciate ligament injury topic, Follow-up section (March 25, 2019)	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	2	0

* Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review that includes a single randomized trial (the KANON trial). We refer to the combination of these sources as KANON 2010 in Parts 3 and beyond.

Second-round searching – searches for intervention-specific systematic reviews:

Database	Search string	Relevant for FAQ(s)	Number of search results	Number of references included
PubMed March 25, 2019	(ACL reconstruction OR anterior cruciate ligament reconstruction OR ACL surgery OR anterior cruciate ligament surgery) AND (complication[tiab] OR adverse[tiab] OR infection[tiab] OR rupture[tiab] OR donor[tiab] OR failure[tiab] OR venous thrombo*[tiab] OR deep venous thrombo*[tiab] OR pulmonary emboli*[tiab]) AND systematic[sb] AND (2013/01/01[PDAT] : 3000/12/31[PDAT])	FAQ3, FAQ5, FAQ6	124	(Crawford 2013, DiSilvestro 2016*, Janssen 2016, Kim 2014, Monk 2016†, Nawasreh 2018)

* DiSilvestro 2016 pertains to FAQ4, but it was retrieved during a search pertaining to FAQs 3, 5, and 6. We therefore do not list FAQ4 in the "Relevant for FAQ(s)" column above, but we count this search in the Part 5 recap of Part 2.
† Already captured in first-round searching. See note in first-round searching regarding referring to Monk 2016 as KANON 2010 in Parts 3 and beyond.

Third-round searching – original study tracing from systematic reviews:

Source	Tracing	Relevant for FAQ(s)	Number of search results	Number of references included
Not applicable				

Fourth-round searching – searches for original evidence reports:

Database	Search string	Relevant for FAQ(s)	Number of search results	Number of references included
PubMed March 25, 2019	(ACL reconstruction OR anterior cruciate ligament reconstruction OR ACL surgery OR anterior cruciate ligament surgery) AND (conservative OR non-surg* OR nonsurg* OR non-operat* or nonoperat* OR non-invasive OR noninvasive OR delay*) AND randomized controlled trial[ptyp] AND (2015/12/01[PDAT]:3000/12/31[PDAT])	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	15	1 (Tsoukas 2016)
PubMed April 08, 2019	(ACL reconstruction OR anterior cruciate ligament reconstruction OR ACL surgery OR anterior cruciate ligament surgery) AND return to work[tiab]	FAQ4	35	5 (Groot 2017, Jenny 2016, Minzlaff 2018, Obermeier 2018, Tiftikci 2015)*

* This is a search beyond specified scoping added to investigate descriptive summaries concerning time to return to work.

Evidence report for management of anterior cruciate ligament rupture

Part 3 - Critical Appraisal of Evidence Reports

Prepared by EBSCO Information Services

March 25, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

For each study selected for critical appraisal, we assessed for criteria needed for Level 1 [likely reliable] evidence ratings in DynaMed's Levels of Evidence criteria in which evidence quality is labeled in 1 of 3 levels:

- **(level 1 [likely reliable] evidence)** for studies with clinical outcomes and minimal risk of bias;
- **(level 2 [mid-level] evidence)** for studies with clinical outcomes and significant methodological or statistical limitations; and
- **(level 3 [lacking direct] evidence)** for reports that do not include scientific analysis of clinical outcomes or for study types that do not include comparisons between groups.
-

The specific concepts we critically assessed are fully mapped to cover all the criteria used in GRADE. We summarized key concerns identified that reduce the certainty of evidence in categories used for GRADE methods (i.e., risks of bias, indirectness, imprecision, inconsistency, and other considerations if relevant). In the study-level summaries inconsistency assessment was applied to consistency of within-study results – this applies to consistency across related outcomes for both original studies and for systematic reviews, and also applies to consistency across studies when applied to systematic reviews.

FAQ Summary

Results

Characteristics and Results of Critically Appraised Studies/Sources

CRAWFORD 2013
Crawford SN, Waterman BR, Lubowitz JH. Long-term failure of anterior cruciate ligament reconstruction. Arthroscopy. 2013 Sep;29(9):1566-71. Epub 2013 Jun 29. PubMed

Relevant to FAQ3, FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients who had ACL reconstruction
- **Intervention:** intra-articular allograft or autograft ACL reconstruction
- **Comparison:** Not applicable

- **Study inclusion criteria:**
  - English-language publication
  - ≥ 10-year follow-up
  - reported re-rupture rate and objective International Knee Documentation Committee grade and/or stability examination at final follow-up
  - conducted between 1980 and 2012

- **Number of studies:** 14
- **Number of participants:** 2,782
- **Duration of follow-up:** ≥ 10 years
  - range of 10.2 to 15.3 years

- **Certainty: Low**
  - **Certainty by outcome: Low for all outcomes**
  - **Risk of bias:** Serious concern
    - limitations of some studies included
      - high loss to follow-up
      - possible missed treatment failures (treatment failures not classified as such because failure rate did not account for functional or subjective outcome measures)
      - lack of blinding for instrumented and manual laxity testing for some studies, which may have introduced detection bias
  - **Imprecision:** No serious concern
  - **Indirectness:** No serious concern
  - **Inconsistency:** Serious concern
    - wide range of failure rates across studies for all 3 failure rate outcomes
  - **Other considerations:** heterogeneity in patient characteristics, surgical techniques, and tissue graft

- **Results:**
  - pooled failure rates at > 10 years follow-up
    - 6.2% (173/2,782) ACL graft rupture rate

        - range, 0% to 13.4% across studies
    - 10.3% (158/1,532) clinical failure rate
        - based on poor clinical outcomes as indicated by 1 of the following established objective clinical measures (in cases exclusive of graft rupture)
            - overall IKDC objective score of C or D
            - IKDC grade C or D pivot shift (ie, > 2 + or pivot shift)
            - IKDC grade C or D Lachman examination or KT arthrometer measurement (ie, >5 mm)
            - identified grossly abnormal stability examination without IKDC scoring available
        - range, 1.9% to 25.6%
    - 11.9% (331/2,782) overall cumulative ACL failure rate
        - based on sum of ACL graft rupture rate plus clinical failure rate
        - range, 3.2% to 29.9%

DISILVESTRO 2016

DiSilvestro KJ, Santoro AJ, Tjoumakaris FP, Levicoff EA, Freedman KB. When Can I Drive After Orthopaedic Surgery? A Systematic Review. Clin Orthop Relat Res. 2016 Dec;474(12):2557-2570. Epub 2016 Aug 4. PubMed

Relevant to FAQ4

- **Study design:** systematic review of observational studies
- **Population:** patients undergoing ACL reconstruction
    - This systematic review considered many other orthopedic surgeries, but these are beyond the scope of this evidence review, so we only consider the studies on ACL reconstruction here
- **Intervention:** ACL reconstruction
- **Comparison:** not applicable
    - The studies included used healthy controls to inform braking response times, but there was no 'comparison'

- **Study inclusion criteria:**
    - One of 20 most common orthopedic surgeries
        - This systematic review considered many other orthopedic surgeries, but these are beyond the scope of this evidence review, so we only consider the studies on ACL reconstruction here
    - Had to report either observer-reported outcomes (objective measurements pertaining to driver function, such as brake reaction time) or survey data about return to driving
    - Restricted to English language
    - Search period was from inception to July 2015

- **Number of studies:** 2
    - This systematic review considered many other orthopedic surgeries, but these are beyond the scope of this evidence review, so we only consider the studies on ACL reconstruction here
- **Number of participants:** 87

- **Duration of follow-up:** 8 to 10 weeks
    - Following preoperative assessments, both studies had postoperative assessments every 2 weeks for a total of 8 weeks in one study and 10 weeks in the other.

- **Certainty and results:**

Reference (no. of patients)*	Results	Recommendations about driving	Certainty (reasons for downgrade)†
Nguyen et al. 2000 (73)	R BRT: preoperative, 738 ms; 6 weeks postoperative, 733 ms; L BRT: preoperative, 662 ms; 2 weeks, 660 ms	R: 6 weeks; L: 2 weeks	Very low (very serious concern for indirectness, serious concern for imprecision)
Gotlin et al. 2000 (14)	BRT reached the 50th percentile of national BRT data 4 weeks postoperative	R: 4 to 6 weeks	Very low (very serious concern for indirectness, serious concern for imprecision)

BRT, braking reaction time; L, left; ms, milliseconds; R, right
* For both studies, sample size is for ACL reconstruction cohort. Both studies are also reported to have used "preoperative, healthy volunteers" for comparison, but further details (including sample size) are not provided.
† For both studies, Very serious concern for indirectness results from braking reaction time being a surrogate for return to driving, and as the authors note, such measures "are only one aspect of safe driving, and do not include other crucial factors such as the use of scheduled narcotics". Serious concern for imprecision results from total sample size of 87 patients undergoing ACL reconstruction across the 2 studies.

GROOT 2017
Groot JA, Jonkers FJ, Kievit AJ, Kuijer PP, Hoozemans MJ. Beneficial and limiting factors for return to work following anterior cruciate ligament reconstruction: a retrospective cohort study. Arch Orthop Trauma Surg. 2017 Feb;137(2):155-166. doi: 10.1007/s00402-016-2594-6. Epub 2016 Nov 21. PubMed

Relevant to FAQ4

- **Study design:** observational study
    - retrospective cohort study
- **Population:** patients undergoing ACL reconstruction
- **Intervention:** ACL reconstruction
    - single bundle semitendinosus-gracilis autograft
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - consecutively referred
    - aged 18–65 years
    - underwent primary ACL reconstruction (single bundle semitendinosus-gracilis autograft)
    - surgery at Noordwest Ziekenhuisgroep, Alkmaar, the Netherlands
    - surgery between April 1st 2012 and April 1st 2014
    - part of the working population
    - could not have concomitant collateral ligament or posterior cruciate ligament injury

- **Number of studies:** not applicable
- **Number of participants:** 89
    - 125 patients included, but 36 were not members of working population
- **Certainty:** not applicable
    - **Other considerations:** certainty not assessed; this source was sought for basic concepts (e.g., ranges), with no expectation for precision or 'accuracy' for this particular outcome (return to work)

- **Results:**
    - median time to return fully to work 78 days (IQR 49 to 112 days)
    - 82 patients (92%) had returned fully to work, 7 (8%) had returned, but not fully
    - demands placed on the knee as a result of the work associated with time to return to work

JANSSEN 2016

Janssen RP, Reijman M, Janssen DM, van Mourik JB. Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review. World J Orthop. 2016 Sep 18;7(9):604-17. eCollection 2016 Sep 18. PubMed

Relevant to FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients having ACL reconstruction
    - ACL reconstruction involving any arthroscopic surgical method of primary or revision intra-articular using any type of graft
- **Intervention:** ACL reconstruction
- **Comparison:** Not applicable

- **Study inclusion criteria:**
    - included all study designs that evaluated vascular and thromboembolic complications following ACL reconstruction

- **Number of studies:** 47
    - 2 randomized trials
    - 8 prospective cohort studies
    - 9 retrospective cohort studies
    - 28 case reports
- **Number of participants:** Not reported
- **Duration of follow-up:** <1 year in 9 studies, unclear in 1 study, and ≥1 year in 1 study
    - Based on Table 2, and only considers the 11 studies that contributed to estimates for venous thrombotic events (estimate for pseudoaneurysm is based on case series)

- **Certainty: Varies by outcome**
    - **Certainty by outcome:** Moderate for symptomatic deep venous thrombosis and pulmonary embolism; Very low for arterial pseudoaneurysm outcome
    - **Risk of bias: Varies by outcome**

        - For symptomatic deep venous thrombosis and pulmonary embolism, no serious concern when limiting to studies where thromboprophylaxis was reported *not* to be given, and serious concern if using all available data (irrespective of whether thromboprophylaxis was used)
            - the 11 studies contributing to estimates of venous thrombotic event rates were either cohort studies (5 prospective, 4 retrospective) or randomized trials (2)
                - 3 studies judged by authors as being at low risk of bias (totaling 443 patients) contributed to estimates of any deep venous thrombosis and pulmonary embolism; 2 studies judged by authors as being at low risk of bias (totaling 212 patients) contributed to estimate of symptomatic deep venous thrombosis. We concern ourselves mainly with symptomatic deep venous thrombosis and pulmonary embolism given their clinical relevance (i.e., the incidence of *any* deep venous thrombosis is of unclear clinical relevance)
                    - For estimates from studies that reported thromboprophylaxis *not* being given, data from the low-risk-of-bias studies comprised a majority of the evidence and/or estimates from considering only the low-risk-of-bias studies yielded estimates comparable to those using all the evidence
                    - For estimates from all studies (irrespective of whether thromboprophylaxis was given), the data from the low-risk-of-bias studies contribute only a small minority of the evidence, and estimates from considering only the low-risk-of-bias studies yield inconsistent estimates compared to using all the evidence (though we note this may be due to all 3 low-risk-of-bias studies being studies reporting thromboprophylaxis *not* being used)
        - Very serious concern for arterial pseudoaneurysm outcome
            - based on one case series of 299 patients
    - **Imprecision:** Serious concern for symptomatic deep venous thrombosis and pulmonary embolism estimates from studies where thromboprophylaxis was reported as *not* being given; No serious concern for other outcomes
    - **Indirectness:** No serious concern
    - **Inconsistency:** No serious concern

- **Results:**
    - incidence of arterial pseudoaneurysm 0.3% (based on 1 case series of 299 patients)
    - incidence of thromboembolic complications following ACL reconstruction, irrespective of whether thromboprophylaxis was used (reported as not used in 7 studies, used in 1 study, and not reported in 3 studies, including the 2 studies that were by far the largest)
        - 0.6% (182/30368) for all deep venous thrombosis (11 studies)
        - 0.3% (48/14506) for symptomatic deep venous thrombosis (5 studies)
        - 0.1% (42/30216) for pulmonary embolism (10 studies)

        - proportion of data from studies judged to be at low risk of bias for symptomatic deep venous thrombosis and pulmonary embolism: 1.46% to 1.47%, respectively
    - incidence of thromboembolic complications following ACL reconstruction, among studies where thromboprophylaxis was reported as *not* being given
        - 9.7% (83/856) for all deep venous thrombosis (7 studies)
            - If including data from one study where patients received thromboprophylaxis while in the hospital, but not after discharge from the hospital, this estimate becomes 12.0% (111/924; 8 studies)
        - 2.1% (5/235) for symptomatic deep venous thrombosis (3 studies)
            - proportion of data from studies judged to be at low risk of bias: 90%
            - estimate if restricting to low-risk-of-bias studies: 2.4% (5/212)
        - 0.1% (1/704) for pulmonary embolism (6 studies)
            - proportion of data from studies judged to be at low risk of bias: 63%
            - estimate if restricting to low-risk-of-bias studies: 0.2% (1/443)
            - If including data from one study where patients received thromboprophylaxis while in the hospital, but not after discharge from the hospital, this estimate remains 0.1%, but the denominator changes (1/772; 7 studies)

JENNY 2016

Jenny JY, Clement X. Patient-based decision for resuming activity after ACL reconstruction: a single-centre experience. Eur J Orthop Surg Traumatol. 2016 Dec;26(8):929-935. Epub 2016 Sep 26. PubMed

Relevant to FAQ4

- **Study design:** observational study
    - retrospective cohort study
- **Population:** patients undergoing ACL reconstruction
- **Intervention:** ACL reconstruction
    - semitendinosus graft
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - consecutively referred
    - surgery for primary ACL repair between 2007 and 2012 at a single center
    - must have been practicing recreational or professional sports prior to reconstruction

- **Number of studies:** not applicable
- **Number of participants:** 72

- **Certainty:** not applicable
    - **Other considerations:** certainty not assessed; this source was sought for basic concepts (e.g., ranges), with no expectation for precision or 'accuracy' for this particular outcome (return to work)

- **Results:**
    - return to work in 69 (96%) after a mean delay of 2.3 ± 0.8 months (50% returned within 2 months)

- delay not different for “sedentary” (2.0 months) versus “strenuous” (2.4 months) work

KIM 2014
Kim SJ, Postigo R, Koo S, Kim JH. Infection after arthroscopic anterior cruciate ligament reconstruction. Orthopedics. 2014 Jul;37(7):477-84. PubMed

Relevant to FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients who had ACL reconstruction
- **Intervention:** ACL reconstruction
- **Comparison:** not applicable

- **Study inclusion criteria:**
  - published in English
  - reported rates of septic arthritis infection
  - published between January 1, 1950 and November 1, 2012

- **Number of studies:** 14
- **Number of participants:** not reported
  - number of knees reported (22,836), not number of patients
- **Duration of follow-up:** 53.6 months mean duration after ACL reconstruction surgery
  - range 4 to 218 months

- **Certainty: Moderate**
  - **Certainty by outcome:** Not applicable
  - **Risk of bias:** No serious concern
  - **Imprecision:** No serious concern
  - **Indirectness:** No serious concern
  - **Inconsistency:** Serious concern
    - The incidence across included studies ranged from a low of 0.23% to a high of 1.7%. Although overall these rates are low, a rate of slightly more than 2/1000 and a rate of slightly less than 2/100 for a potentially-serious outcome like septic arthritis seems important enough to reduce our certainty in the overall estimate.

- **Results:**
  - 0.5% (121/22,836) pooled risk of postoperative septic arthritis in analysis of 14 studies
    - mean interval between ACL reconstruction and presentation for examination for infection was 19.1 days (range of 2 to 450 days, but we note the 450 days is an outlier and septic arthritis resulting from ACL reconstruction is considered a postoperative complication, so a presentation 450 days after ACL reconstruction does not make sense in terms of being causally-linked to the index surgery)

KANON 2010

This reference header represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations below). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, we grouped these three references and refer to the combination of these sources as KANON 2010.

Frobell RB, Roos EM, Roos HP, Ranstam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. N Engl J Med. 2010 Jul 22;363(4):331-42. Erratum in: N Engl J Med. 2010 Aug 26;363(9):893. PubMed

Frobell RB, Roos HP, Roos EM, Roemer FW, Ranstam J, Lohmander LS. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. BMJ. 2013 Jan 24;346:f232. PubMed

Monk AP, Davies LJ, Hopewell S, Harris K, Beard DJ, Price AJ. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. Cochrane Database Syst Rev. 2016 Apr 3;4:CD011166. PubMed

Relevant to FAQ2, FAQ3, FAQ4

- **Study design:** randomized trial
- **Population:** patients with ACL rupture
- **Intervention:** structured rehabilitation plus early ACL reconstruction
- **Comparison:** structured rehabilitation with the option of later ACL reconstruction if needed

- **Study inclusion criteria:**
  - aged 18 to 35 years old
  - had rotational trauma to previously uninjured knee within previous 4 weeks
  - evidence of ACL insufficiency on clinical exam
  - score of 5 to 9 on Tegner Activity Scale before injury (range is 1 to 10, with 5 indicating participation in recreational sports and 9 indicating participation in competitive, nonprofessional sports)
- **Number of studies:** 1
- **Number of participants:** 141
  - 141 were originally randomized, but due to subsequent exclusions (consistent with inclusion/exclusion criteria) as a result of MRI findings or extensive meniscal fixation or intact ACL at surgery, the study population amounted to 121 patients (62 in structured rehabilitation plus early ACL reconstruction, 59 rehabilitation and option of later ACL reconstruction if needed)
- **Duration of follow-up:** 5 years

- **Certainty: Low**
  - **Certainty by outcome:** Low for all outcomes
  - **Risk of bias:** serious concern
    - no blinding

        - high cross-over from conservative treatment control group to surgery (39% [23/59] at 2 years; 51% [30/59] at 5 years); however, we did not add second risk of bias downgrade due to these cross-overs because as-treated analysis found no significant differences at 2 years or 5 years in patient-reported outcomes among patients treated with rehabilitation plus early ACL reconstruction, rehabilitation plus delayed ACL reconstruction, and rehabilitation alone; additionally, the crossover actually serves to answer the clinically-relevant question of whether people can pursue rehab alone with the option for delayed surgery if necessary, and from this perspective, the crossovers in this trial indicate that by providing rehab alone, 61% of patients can avoid surgery at 2 years and 49% at 5 years, without compromising results.
    - **Imprecision:** serious concern
        - evidence for all outcomes was downgraded due to imprecision because single small trial
    - **Indirectness:** no serious concern
    - **Inconsistency:** no serious concern
    - **Other considerations:**
        - The 2-year results of KANON trial were published in 2010 (Frobell 2010 N Engl J Med) and the 5-year results were published in 2013 (Frobell 2013 BMJ). To consolidate all information from this trial into a single summary with data reported in a standard format, outcome data from both trial publications have been added to this summary. In addition, we consulted a Cochrane review which included only the KANON trial (Monk 2016), but no further information was extracted from it for this summary.

- **Results and certainty:**

Patient-reported outcomes comparing ACL reconstruction vs. conservative therapy at 2 and 5 years*

Outcome	Early ACL reconstruction	Delayed optional ACL reconstruction	Mean difference (95% CI)
At 2 years			
Number of patients	62	59	-
Mean (95% CI) follow-up after randomization (months)	25 (24 to 25)	25 (25 to 25)	Not reported
Mean change in $KOOS_4$ score† from baseline (95% CI)‡	39 (35 to 44)	39 (35 to 44)	0.18 (95% CI -6.5 to 6.8)
Mean (95% CI) KOOS§			
$KOOS_4$ (from Figure 2A)	76 (71 to 81)	76 (71 to 81)	Not reported
Pain	87 (83 to 91)	88 (84 to 92)	Not reported
Symptoms	79 (74 to 84)	83 (78 to 88)	Not reported
Activities of daily living	94 (91 to 97)	95 (92 to 97)	Not reported
Sport and recreation	72 (65 to 79)	71 (64 to 79)	Not reported
Knee related QoL	67 (61 to 73)	63 (57 to 69)	Not reported
Mean (95% CI) SF-36¶			
Physical component	82 (77 to 87)	78 (73 to 83)	Not reported
Mental component	88 (85 to 92)	84 (80 to 88)	Not reported

No (%) active at pre-injury Tegner activity scale level**	27 (44)	21 (36)	Not reported
At 5 years			
Number of patients	61	59	-
Mean (95% CI) follow-up after randomization (months)	60 (59 to 61)	59 (57 to 60)	1.2 (−0.6 to 3.0)
Mean change in $KOOS_4$ score† from baseline (95% CI)‡	42.9 (CI not reported)	44.9 (CI not reported)	-2 (95% CI -8.5 to 4.5)
Mean (95% CI) KOOS§			
$KOOS_4$	80 (76 to 84)	82 (77 to 86)	−1.5 (−7.4 to 4.4)
Pain	91 (88 to 94)	91 (88 to 94)	−0.3 (−4.6 to 4.0)
Symptoms	83 (78 to 87)	87 (83 to 91)	−4.4 (−10.2 to 1.4)
Activities of daily living	95 (93 to 98)	97 (95 to 99)	−1.5 (−4.3 to 1.4)
Sport and recreation	76 (70 to 82)	79 (73 to 86)	−3.3 (−11.7 to 5.2)
Knee related QoL	71 (66 to 76)	69 (63 to 75)	1.8 (−6.2 to 9.8)
Mean (95% CI) SF-36¶			
Physical component	85 (81 to 89)	84 (80 to 89)	0.9 (−4.9 to 6.7)
Mental component	87 (84 to 91)	85 (84 to 91)	2.8 (−2.7 to 8.3)
No (%) active at pre-injury Tegner activity scale level**	14 (23)	12 (20)	2.6 (−12.4 to 17.6)††
Median Tegner scores (IQR)	4 (2.5 to 7)	4 (2 to 7)	0.1 (−0.8 to 1.1)

ACL=anterior cruciate ligament; CI = confidence interval; IQR = interquartile range; KOOS=knee injury and osteoarthritis outcome score; QOL=quality of life; SF-36 Medical Outcomes Study 36-Item Short-Form Health Survey

* 2-year results were extracted directly from Frobell 2010 NEJM KANON trial publication and 5-year results were extracted directly from BMJ 2013 Frobell KANON trial publication

† KOOS4 includes four KOOS subscales: pain, symptoms, function in sports and recreation, and knee-related quality of life. Scores range from 0 to 100, with higher scores indicating better results.

‡ adjusted for baseline $KOOS_4$ score

§ KOOS ranges from 0 to 100, with higher scores indicating better results.

¶ Scores range from 0 to 100, with higher scores indicating better results.

** Patients with score at follow-up (2-year or 5-years) that was same as or higher (ie, better) than pre-injury score on Tegner scale, which assesses activity level with specific emphasis on knee

††Values shown, including 95% confidence interval, are for the percentage

- Graft rupture rates in as-treated analysis including only patients who had ACL reconstruction (either early or delayed) were:
    - 4.8% (4/84) at 2-years – Moderate Certainty with downgrade for imprecision
        - 61 had early ACL reconstruction, 23 had delayed ACL reconstruction
    - 4.4% (4/91) at 5- years – Moderate Certainty with downgrade for imprecision
        - 7 more patients had delayed ACL reconstruction between the 2- and 5-year point (total of 30 receiving delayed ACL reconstruction)
    - Of 4 patients with graft rupture, 2 had revision surgery, and 2 declined revision surgery
- There were 5 donor site problems among the 84 patients who received surgery within 2 years (not reported at 5-year point)
    - The specific donor site issue for these 5 events was not reported, and although it is not explicitly reported whether each donor site problem was in a unique individual (as opposed to >1 donor site problem occurring in the same individual), it is not clear how a given individual could have >1 donor site problem, so we consider the number of events to be equal to the number of patients who had an event (additionally, even if a given

patient could have had >1 donor site problem, treating the number of events as the number of patients with an event would still yield a conservative estimate, because it would represent the highest possible rate of donor site problems)
        - This yields an estimate for donor site morbidity of 6.0% (5/84) within 2 years and provides Moderate certainty evidence (downgrade due to imprecision)
- The proportion of patients randomly assigned to the control group who had delayed ACL reconstruction was 39% (23/59) at 2-year follow-up and 51% (30/59) at 5-year follow-up. Thus, 61% of patients avoided surgery at 2 years and 49% avoided surgery at 5 years, without compromising outcomes in intention-to-treat or as-treated analyses. This provides Moderate certainty evidence for eventual need for surgery among patients who initially pursue conservative (non-surgical) treatment, with downgrade due to imprecision.

MINZLAFF 2018
Minzlaff P, Heidt T, Feucht MJ, Plath JE, Hinterwimmer S, Imhoff AB, Saier T. Patient satisfaction with health is substantially improved following ACL reconstruction. Knee Surg Sports Traumatol Arthrosc. 2018 Feb;26(2):582-588. doi: 10.1007/s00167-017-4623-6. Epub 2017 Jun 26. PubMed

Relevant to FAQ4

- **Study design:** observational study
    - prospective cohort study
- **Population:** patients undergoing ACL reconstruction
- **Intervention:** ACL reconstruction
    - anatomic single-bundle technique with autologous hamstring grafts was performed in all patients
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - isolated and symptomatic full ACL tear
    - aged 18–60 years
    - had to be working on a regular basis before the injury
    - did not receive income from or plan to file for workers' compensation
    - treated between 2011 and 2013 in a single specialized orthopedic sports medicine unit
    - anatomic single-bundle technique with autologous hamstring grafts was performed in all patients
    - no other procedures permitted

- **Number of studies:** not applicable
- **Number of participants:** 60
    - 69 originally eligible, but 6 lost to follow-up, 2 suffered traumatic re-rupture, and 1 required removal of a meniscal ganglion 3 months post-operatively

- **Certainty:** not applicable
    - **Other considerations:** certainty not assessed; this source was sought for basic concepts (e.g., ranges), with no expectation for precision or 'accuracy' for this particular outcome (return to work)

- **Results:**

    - mean time to return to work was 7 weeks (range 1 to 34 weeks; SD 6 weeks).
    - 40 patients (66.7%) worked in desk jobs, and 20 patients (23.3%) had occupations involving a heavy physical workload.
        - 5 weeks (range 1 to 18 weeks; SD 3.1 weeks) for those who worked a desk job versus 10 weeks (range 1 week to 34 weeks; SD 5.55 weeks) for those who had occupations with a heavy physical workload, noted to be "a significant difference in time to return to work ($p < 0.05$)."

NAWASREH 2018

Nawasreh Z, Adams G, Pryzbylkowski O, Logerstedt D. influence of patient demographics and graft types on acl second injury rates in ipsilateral versus contralateral knees: a systematic review and meta-analysis. Int J Sports Phys Ther. 2018 Aug;13(4):561-574. PubMed

Relevant to FAQ3, FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients who had primary ACL reconstruction
- **Intervention:** primary ACL reconstruction
- **Comparison:** Not applicable

- **Study inclusion criteria:**
    - English language
    - reported number or proportion of ipsilateral graft and/or contralateral ACL injuries within five years after ACL reconstruction
    - mean follow-up of ≤5 years

- **Number of studies:** 11
- **Number of participants:** 23,579
    - number reported is number of patients who completed follow-up and were included in analysis
- **Duration of follow-up:** mean (SD) 45.7 (19.4) months (range 12 to 60 months) after ACL reconstruction
    - included studies reported rates of second ACL injury collected within the first 5 years after ACLR; rates are not time specific as second ACL injury may have occurred at any time within the 5 years following surgery

- **Certainty: Low**
    - **Certainty by outcome:** Not applicable
        - pooled rate of second ACL injury was only outcome evaluated for certainty
    - **Risk of bias: Serious concern**
        - publication did not include description of the completeness of follow-up nor of the method used to diagnose second ACL injury nor other components related to study quality, so risk of bias could not be adequately evaluated
            - although the publication included a table reporting ratings for each included study on 13 items included in a "Modified Downs and Black checklist" for study quality, the study quality domain represented by each of the 13 items was not reported in the Nawasreh 2018 publication, and a copy of the referenced study describing this checklist was obtained

(https://jech.bmj.com/content/52/6/377.long) but the checklist (included as Appendix) includes 27 items, not 13, so it was still unclear what quality domains the 13 items represent
    - **Imprecision:** No serious concern
    - **Indirectness:** No serious concern
    - **Inconsistency:** Serious concern
        - rate of second ACL injury (ipsilateral or contralateral) were not reported for each trial, nor was a range of rates reported, and therefore heterogeneity could not be evaluated

- **Results:**
    - 6.11% (n = 1,441) rate of second ACL injuries (ipsilateral graft and contralateral ACL) in analysis of 11 studies with 23,579 patients
        - 3.29% (775/23,579) rate of ipsilateral graft injuries
        - 2.82% (666/23,579) rate of contralateral ACL injuries
    - time of second ACL injury outcome
        - for ipsilateral graft injuries in analysis of 5 studies
            - pooled mean time 25.56 months
            - median 20 months
            - range 7-60 months
        - for contralateral ACL injury in analysis of 6 studies
            - pooled mean time 47.3 months
            - median 36.3 months
            - range 16 to 84 months

OBERMEIER 2018

Obermeier MC, Sikka RS, Tompkins M, Nelson BJ, Hamilton A, Reams M, Chmielewski TL. Examination of Early Functional Recovery After ACL Reconstruction: Functional Milestone Achievement and Self-Reported Function. Sports Health. 2018 Jul/Aug;10(4):345-354. doi: 10.1177/1941738118779762. Epub 2018 Jun 4. PubMed

Relevant to FAQ4

- **Study design:** observational study
    - prospective cohort study
- **Population:** patients undergoing ACL reconstruction
- **Intervention:** ACL reconstruction
    - performed arthroscopically by 1 of 7 board-certified orthopedic surgeons
    - autograft or allograft tissue
        - autograft sources consisted of bone–patellar tendon–bone or semitendinosus and gracilis tendons; allograft sources consisted of the tibialis anterior, tibialis posterior, or Achilles tendon
    - surgical technique varied by surgeon preference and was not controlled for
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - between 12 and 59 years of age
    - treated for primary ACL reconstruction between January 2012 and April 2014 in a single institution

    - prior surgery on the index knee
    - need for concomitant procedures that would result in protocol deviation (e.g., meniscal repair, multiligament reconstruction)

- **Number of studies:** not applicable
- **Number of participants:** 98
    - full sample size is 182 patients, but 98 were employed, 81 were full-time students, and 3 were unemployed, and the latter 2 groups did not inform the return to work outcome

- **Certainty:** not applicable
    - **Other considerations:** certainty not assessed; this source was sought for basic concepts (e.g., ranges), with no expectation for precision or 'accuracy' for this particular outcome (return to work)

- **Results:**
    - time to return to work was a median of 11 days (no IQR or range provided)
    - about 40% returned to work within 1 week and 68% within 2 weeks
        - the surgical protocol in this study did not allow return to work before approximately 1 week following surgery
    - occupational demands on the knee were associated with time to return to work

TIFTIKCI 2015
Tiftikci U, Serbest S, Kilinc CY, Karabicak GÖ, Vergili Ö. Return to work in miners following anterior cruciate ligament reconstruction. Pan Afr Med J. 2015 Oct 22;22:173. doi: 10.11604/pamj.2015.22.173.7979. eCollection 2015. PubMed

Relevant to FAQ4

- **Study design:** observational study
    - retrospective cohort study
- **Population:** miners undergoing ACL reconstruction
- **Intervention:** ACL reconstruction
    - pes anserinus, gracilis, and semitendinosus tendons
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - miners who had arthroscopic ACL reconstruction
    - could not be over 40 years of age
    - treated between 2009 and 2014
    - could not have multiple ligament injuries, total meniscectomy, contralateral knee or lower extremity injury

- **Number of studies:** not applicable
- **Number of participants:** 33

- **Certainty:** not applicable

- **Other considerations:** certainty not assessed; this source was sought for basic concepts (e.g., ranges), with no expectation for precision or 'accuracy' for this particular outcome (return to work)

- **Results:**
  - average time for returning to work was 15.3 ± 4 (range 10 to 27) weeks

TSOUKAS 2016
Tsoukas D, Fotopoulos V, Basdekis G, Makridis KG. No difference in osteoarthritis after surgical and non surgical treatment of ACL-injured knees after 10 years. Knee Surg Sports Traumatol Arthrosc. 2016 Sep;24(9):2953-2959. Epub 2015 Apr 9. PubMed

Relevant to FAQ2, FAQ3, FAQ5

- **Study design:** randomized trial
- **Population:** patients with ACL rupture
  - median time between initial injury and beginning of treatment was 6 weeks for both groups
  - median age about 32 years old
  - all patients were male
- **Intervention:** ACL reconstruction surgery
  - hamstrings tendon graft used for surgery
  - patients in surgery group also participated in rehabilitation program
  - 1 surgeon performed all procedures
- **Comparison:** conservative treatment
  - rehabilitation program alone

- **Study inclusion criteria:**
  - Isolated ACL injury
  - Body mass index <30
  - No prior knee surgery or major knee injury
  - "[P]atients who successfully complete the final follow-up"

- **Number of studies:** Not applicable
- **Number of participants:** 32
  - 15 conservative treatment
  - 17 surgery
- **Duration of follow-up:** 10.1 years median

- **Certainty: Very low**
  - **Certainty by outcome:** Not applicable
  - **Risk of bias:** Very serious concern
    - no patient blinding
    - risk of selective outcome reporting because Lysholm activity scale score was reported as being used in Abstract and Methods, but results were not reported in Results section
  - **Imprecision:** Serious concern

        - evidence downgraded due to imprecision because small sized trial and lower bound of CI would not be clinically significant
    - **Indirectness:** Serious concern
        - 1 surgeon performed all the procedures
    - **Inconsistency:** No serious concern

    - **Other considerations:**
        - did not cite KANON 2010
        - reported there were no complications, revision surgeries, and further meniscus surgeries or surgeries due to persistent instability over 10-year follow-up
        - reported "patients who successfully completed the final follow-up" as part of the inclusion criteria

- **Results:**
    - comparing ACL reconstruction vs. conservative therapy
        - ACL reconstruction associated with improvement in 2000 Revised International Knee Documentation Committee (IKDC) Subjective Form, a measure of symptoms, function, and activity in patients with knee disorders
            - score range not reported in publication, but results on this measure are typically transformed to a scaled number that ranges from 0 to 100
            - between groups comparison
                - post-treatment means and standard deviations in each group
                    - ACL reconstruction – mean 86.7; standard deviation 6.5
                    - conservative treatment – mean 77.5; standard deviation 13
                        - p = 0.04 comparing groups at final follow-up
                        - we calculated MD using 2 different assumptions about variance
                            - MD 9.2 points (95% CI 1.9 to 16.5 points) assuming homoscedasticity
                            - MD 9.2 points (95% CI 1.5 to 16.9 points) assuming heteroscedasticity
        - Tegner scale values were reported as medians (range) for each group before surgery and at final follow-up
            - within group analysis reported significant decrease in conservative therapy group and no significant difference in ACL reconstruction group
            - no between group analyses performed
            - data on this outcome could not be used because of inadequate outcome reporting
    - no complications occurred and no revision surgeries were performed

Evidence report for management of anterior cruciate ligament rupture

Part 4 - Evidence Review

Prepared by EBSCO Information Services

March 26, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

For each FAQ, the key concepts (results and factors affecting certainty of the results) from the included studies that are most relevant to evidence synthesis will be summarized in Evidence Review Tables. Where evidence is very limited, or the FAQ is for descriptive summary, summary text will be provided.

Results

FAQ 1: What does the treatment involve?

FAQ1a: ACL reconstruction surgery

Descriptive Summary

If a patient is going to have reconstructive surgery, it is often scheduled 2 to 6 weeks after the injury. This is due to concerns about performing the surgery when inflammation is still prominent and the resultant concern of developing prominent scar tissue (arthrofibrosis). Before undergoing surgery, patients will also likely undergo several weeks of rehabilitation/physical therapy, with the goal of reducing swelling, restoring the knee's full range of motion, and strengthening the muscles contributing to healthy knee function prior to having surgery.

General anesthesia is typically used for the surgery, but regional anesthesia may be used in some cases. The surgery itself often takes less than 2 hours and is typically done arthroscopically through small incisions for the arthroscope and to allow the surgeon to use the required instruments to perform the surgery.

The damaged ACL will be removed and replaced with a segment of tendon. The tendon segment can either come from another part of the person’s body or from a deceased donor.

In the most common form of the surgery, the surgeon will drill sockets or tunnels into the thighbone and shinbone to position the graft. The graft is then secured with screws or other fixation devices. The graft serves as scaffolding on which new ligament tissue can grow.

ACL reconstruction is an outpatient procedure, so patients should be able to go home the same day after recovering from anesthesia (this often takes at least an additional 2 hours).

Following surgery, a rehabilitation program will be important for ensuring optimal outcomes. This rehabilitation may continue for anywhere from 4 to 12 months depending on the patient’s specific case. This is addressed in greater detail in ‘FAQ 4: When will I recover?’.

Patients may have some pain and swelling after surgery, and pain medication can be prescribed to help with this. These symptoms should subside within a week or two. This is addressed in greater detail in ‘FAQ 6: What are the side effects?’.

(AAOS 2009, Allen 2009, DiSilvestro 2016, Emory Healthcare nd, Mayo Clinic 2018, NHS 2018, NIH 2017, UCSF Health nd)

FAQ1b: Conservative (non-surgical) treatment

Descriptive Summary

The section Nonoperative management (rehabilitation) within the DynaMed Plus topic Management of anterior cruciate ligament (ACL) injury includes the following:

- goals of rehabilitation include
  - minimizing risk of damage to secondary knee structures
  - reestablishing full range of motion
  - regaining muscle strength of lower extremities and core muscles
  - improving neuromuscular control
  - returning to preinjury levels of function
- proposed rehabilitation protocol
  - acute phase
    - therapeutic strategies
      - modalities - cryotherapy and electrical stimulation
      - range of motion - active-assisted flexion and passive extension
      - exercises - isometric quadriceps (90 degrees-45 degrees) contractions, dynamic hamstring exercises, straight-leg raises
      - general conditioning
      - crutch ambulation
    - criteria for advancement
      - decreased pain
      - obtaining 90 degrees of flexion and full extension
      - satisfactory knee muscle control
      - ability to tolerate strengthening exercises
  - recovery phase
    - therapeutic strategies
      - modalities - superficial heat, pulsed ultrasound, and electrical stimulation
      - range of motion/stretching - active flexion and extension exercises, flexibility training
      - exercises
        - dynamic quadriceps (90 degrees-30 degrees) exercises, hamstring strengthening
        - closed kinetic chain exercises (open kinetic chain exercises may be introduced in functional phase), multiplanar lower extremity joint exercises
      - conditioning - aquatic exercises, bicycle, swimming, elliptical trainer
      - gradual return to sport-specific training, with optional functional brace use
    - criteria for advancement
      - full flexion and extension
      - symmetric quadriceps and hamstring strength
      - symptom-free progression in a sport-specific program
  - functional phase
    - therapeutic strategies
      - general flexibility training
      - exercises
        - general strengthening exercise program
        - lower extremities power and endurance exercises (such as plyometrics)
      - neuromuscular control, proprioceptive training

    - return to sport-specific participation
    - optional functional brace use
- criteria for advancement
    - no symptoms
    - normal mechanics while running and jumping
    - normal kinetic chain integration
    - completed sport-specific program

This is based on Micheo W, Hernández L, Seda C. Evaluation, management, rehabilitation, and prevention of anterior cruciate ligament injury: current concepts. PM R. 2010 Oct;2(10):935-44. (DynaMed Plus 2018)

FAQ 2: Will my symptoms get better?

FAQ2a vs. FAQ2b: ACL reconstruction vs conservative (non-surgical) treatment

As used throughout this evidence report, the reference KANON 2010 represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations below). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, we grouped these three references and refer to the combination of these sources as KANON 2010.

Evidence Review Table – randomized trials

Citation, Intervention, Comparator, Follow-up (years after surgery), and Number of participants	**Outcome***	**Mean in intervention group (95% CI) Mean in control group (95% CI) Mean difference (95% CI)**	**Certainty of evidence (reason for downgrade)**
KANON 2010 Intervention: early ACL reconstruction Comparator: optional delayed reconstruction surgery Follow-up: 5 years† (mean) No. of participants: 121	$KOOS_4$‡ (between-group difference in mean change from baseline)	42.9 (CI not reported) 44.9 (CI not reported) −2 (−8.5 to 4.5)	Low (risk of bias from no blinding and imprecision)
	$KOOS_4$‡ (between-group difference in mean post-treatment score)	80 (76 to 84) 82 (77 to 86) −1.5 (−7.4 to 4.4)	Low (risk of bias from no blinding and imprecision)
	$KOOS_4$ - Pain subscale§	91 (88 to 94) 91 (88 to 94) −0.3 (−4.6 to 4.0)	Low (risk of bias from no blinding and imprecision)
	$KOOS_4$ - Symptoms subscale§	83 (78 to 87) 87 (83 to 91) −4.4 (−10.2 to 1.4)	Low (risk of bias from no blinding and imprecision)
	$KOOS_4$ - Knee-related quality of life subscale§	71 (66 to 76) 69 (63 to 75) 1.8 (−6.2 to 9.8)	Low (risk of bias from no blinding and imprecision)
	SF-36 - Physical component§	85 (81 to 89) 84 (80 to 89) 0.9 (−4.9 to 6.7)	Low (risk of bias from no blinding and imprecision)
	SF-36 - Mental component§	87 (84 to 91) 85 (84 to 91) 2.8 (−2.7 to 8.3)	Low (risk of bias from no blinding and imprecision)

Tsoukas 2016 Intervention: early ACL reconstruction Comparator: conservative treatment (rehabilitation program alone) Follow-up: 10.1 years (median) No. of participants: 32	2000 Revised International Knee Documentation Committee (IKDC) Subjective Form§ ¶	86.7 (standard deviation 6.5) 77.5 (standard deviation 13) 9.2 (1.9 to 16.5)	Very low (very serious concerns about risk of bias from no blinding and risk of selective outcome reporting, imprecision, and indirectness)

* Scores range from 0 to 100 for all outcomes, with higher scores indicating better results; positive mean differences favor intervention group and negative mean differences favor control group.

† At 2-year follow-up, the results were very similar to those at 5-years and are not included in this summary table. As-treated analyses among patients treated with rehabilitation plus early ACL reconstruction, rehabilitation plus delayed ACL reconstruction, and rehabilitation alone also found results comparable to those shown in the table at both 2 and 5 years. See table and discussion of certainty in Part 3 for further detail.

‡ KOOS4 includes four KOOS subscales: pain, symptoms, function in sports and recreation, and knee-related quality of life. Scores range from 0 to 100, with higher scores indicating better results.

§ Results reported as between-group difference in mean post-treatment scores.

¶ Measure of symptoms, function, and activity in patients with knee disorders. Scores range from 0 to 100, with higher scores indicating better results.

FAQ 3: Will I need to get surgery later?

The outcomes of interest are surgery failure in the surgical treatment group and eventual need for surgery (delayed surgery) in the conservative treatment group.

As used throughout this evidence report, the reference KANON 2010 represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations below). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, we grouped these three references and refer to the combination of these sources as KANON 2010.

FAQ3a: ACL reconstruction

Evidence Review Table

We summarized three different evidence sources that estimate the proportion of surgery patients who may need subsequent revision surgery, based on failure of initial surgery or ipsilateral graft injury. In the KANON 2010 randomized trial, surgery failure rate was estimated based on the proportion of surgery patients who had a graft re-rupture at 2-year and 5-year follow-up times. In the Crawford 2013 systematic review of observational studies, surgery failure rate was estimated based on the proportion of surgery patients at > 10 years with treatment failure (defined as graft re-rupture, clinical failure based on objective tests, or the sum of both). In the Nawasreh 2018 systematic review of observational studies, the outcome was ipsilateral graft injury at up to 5 years. 'Ipsilateral graft injury' was not further defined by Nawasreh 2018, and therefore it was not clear whether these injuries would be sufficiently severe to warrant a revision surgery. Although we have included the ipsilateral graft injury rates from Nawasreh 2018 in the table below, in our summary in Part 5, we focus only on the graft rupture and clinical failure rates because we have judged these to provide better estimates of the possible need for revision surgery, which is ultimately a preference-sensitive decision (see, for instance, KANON 2010).

Citation	Study design	No of participants (studies)	Follow-up (years after surgery)	Outcome and results	Certainty of evidence (reason for downgrade)
KANON 2010	randomized trial (as-treated analysis)	84 (1)	2-year	graft re-rupture*: 4.8% (4/84)†	Moderate (imprecision)
		91 (1)	5-year	graft re-rupture*: 4.4% (4/91)†	Moderate (imprecision)
Crawford 2013	systematic review of observational studies			Failure rates‡ (measured 3 different ways):	
		2,782 (14)	> 10-years (range 10.2 to 15.3 years)	• 6.2% (173/2,782) ACL graft rupture rate; range 0% to 13.4%	Low (risk of bias and inconsistency)
		1,532 (14)	> 10-years (range 10.2 to 15.3 years)	• 10.3% (158/1,532) clinical failure rate; range 1.9% to 25.6%§	Low (risk of bias and inconsistency)
		2,782 (14)	> 10-years (range 10.2 to 15.3 years)	• 11.9% (331/2,782) overall cumulative ACL failure rate; range 3.2% to 29.9%¶	Low (risk of bias and inconsistency)
Nawasreh 2018	systematic review of observational studies	23,579 (11)	≤ 5 years**	Ipsilateral graft injury rate 3.29% (775/23,579)††	Low (unclear risk of bias and inconsistency) ‡‡

* Among patients who had surgery (as-treated analysis).
† Among the 4 patients with graft re-rupture, 2 had revision surgery and 2 declined revision surgery.
‡ Systematic review did not report the surgery revision rates among patients with treatment failure.
§ Based on poor clinical outcomes as indicated by established objective clinical measures (e.g., International Knee Documentation Committee grade C or D pivot shift or Lachman test on examination) and excluding patients with graft ruptures, who are already considered as failures and included in category above).
¶ Based on sum of ACL graft rupture rate plus clinical failure rate.
** Second ACL injury may have occurred at any time within the 5 years following surgery.
†† Rate of contralateral ACL injuries was only slightly lower (2.82%)
‡‡ Insufficient information was reported in publication to allow for a satisfactory evaluation of either risk of bias or inconsistency.

Descriptive Evidence Review

Tsoukas 2016 is a randomized trial of ACL reconstruction plus rehabilitation (n = 17) versus rehabilitation alone (n = 15) and represents a potential fourth evidence source concerning potential need for surgery later. Tsoukas 2016 reported no subsequent surgeries among participants but provides only Very low certainty evidence (due to very serious concern for risk of bias and indirectness).

FAQ3b: Conservative (non-surgical) treatment

Descriptive Evidence Review

Eventual need for surgery (delayed surgery) in the conservative treatment group was addressed in the KANON 2010 trial. Patients in KANON 2010 were randomized to ACL reconstruction surgery (intervention) vs conservative treatment with the option for delayed-reconstruction surgery (control). Patients randomized to the control group were referred for delayed surgery if they selected this option and met prespecified criteria. The proportion of patients randomly assigned to the control group who had delayed ACL reconstruction was 39% (23/59) at 2-year follow-up and 51% (30/59) at 5-year follow-up. Thus, 61% of patients avoided surgery at 2 years and 49% avoided surgery at 5 years, without compromising outcomes in intention-to-treat or as-treated analyses. This provides Moderate certainty evidence for eventual need for surgery among patients who initially pursue conservative (non-surgical) treatment, with downgrade due to imprecision. (As-treated analyses indicated no significant difference in patient-reported outcomes at 2-year or 5-year follow-up times among patients treated with rehabilitation plus early ACL reconstruction, patients treated with rehabilitation alone.)

FAQ 4: When will I recover?

Key outcomes of interest are return to usual activities and return to sports, both summarized below based on the findings of KANON 2010. Other recovery-related concepts including return to work and return to driving are not addressed in randomized trials, and descriptive evidence reviews or descriptive summaries for these concepts are provided below.

As used throughout this evidence report, the reference KANON 2010 represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations below). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, we grouped these three references and refer to the combination of these sources as KANON 2010.

FAQ4a vs. FAQ4b: ACL reconstruction vs conservative (non-surgical) treatment

Evidence Review Table

Comparing early ACL reconstruction vs. optional delayed ACL reconstruction on activity- and sports-related outcomes (KANON 2010; n = 121 patients)

Outcome at 5 years*	**Difference (95% CI)†**	**Certainty of evidence (reason for downgrade)**
Activities-related outcomes		
Tegner activity scale‡		
Proportion active at pre-injury level§	2.6% (−12.4% to 17.6%)	Low (risk of bias from no blinding and imprecision)
Median scores	0.1 (-0.8 to 1.1)	Low (risk of bias from no blinding and imprecision)
Mean $KOOS_4$ - Activities of daily living subscale scores¶	−1.5 (−4.3 to 1.4)	Low (risk of bias from no blinding and imprecision)
Sports-related outcome		
Mean $KOOS_4$ – sports and recreation subscale scores¶	−3.3 (−11.7 to 5.2)	Low (risk of bias from no blinding and imprecision)

* At 2-year follow-up, the results were very similar to at 5-year follow-up and are not included in this summary table. Further detail about 2-year results are included in Part 3 summary.

† Between-group mean and median differences are differences in post-treatment scores. Positive differences favor the intervention group.

‡ Assesses activity level with specific emphasis on knee; scores range from 1 (least strenuous activity) to 10 (high knee demanding activity on professional sports level).

§ Proportion with score at five years that was same as or higher (ie, better) than pre-injury score on Tegner scale.

¶ Scores range from 0 to 100, with higher scores indicating better results.

FAQ4a: ACL reconstruction

Descriptive Evidence Review – systematic review of observational studies

Braking reaction time

In a systematic review of observational studies, DiSilvestro 2016 found 2 cohort studies that investigated braking reaction time (BRT) as a surrogate for return to driving among patients who had ACL reconstruction. One study (n = 73 patients receiving ACL reconstruction) differentiated right versus left ACL reconstruction: BRTs were 738 milliseconds preoperatively and 733 milliseconds at the 6-week postoperative period among patients who received right ACL reconstruction; BRTs were 662 milliseconds preoperatively and 660 milliseconds at the 2-week postoperative period among patients who received left ACL reconstruction. Based on these results, the cohort study authors recommended return to driving at 6 weeks for right ACL reconstruction and 2 weeks for left ACL reconstruction. In another study (n = 14 patients receiving ACL reconstruction), BRTs reached the 50th percentile of national BRT data at the 4-week postoperative point, so the cohort study authors recommended return to driving at 4 to 6 weeks after ACL reconstruction. As the systematic review authors note, measures such as BRT "are only one aspect of safe driving, and do not include other crucial factors". Accordingly, and also as a result of the small sample sizes, this is Very low certainty evidence concerning return to driving. We therefore also considered descriptive summaries of return to driving.

Return to work

Although beyond scoping, we conducted a PubMed search for reports on time to return to work among people who have ACL reconstruction. These reports are consistent with the range given in the descriptive summary below for return to work. Briefly, these reports suggest most patients will return to work (100% in Groot 2017, with 92% returning fully and 8% returning, but not yet in a full capacity compared to their pre-injury capacity; 96% in Jenny 2016). However, the time to return to work seems variable:

- Groot 2017 (n = 125, but 36 were not working preoperatively, thus yielding 89 who were working preoperatively) found a median of 78 days (IQR 49 to 112 days)
- Jenny 2016 (n = 72) found a mean of 2.3 ± 0.8 months
- Minzlaff 2018 (n = 60) found a mean of 7 weeks (range 1 to 34 weeks)
- Obermeier 2018 (n = 182, but only 98 were employed, with 81 being full-time students and 3 being unemployed) found a median of 11 days (no IQR or range provided), with about 40% returning to work within 1 week and 68% within 2 weeks (the surgical protocol in this study did not allow return to work before approximately 1 week following surgery)
- Tiftikci 2015 (n = 33 miners) found a mean of 15.3 ± 4 weeks (range 10 to 27 weeks)

As would be expected, time to return to work was found to be associated with the demands the work placed on the knee in most (Groot 2017, Minzlaff 2018, Obermeier 2018) but not all (Jenny 2016) studies. We also note that, given the high prior probability that time to return to work

would depend on the type of work a person does, giving average times may be misleading, and ranges may be more appropriate to capture the heterogeneity. Means are most appropriate for normally-distributed data and are thus susceptible to influence from extreme values. For this outcome, they will also depend heavily on the type of people enrolled, their general health, and the type of work they do. Although medians are resistant to extreme values, they will still depend heavily on the type of people enrolled, their general health, and the type of work they do. Means and medians can also obfuscate multimodal data where they exist.

The overall range across 5 studies for return to work is from 1 week to 34 weeks.

Descriptive Summary

Importance of postsurgical physical therapy/rehabilitation

Continued rehabilitation/physical therapy is important after surgery. This rehabilitation program may continue for anywhere from 4 to 12 months, with the exact time varying from patient to patient based on his/her specific case.

Within the first few weeks after surgery, patients are generally encouraged to strive to regain a range of motion that is comparable to the unaffected knee. Patients may also have to wear a knee brace and/or walk with crutches for the first 1 to 4 weeks after surgery.

Returning to work, normal activities, and sports

When a person can return to work will depend on the kind of work s/he does. It can range from a few days to a few months, with longer periods typically being for jobs involving manual labor. Returning fully to activities and sports may take about 4 to 6 months, but some suggest 6 to 9 months as an average rehabilitation period, and in some cases, full recovery may take a year. The specifics of the person are a key factor. For instance, returning to sports that involve quick changes in direction (e.g., basketball, football, soccer) may require up to 9 to 12 months of rehabilitation.

Returning to driving

Recommendations about returning to driving vary. Some sources suggest not returning to driving for 4 to 6 weeks if the right knee was affected based on braking reaction times in a driving simulation test from a small number of patients who had right-sided ACL reconstruction. However, this is not clearly a direct match for returning to driving. Others suggest returning to driving when cleared to do so by the surgeon or the general practitioner, which may be 2 to 4 weeks or whenever a person can comfortably put weight on the foot on the affected side.

As always, each patient should seek individualized recommendations from his/her surgical team.

(See FAQ1 for references.)

FAQ4b: Conservative (non-surgical) treatment

Descriptive Summary

Available descriptive summaries focus on rehabilitation and return to activities after ACL reconstruction, but it is not just the ACL reconstruction *per se* that leads to the timelines below, but rather, the full rehabilitation of the ACL. Therefore, perhaps especially with the available evidence suggesting no clear difference in efficacy between early ACL reconstruction plus rehabilitation vs rehabilitation alone with the option for delayed surgery if needed, the timelines above (FAQ4a) may reasonably apply to those who pursue conservative (non-surgical) treatment as well, but this is not explicitly addressed in available descriptive summaries.

FAQ 5: What are the risks?

Outcomes of interest include septic arthritis, venous thromboembolic events, donor site problems, and failure of graft (including re-rupture). Septic arthritis and venous thromboembolic events following ACL reconstruction have each been evaluated in systematic reviews of observational studies. Donor site problems were reported in the KANON 2010 trial. Key findings are summarized below. Failure of graft (including re-rupture) is addressed in 'FAQ 3: Will I need to get surgery later?'.

As used throughout this evidence report, the reference KANON 2010 represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations below). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, we grouped these three references and refer to the combination of these sources as KANON 2010.

FAQ5a: ACL reconstruction

Evidence Review Tables – systematic reviews of observational studies

Incidence of septic arthritis infection following ACL reconstruction (Kim 2014)

No of knees (studies)	Interval between ACL reconstruction and examination for infection	Pooled incidence of septic arthritis infection	Certainty of evidence (reason for downgrade)
22,836 (14)	mean 19.1 days (range 2 to 450 days, with 450 days being an outlier and not consistent with a strong link to index ACL reconstruction)	0.5% (121/22,836)	Moderate (inconsistency)

Incidence of thromboembolic complications at <1 year* following ACL reconstruction (Janssen 2016)

Type of thromboembolic complication	No of patients (studies)	Pooled incidence	Certainty of evidence (reason for downgrade)
All studies, irrespective of whether thromboprophylaxis was given			
symptomatic deep venous thrombosis	14,506 (5)	0.3% (48/14,506)	Moderate (risk of bias)
pulmonary embolism	30,216 (10)	0.1% (42/30,216)	Moderate (risk of bias)
Studies reporting thromboprophylaxis *not* given			
symptomatic deep venous thrombosis	235 (4)	2.1% (5/235)	Moderate (imprecision)
pulmonary embolism	704 (6)	0.1% (1/704)	Moderate (imprecision)

* Unclear in 1 study, ≥1 year in 1 study, and <1 year in all other studies contributing to the above estimates

Descriptive Evidence Review

KANON 2010 reported on donor site problems but reported the number of events rather than the number of people experiencing an event. There were a total of 5 donor site problem events among 84 patients having surgery within 2 years (6.0%; Moderate certainty evidence with downgrade due to imprecision). No additional information was reported on this outcome, and it was not reported at the 5-year point.

Tsoukas 2016 reported no complications over about 10 years of follow-up among the 17 patients who were randomized to receive ACL reconstruction (Very low certainty evidence due to very serious concern for risk of bias and indirectness).

FAQ 6: What are the side effects?

FAQ6a: ACL reconstruction

Descriptive Summary

Pain and swelling after surgery

Patients will be instructed on postsurgical care for the knee, and they may be given medication to help with postoperative pain. This may include some painful bruising, swelling, and redness that can extend down the front of the shin and ankle, which is caused by the fluid inside the knee joint (synovial fluid and blood) leaking down the shin. These symptoms are temporary and should start to improve after about a week or two.

(See FAQ1 for references.)

Evidence report for management of anterior cruciate ligament rupture

Part 5 - Evidence Synthesis

Prepared by EBSCO Information Services

March 29, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

Evidence synthesis process

Synthesis methods will be based on the most appropriate methods matching the available evidence. We will systematically consider synthesis methods with the following questions:

Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

State "Yes" or "No". Provide justification if "No".

If "Yes", what method is the best approach?

Pick one of the following and justify:

(1) meta-analysis already done

(2) meta-analysis created from the evidence results

(3) median of sufficiently-valid results, stating cutoff for validity

(4) median of all results

If "No", what method is best to represent the evidence synthesis?

Pick one of the following and justify:

(1) range of all results

(2) range of sufficiently valid results

(3) descriptive summary without quantitative representation (e.g., consistency in direction, but inconsistency in magnitude)

(4) statement of inconsistency too limiting for single synthesized conclusion

Where evidence is very limited, or the FAQ is for descriptive summary, such that summary text was provided instead of Evidence Review Tables, the Descriptive Evidence Summary will be noted.

Results

FAQ 1: What does the treatment involve?

FAQ1a: ACL reconstruction surgery

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

If a patient is going to have reconstructive surgery, it is often scheduled 2 to 6 weeks after the injury. This is due to concerns about performing the surgery when inflammation is still prominent and the resultant concern of developing prominent scar tissue (arthrofibrosis). Before undergoing surgery, patients will also likely undergo several weeks of rehabilitation/physical therapy, with the goal of reducing swelling, restoring the knee's full range of motion, and strengthening the muscles contributing to healthy knee function. This is thought to help improve outcomes from having surgery.
General anesthesia is typically used for the surgery, but regional anesthesia may be used in some cases. The surgery itself often takes less than 2 hours and is typically done arthroscopically through small incisions for the arthroscope and to allow the surgeon to use the required instruments to perform the surgery.

The damaged ACL will be removed and replaced with a segment of tendon. The tendon segment can either come from another part of the person's body or from a deceased donor.
In the most common form of the surgery, the surgeon will drill sockets or tunnels into the thighbone and shinbone to position the graft. The graft is then secured with screws or other fixation devices. The graft serves as scaffolding on which new ligament tissue can grow.

ACL reconstruction is an outpatient procedure, so patients should be able to go home the same day after recovering from anesthesia (this often takes at least an additional 2 hours).

Following surgery, a rehabilitation program will be important for ensuring optimal outcomes. This rehabilitation may continue for anywhere from 4 to 12 months depending on the patient's specific case. This is addressed in greater detail in 'FAQ 4: When will I recover?'.

Patients may have some pain and swelling after surgery, and pain medication can be prescribed to help with this. These symptoms should subside within a week or two. This is addressed in greater detail in 'FAQ 6: What are the side effects?'.

(AAOS 2009, Allen 2009, DiSilvestro 2016, Emory Healthcare nd, Mayo Clinic 2018, NHS 2018, UCSF Health nd)

You will likely have several weeks of exercises and physical therapy before having surgery. Most people are put to sleep for the surgery, but some just have their leg numbed. The surgeon will replace the damaged part of your knee with healthy tissue (called a 'graft'). The graft can come from you or another person. After surgery, it is important to continue with exercises and physical therapy. This often lasts for 4 months or longer, up to a year.

FAQ1b: Conservative (non-surgical) treatment

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

The section Nonoperative management (rehabilitation) within the DynaMed Plus topic Management of anterior cruciate ligament (ACL) injury includes the following:

- goals of rehabilitation include
  - minimizing risk of damage to secondary knee structures
  - reestablishing full range of motion
  - regaining muscle strength of lower extremities and core muscles
  - improving neuromuscular control
  - returning to preinjury levels of function
- proposed rehabilitation protocol
  - acute phase
    - therapeutic strategies
      - modalities - cryotherapy and electrical stimulation
      - range of motion - active-assisted flexion and passive extension
      - exercises - isometric quadriceps (90 degrees-45 degrees) contractions, dynamic hamstring exercises, straight-leg raises
      - general conditioning
      - crutch ambulation
    - criteria for advancement
      - decreased pain
      - obtaining 90 degrees of flexion and full extension
      - satisfactory knee muscle control
      - ability to tolerate strengthening exercises
  - recovery phase
    - therapeutic strategies
      - modalities - superficial heat, pulsed ultrasound, and electrical stimulation
      - range of motion/stretching - active flexion and extension exercises, flexibility training
      - exercises
        - dynamic quadriceps (90 degrees-30 degrees) exercises, hamstring strengthening
        - closed kinetic chain exercises (open kinetic chain exercises may be introduced in functional phase), multiplanar lower extremity joint exercises
      - conditioning - aquatic exercises, bicycle, swimming, elliptical trainer
      - gradual return to sport-specific training, with optional functional brace use
    - criteria for advancement
      - full flexion and extension
      - symmetric quadriceps and hamstring strength
      - symptom-free progression in a sport-specific program
  - functional phase
    - therapeutic strategies
      - general flexibility training
      - exercises
        - general strengthening exercise program
        - lower extremities power and endurance exercises (such as plyometrics)

    - neuromuscular control, proprioceptive training
    - return to sport-specific participation
    - optional functional brace use
- criteria for advancement
    - no symptoms
    - normal mechanics while running and jumping
    - normal kinetic chain integration
    - completed sport-specific program

This is based on Micheo W, Hernández L, Seda C. Evaluation, management, rehabilitation, and prevention of anterior cruciate ligament injury: current concepts. PM R. 2010 Oct;2(10):935-44. (DynaMed Plus 2018)

You will do exercises and go to physical therapy to help your knee heal. Doing the exercises and physical therapy as directed will give you the best chance of your knee healing without surgery. The exercises and physical therapy often last for several months or longer, up to a year. You will not have surgery now, but you may decide to have surgery later if your knee does not get better.

FAQ 2: Will my symptoms get better?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	3 (Frobell 2010, Frobell 2013, Monk 2016)
Second-round (Systematic review searches)	Not applicable	
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	15	1 (Tsoukas 2016)

Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review that includes a single trial (the KANON trial). We refer to the combination of these sources as KANON 2010 in Parts 3 and beyond.

Part 3 Critical Appraisal (evidence evaluated for FAQ2):

Certainty	**Systematic reviews**	**Randomized trials**	**Other article types**
High			
Moderate			
Low		KANON 2010	
Very low		Tsoukas 2016	
Unusable			
Not applicable			

Part 4 Results for FAQ2: Will my symptoms get better?

Evidence Review Table – randomized trials

Citation, Intervention, Comparator, Follow-up (years after surgery), and Number of participants	**Outcome***	**Mean in intervention group (95% CI); Mean in control group (95% CI); Mean difference (95% CI)†**	**Certainty of evidence**
KANON 2010 *Intervention:* early ACL reconstruction *Comparator:* optional delayed reconstruction surgery *Follow-up*: 5 years‡ (mean) *No. of participants:* 121	$KOOS_4$§	80 (76 to 84); 82 (77 to 86); −1.5 (−7.4 to 4.4)	Low**
	$KOOS_4$ - Pain subscale	91 (88 to 94); 91 (88 to 94); −0.3 (−4.6 to 4.0)	Low**
	$KOOS_4$ - Symptoms subscale	83 (78 to 87); 87 (83 to 91); −4.4 (−10.2 to 1.4)	Low**
	$KOOS_4$ - Knee-related quality of life subscale	71 (66 to 76); 69 (63 to 75); 1.8 (−6.2 to 9.8)	Low**
	SF-36 - Physical component	85 (81 to 89); 84 (80 to 89); 0.9 (−4.9 to 6.7)	Low**
	SF-36 - Mental component	87 (84 to 91);85 (84 to 91); 2.8 (−2.7 to 8.3)	Low**
Tsoukas 2016 *Intervention:* early ACL reconstruction *Comparator:* conservative treatment (rehabilitation program alone) *Follow-up:* 10.1 years (median) *No. of participants:* 32	2000 Revised International Knee Documentation Committee (IKDC) Subjective Form¶	86.7 (standard deviation 6.5); 77.5 (standard deviation 13); 9.2 (1.9 to 16.5)	Very low††

* All mean differences are between-group difference in mean post-treatment scores. Scores range from 0 to 100 for all outcomes, with higher scores indicating better results.
† Positive mean difference favors intervention group.
‡ At 2-year follow-up, results were very similar to those at 5-years and are not included in this summary table. As-treated analyses among patients treated with rehabilitation plus early ACL reconstruction, rehabilitation plus delayed ACL reconstruction, and rehabilitation alone also found results comparable to those shown in the table at both 2 and 5 years. See table and discussion of certainty in Part 3 for further detail.
§KOOS4 includes four KOOS subscales: pain, symptoms, function in sports and recreation (see FAQ4), and knee-related quality of life. Scores range from 0 to 100, with higher scores indicating better results.
¶ Measure of symptoms, function, and activity in patients with knee disorders. Scores range from 0 to 100, with higher scores indicating better results.
** All outcomes are Low certainty due to lack of blinding, high crossover rate, and imprecision.
†† Very low certainty due to lack of blinding, selective outcome reporting, indirectness, and small sample size.

Evidence Synthesis Process for FAQ2
Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

No. Although 2 randomized trials have addressed this comparison (KANON 2010, Tsoukas 2016), Tsoukas 2016 was small and provides only Very low certainty evidence, so we consider KANON 2010 to be the more useful and appropriate representation of the body of evidence. Additionally, KANON 2010 provides numerous outcome measures (including subscales of composite measures) that consistently fail to demonstrate a clear difference between early surgery plus rehabilitation versus rehabilitation alone with the option for delayed surgery if needed, whereas Tsoukas 2016 provides only one useable outcome measure of unclear clinical relevance.

If "No", what method is best to represent the evidence synthesis?

Pick one of the following and justify:

(3) descriptive summary without quantitative representation (e.g., consistency in direction, but inconsistency in magnitude)

KANON 2010 found that in young adults with ACL tear, a strategy of structured rehabilitation plus early ACL reconstruction did not provide better results on a range of patient-reported outcomes vs. structured rehabilitation with the option of later ACL reconstruction. Results were consistently similar between groups on various patient-reported outcomes, including an overall measure of symptoms and disabilities ($KOOS_4$) as well as the $KOOS_4$ subscales that specifically measure pain, symptoms, and quality of life; the scores on these scales within each group also suggest that people generally improve over time. As-treated analyses among patients treated with rehabilitation plus early ACL reconstruction, rehabilitation plus delayed ACL reconstruction, and rehabilitation alone also found results comparable to those for the intention-to-treat analyses at both 2 and 5 years. In addition, the proportion of patients randomly assigned to the control group who had delayed ACL reconstruction was 39% at 2-year follow-up and 51% at 5-year follow-up. Thus, 61% of patients avoided surgery at 2 years and 49% avoided surgery at 5 years without worsening symptoms (in either intention-to-treat or as-treated analyses).

Symptoms appear to improve over time with either option, even if you decide to have surgery later.

Having ACL reconstruction surgery early may not improve symptoms better than doing exercises and physical therapy alone with the option for getting surgery later if needed.

Doing exercises and physical therapy alone with the option for getting surgery later if needed may improve symptoms as much as having ACL reconstruction surgery early.

FAQ 3: Will I need to get surgery later?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	3 (Frobell 2010, Frobell 2013, Monk 2016)
Second-round (Systematic review searches)	124	2 (Crawford 2013, Nawasreh 2018)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	15	1 (Tsoukas 2016)

Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review that includes a single trial (the KANON trial). We refer to the combination of these sources as KANON 2010 in Parts 3 and beyond.

Part 3 Critical Appraisal (evidence evaluated for surgery failure or eventual need for surgery for FAQ3):

Certainty	Systematic reviews	Randomized trials	Other article types
High			
Moderate		KANON 2010	
Low	Crawford 2013		
Very low		Tsoukas 2016†	
Unusable	Nawasreh 2018*		
Not applicable			

* Nawasreh 2018 investigated the rate of second injury up to 5 years after ACL reconstruction. Nawasreh 2018 did not further define "injury", so we are not confident whether the injury rate offers a meaningful indication of surgical failure. We therefore did not consider it beyond Part 4. Parts 3 and 4 have further detail.

† Tsoukas 2016 randomized people to either ACL reconstruction plus rehabilitation (n = 17) or rehabilitation alone (n =15) and reported no subsequent surgeries among participants over about 10 years of follow-up. However, it provides only Very low certainty evidence, so we do not consider it beyond Part 4. Parts 3 and 4 have further detail.

FAQ3a: ACL reconstruction

Part 4 Results for FAQ3a: Will I need to get surgery later?

Rates of 'failed' surgeries were reported in 2 different evidence sources. In KANON 2010, surgery failure was estimated based on the proportion of patients who had a graft re-rupture after ACL reconstruction at 2-year and 5-year follow-up times. In Crawford 2013, surgery failure was estimated based on the proportion of patients at > 10 years after ACL reconstruction with graft re-rupture, clinical failure based on objective tests, or the sum of both. We note that not all surgery failures lead to revision surgery, and that the choice for revision surgery is preference-sensitive. For example, among the 4 patients with graft re-rupture in KANON 2010, only 2 elected to have revision surgery. Crawford 2013 did not report surgery revision rates among patients with treatment failure.

Citation	**Study design**	**No of participants (studies)**	**Follow-up (years after surgery)**	**Outcome and results**	**Certainty of evidence**
KANON 2010	randomized trial (as-treated analysis)	84 (1)	2-year	graft re-rupture*: 4.8% (4†/84)	Moderate
		91 (1)	5-year	graft re-rupture*: 4.4% (4†/91)	Moderate
Crawford 2013	systematic review of observational studies			Failure rates‡ (measured 3 different ways):	
		2,782 (14)	> 10-years (range 10.2 to 15.3 years)	• 6.2% ACL graft re-rupture rate	Low
		1,532 (14)	> 10-years (range 10.2 to 15.3 years)	• 10.3% clinical failure rate§	Low
		2,782 (14)	> 10-years (range 10.2 to 15.3 years)	• 11.9% overall cumulative ACL failure rate¶	Low

* Among patients who had surgery (as-treated analysis).
† Among the 4 patients with graft re-rupture, 2 had revision surgery and 2 declined revision surgery.
‡ Did not report the surgery revision rate among patients with treatment failure.
§ Based on poor clinical outcomes as indicated by established objective clinical measures (and excluding patients with graft re-ruptures, who are already considered as failures and included in category above).
¶ Based on sum of ACL graft re-rupture rate plus clinical failure rate.

Evidence Synthesis Process for FAQ3a
Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

Yes, for the follow-up time point of 2 years and 5 years after surgery.

At both 2 years and 5 years, only a single estimate was available, from KANON 2010 (Moderate certainty) which reported surgery failure rates based on graft re-ruptures.

No, for the follow-up points of 10 years after surgery (best method: range of sufficiently-valid results).

At 10 years after surgery, Crawford 2013 (Low certainty) reported surgery failure rates based on three different measures: re-rupture rate, clinical failure rate, and sum of re-rupture rate plus clinical failure rate. As all three of these measures may be meaningful for informing the outcome of failed surgery and the possible need for additional surgery, we report all three.

Out of 100 people who have ACL reconstruction surgery:

- **the graft may tear in about 5 (5%) within 2 years**
- **the graft may tear in about 6 (6%) within 10 to 15 years**
- **about 10 (10%) may have a knee exam that suggests the surgery did not work as hoped within 10 to 15 years**

Whether to have another surgery after a graft tear or a knee exam that suggests the surgery did not work as hoped is a choice that each patient will make with his or her surgeon.

FAQ3b: Conservative (non-surgical) treatment

Part 4 Results for FAQ3b: Will I need to get surgery later?

Descriptive Evidence Review

Eventual need for surgery (delayed surgery) in the conservative treatment group (n = 59) was addressed in KANON 2010. The proportion of patients randomly assigned to the control group who had delayed ACL reconstruction was 39% at 2-year follow-up and 51% at 5-year follow-up. Thus, 61% of patients avoided surgery at 2 years and 49% avoided surgery at 5 years, without compromising outcomes in intention-to-treat or as-treated analyses. (Moderate certainty)

Evidence Synthesis Process for FAQ3b
Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

Yes.

At both 2 years and 5 years, only a single estimate was available. KANON 2010 provides Moderate certainty evidence for the rate of delayed surgery in the control group.

Out of 100 people who have conservative (non-surgical) treatment:

- **about 39 (39%) will have surgery within 2 years**
- **about 51 (51%) will have surgery within 5 years**

The outcome of surgery does not appear to be worse for people who have surgery later.

FAQ 4: When will I recover?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	3 (Frobell 2010, Frobell 2013, Monk 2016)
Second-round (Systematic review searches)	124	1 (DiSilvestro 2016)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	35	5 (Groot 2017, Jenny 2016, Minzlaff 2018, Obermeier 2018, Tiftikci 2015)*

* This search was beyond scoping, but we included it to investigate descriptive summaries for return to work.

Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review that includes a single trial (the KANON trial). We refer to the combination of these sources as KANON 2010 in Parts 3 and beyond.

Part 3 Critical Appraisal (evidence evaluated for recovery for FAQ4):

Certainty	Systematic reviews	Randomized trials	Other article types
High			
Moderate		KANON 2010	
Low			
Very low		DiSilvestro 2016	
Unusable			
Not applicable			Groot 2017, Jenny 2016, Minzlaff 2018, Obermeier 2018, Tiftikci 2015*

* This search was beyond scoping, but we included it to investigate descriptive summaries for return to work. Certainty was not assessed, as these sources were sought for basic concepts (e.g., ranges) with no expectation for precision or 'accuracy' for this particular outcome.

Key outcomes of interest are return to usual activities and return to sports, both summarized below based on the findings of KANON 2010. Other recovery-related concepts including return to work and return to driving are not addressed in randomized trials, and Descriptive Evidence Reviews or Descriptive Summaries for these concepts are provided below.

FAQ4a vs. FAQ4b: ACL reconstruction vs conservative (non-surgical) treatment

Part 4 Results for FAQ4: When will I recover? (activity- and sports-related outcomes)

Evidence Review Table

Comparing early ACL reconstruction vs. optional delayed ACL reconstruction on activity- and sports-related outcomes (KANON 2010; n = 121 patients)

Outcome at 5 years*	**Difference (95% CI)†**	**Certainty of evidence**
Activity-related outcomes		
Tegner activity scale‡		
Proportion active at pre-injury level§	2.6% (−12.4% to 17.6%)	Low
Median scores	0.1 (-0.8 to 1.1)	Low
Mean $KOOS_4$ - Activities of daily living subscale scores¶	−1.5 (−4.3 to 1.4)	Low
Sports-related outcome		
Mean $KOOS_4$ – sports and recreation subscale scores¶	−3.3 (−11.7 to 5.2)	Low

* At 2-year follow-up, the results were very similar to those at 5-year follow-up and are not included in this summary table. Further detail about 2-year results are included in Part 3 summary.
† Between-group mean and median differences are differences in post-treatment scores. Positive differences favor the intervention group.
‡ Assesses activity level with specific emphasis on knee; scores range from 1 (least strenuous activity) to 10 (high knee demanding activity on professional sports level).
§ Proportion with score at five years that was same as or higher (ie, better) than pre-injury score on Tegner scale.
¶ Scores range from 0 to 100, with higher scores indicating better results.

Evidence Synthesis Process for FAQ4a vs. FAQ4b
Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

No. Activity-related outcomes were evaluated using three different outcome measures in KANON 2010, and all three found consistent results of no important differences between groups. Sports-related outcome was evaluated using a single measure in KANON 2010, which also found no important difference between groups.

If "No", what method is best to represent the evidence synthesis?

(3) descriptive summary without quantitative representation (e.g., consistency in direction, but inconsistency in magnitude)

There is no clear difference in your ability to return to usual activities or sports if you have ACL reconstruction surgery early or if you do exercises and physical therapy alone with the option for getting surgery later if needed.

FAQ4a: ACL reconstruction

Part 4 Results for FAQ4: When will I recover? (return to driving, work, normal activities, and sports)

Descriptive Evidence Review

Braking reaction time

DiSilvestro 2016 was a systematic review of observational studies that found 2 cohort studies investigating braking reaction time (BRT) after ACL reconstruction. One study (n = 73 patients receiving ACL reconstruction) found BRTs of 738 milliseconds preoperatively and 733 milliseconds at the 6-week postoperative period among patients who received right ACL reconstruction and 662 milliseconds preoperatively and 660 milliseconds at the 2-week postoperative period among patients who received left ACL reconstruction. Based on these results, the cohort study authors recommended return to driving at 6 weeks for right ACL reconstruction and 2 weeks for left ACL reconstruction. In another study (n = 14 patients receiving ACL reconstruction), BRTs reached the 50th percentile of national BRT data at the 4-week postoperative point, so the cohort study authors recommended return to driving at 4 to 6 weeks after ACL reconstruction. This is Very low certainty evidence for return to driving, so we also consider descriptive summaries.

Return to work

Although beyond scoping, we conducted a PubMed search for reports on time to return to work among people who have ACL reconstruction. These reports are consistent with the range given in the descriptive summary below for return to work. Briefly, these reports suggest most patients will return to work (100% in Groot 2017, with 92% returning fully and 8% returning, but not yet fully; 96% in Jenny 2016). However, the time to return to work seems variable:

- Groot 2017 (n = 125, but 36 were not working preoperatively, thus yielding 89 who were working preoperatively) found a median of 78 days (IQR 49 to 112 days)
- Jenny 2016 (n = 72) found a mean of 2.3 ± 0.8 months
- Minzlaff 2018 (n = 60) found a mean of 7 weeks (range 1 to 34 weeks)
- Obermeier 2018 (n = 182, but only 98 were employed, with 81 being full-time students and 3 being unemployed) found a median of 11 days (no IQR or range provided), with about 40% returning to work within 1 week and 68% within 2 weeks (the surgical protocol in this study did not allow return to work before approximately 1 week following surgery)
- Tiftikci 2015 (n = 33 miners) found a mean of 15.3 ± 4 weeks (range 10 to 27 weeks)

As would be expected, time to return to work was found to be associated with the demands the work placed on the knee in most (Groot 2017, Minzlaff 2018, Obermeier 2018) but not all (Jenny 2016) studies. Means and medians are considered less informative this variable population. The overall range for return to work across 5 studies was from 1 week to 34 weeks.

Descriptive Summary

Importance of postsurgical physical therapy/rehabilitation

Continued rehabilitation/physical therapy is important after surgery. This may continue for anywhere from 4 to 12 months, with the exact time varying from patient to patient based on his/her specific case.

Returning to work, normal activities, and sports

When a person can return to work will depend on the kind of work s/he does. It can range from a few days to a few months, with longer periods typically being for jobs involving manual labor. Returning fully to activities and sports may take about 4 to 6 months, but some suggest 6 to 9 months as an average rehabilitation period, and in some cases, full recovery may take a year. The specifics of the person are a key factor. For instance, returning to sports that involve quick changes in direction (e.g., basketball, football, soccer) may require up to 9 to 12 months of rehabilitation.

Returning to driving

Recommendations about returning to driving vary. Some sources suggest not returning to driving for 4 to 6 weeks if the right knee was affected based on braking reaction times in a driving simulation test from a small number of patients who had right-sided ACL reconstruction. However, this is not clearly a direct match for returning to driving. Others suggest returning to driving when cleared to do so by the surgeon or the general practitioner, which may be 2 to 4 weeks or whenever a person can comfortably put weight on the foot on the affected side.

As always, each patient should seek individualized recommendations from his/her surgical team.

(See FAQ1 for references.)

After an ACL tear, full recovery may take up to a year, but it depends on the person. You may return to driving within 2 to 6 weeks. You may return to work within a few days to a few months depending on the work you do. Fully returning to normal activities and sports also depends on the person. Doing the exercises and physical therapy as directed will help make sure you recover as quickly and fully as possible. The recovery period typically ranges from 4 months to 12 months. The surgeon will give specific advice for each person.

FAQ4b: Conservative (non-surgical) treatment

Descriptive Summary

Available descriptive summaries focus on rehabilitation and return to activities after ACL reconstruction, but it is not just the ACL reconstruction *per se* that leads to the timelines below, but rather, the full rehabilitation of the ACL. Therefore, perhaps especially with the available evidence suggesting no clear difference in efficacy between early ACL reconstruction plus rehabilitation vs rehabilitation alone with the option for delayed surgery if needed, the timelines above (FAQ4a) may reasonably apply to those who pursue conservative (non-surgical) treatment as well, but this is not explicitly addressed in available descriptive summaries.

After an ACL tear, full recovery may take up to a year, but it depends on the person. You may return to driving within 2 to 6 weeks. You may return to work within a few days to a few months depending on the work you do. Fully returning to normal activities and sports also depends on the person. Doing the exercises and physical therapy as directed will help make sure you recover as quickly and fully as possible. The recovery period typically ranges from 4 months to 12 months. The surgeon will give specific advice for each person.

FAQ 5: What are the risks?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	3 (Frobell 2010, Frobell 2013, Monk 2016)
Second-round (Systematic review searches)	124	1 (Janssen 2016, Kim 2014)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	15	1 (Tsoukas)

Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review that includes a single trial (the KANON trial). We refer to the combination of these sources as KANON 2010 in Parts 3 and beyond.

Part 3 Critical Appraisal (evidence evaluated for risks for FAQ5):

Certainty	Systematic reviews	Randomized trials	Other article types
High			
Moderate	Janssen 2016 Kim 2014	KANON 2010	
Low			
Very low		Tsoukas 2016†	
Unusable			
Not applicable			

† Tsoukas 2016 randomized people to either ACL reconstruction plus rehabilitation (n = 17) or rehabilitation alone (n =15) and reported no complications among participants over about 10 years of follow-up. However, it provides only Very low certainty evidence, so we do not consider it beyond Part 4. Parts 3 and 4 have further detail.

Outcomes of interest include septic arthritis, venous thromboembolic events, and donor site problems. Septic arthritis and venous thromboembolic events following ACL reconstruction have each been evaluated in systematic reviews of observational studies, and their key findings are summarized in the tables below. Donor site problems were reported in KANON 2010, and a brief Descriptive Evidence Review for this outcome is included below.

FAQ5a: ACL reconstruction

Part 4 Results for FAQ5a: What are the risks?

Evidence Review Tables – systematic reviews of observational studies

Incidence of septic arthritis following ACL reconstruction (Kim 2014)

No of knees (studies)	Interval between ACL reconstruction and examination for infection	Pooled incidence of septic arthritis infection	Certainty of evidence
22,836 (14)	mean 19.1 days (range 2 to 450 days, with 450 days being an outlier and not consistent with a strong link to index ACL reconstruction)	0.5% (121/22,836)	Moderate (downgrade due to inconsistency)

Incidence of thromboembolic complications* following ACL reconstruction among studies where thromboprophylaxis was reported as not being given (Janssen 2016)

Type of thromboembolic complication	No of patients (studies)	Pooled incidence	Certainty of evidence
symptomatic deep venous thrombosis	235 (4)	2.1% (5/235)	Moderate (downgraded due to imprecision)
pulmonary embolism	704 (6)	0.1% (1/704)	Moderate (downgraded due to imprecision)

* Follow-up time at assessment unclear in 1 study, ≥1 year in 1 study, and <1 year in all other studies contributing to the above estimates. It is not possible to determine a more explicit/precise timeframe for these estimates from the original publication.

Descriptive Evidence Review

KANON 2010 reported a total of 5 donor site problem events among 84 patients having surgery within 2 years (6.0%; Moderate certainty evidence with downgrade due to imprecision). No additional information was reported on this outcome, and it was not reported at the 5-year point.

Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

Yes

If "Yes", what method is the best approach?

(1) meta-analysis already done
(meta-analysis not applicable for donor site problems, as KANON 2010 is the single source reporting on that outcome)

Serious complications following ACL reconstruction surgery are not common. Out of 100 people who have ACL reconstruction surgery:

- **about 6 (6%) may have a problem with the area of their leg from where the graft was taken within two years of surgery**
- **about 2 (2%) may have a blood clot in their leg that causes symptoms within a year of surgery**
- **fewer than 1 (<1%) may have a blood clot in their lung within a year of surgery**
- **fewer than 1 (<1%) may have an infection in their knee joint within about a month after surgery**

Although it is not common to have a blood clot after ACL reconstruction surgery, you may be given medicine for a period of time after surgery to help prevent a blood clot from occurring.

FAQ5b: Conservative (non-surgical) treatment

Descriptive Summary

Risks associated with rehabilitation alone with the option for delayed surgery amount to either one-off/anomalous events (e.g., a slip and fall during an exercise program) or events related to having delayed surgery. One-off/anomalous events related to rehabilitation could also happen in the early surgery group, because they undergo a rehabilitation program as well.

Serious risks from exercise/rehabilitation are not common. If you decide to have surgery later, the risks of surgery will apply.

FAQ 6: What are the side effects?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	0
Second-round (Systematic review searches)	124	0
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	15	0

Because we did not find evidence to further inform side effects of pain and swelling after surgery, we use descriptive summaries.

FAQ6a: ACL reconstruction surgery

Descriptive Summary

Patients will be instructed on postsurgical care for the knee, and they may be given medication to help with postoperative pain. This may include some painful bruising, swelling, and redness that can extend down the front of the shin and ankle, which is caused by the fluid inside the knee joint (synovial fluid and blood) leaking down the shin. These symptoms are temporary and should start to improve after about a week or two.

(See FAQ1 for references.)

You may have some pain, bruising, swelling, and redness. This can run down the front of your lower leg and ankle. It should start to get better within a week or two. You can be given medicine to help with the pain if needed.

FAQ6b: Conservative (non-surgical) treatment

Descriptive Summary

People may have soreness or discomfort during the rehabilitation program regardless of whether they pursue early surgery or rehabilitation alone with the option for delayed surgery. If people eventually decide to have surgery, side effects from surgery would apply.

Serious side effects from exercise/rehabilitation are not common. If you decide to have surgery later, the side effects of surgery will apply.

Evidence report for management of anterior cruciate ligament rupture

Reference list

Prepared by EBSCO Information Services

March 26, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

AAOS 2009
American Academy of Orthopedic Surgeons. ACL Injury: Does It Require Surgery?. Last updated/reviewed September 2009. Accessed March 26, 2019. Available at https://orthoinfo.aaos.org/en/treatment/acl-injury-does-it-require-surgery/.

ALLEN 2009
Allen AA, Altchek DW, Rodeo SA. ACL Reconstruction | New Advances in ACL Surgery: An Overview by the HSS Sports Medicine Service. Last updated/reviewed March 2, 2009. Accessed March 26, 2019. Available at https://www.hss.edu/conditions_acl-reconstruction-new-advances.asp.

CRAWFORD 2013
Crawford SN, Waterman BR, Lubowitz JH. Long-term failure of anterior cruciate ligament reconstruction. Arthroscopy. 2013 Sep;29(9):1566-71. Epub 2013 Jun 29. PubMed

DISILVESTRO 2016
DiSilvestro KJ, Santoro AJ, Tjoumakaris FP, Levicoff EA, Freedman KB. When Can I Drive After Orthopaedic Surgery? A Systematic Review. Clin Orthop Relat Res. 2016 Dec;474(12):2557-2570. Epub 2016 Aug 4. PubMed

DYNAMED PLUS 2018
DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T909086, Management of anterior cruciate ligament (ACL) injury; [updated 2018 Nov 30, cited March 26, 2019]. Available from https://www.dynamed.com/topics/dmp~AN~T909086. Registration and login required.

EMORY HEALTHCARE ND
Emory Healthcare. Rehab timeline expectations. Date last updated/reviewed not provided. Accessed March 26, 2019. Available at https://www.emoryhealthcare.org/centers-programs/acl-program/recovery/rehab-timeline.html.

FROBELL 2010
Frobell RB, Roos EM, Roos HP, Ranstam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. N Engl J Med. 2010 Jul 22;363(4):331-42. Erratum in: N Engl J Med. 2010 Aug 26;363(9):893. PubMed

FROBELL 2013
Frobell RB, Roos HP, Roos EM, Roemer FW, Ranstam J, Lohmander LS. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. BMJ. 2013 Jan 24;346:f232. PubMed

GROOT 2017
Groot JA, Jonkers FJ, Kievit AJ, Kuijer PP, Hoozemans MJ. Beneficial and limiting factors for return to work following anterior cruciate ligament reconstruction: a retrospective cohort study. Arch Orthop Trauma Surg. 2017 Feb;137(2):155-166. doi: 10.1007/s00402-016-2594-6. Epub 2016 Nov 21. PubMed

JANSSEN 2016
Janssen RP, Reijman M, Janssen DM, van Mourik JB. Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review. World J Orthop. 2016 Sep 18;7(9):604-17. eCollection 2016 Sep 18. PubMed

JENNY 2016
Jenny JY, Clement X. Patient-based decision for resuming activity after ACL reconstruction: a single-centre experience. Eur J Orthop Surg Traumatol. 2016 Dec;26(8):929-935. Epub 2016 Sep 26. PubMed

KANON 2010
This reference header represents three related references: Frobell 2010, Frobell 2013, and Monk 2016 (full citations are included herein). Frobell 2010 and 2013 are the 2-year and 5-year results from the KANON trial. Monk 2016 is a Cochrane review of randomized, controlled trials of early surgical versus conservative management of anterior cruciate ligament rupture, and it found only a single eligible trial (the KANON trial). As such, for this evidence report, we grouped these three references and refer to the combination of these sources as KANON 2010.

KIM 2014
Kim SJ, Postigo R, Koo S, Kim JH. Infection after arthroscopic anterior cruciate ligament reconstruction. Orthopedics. 2014 Jul;37(7):477-84. PubMed

MAYO CLINIC 2018
Mayo Clinic. ACL reconstruction. Last updated/reviewed December 11, 2018. Accessed March 26, 2019. Available at https://www.mayoclinic.org/tests-procedures/acl-reconstruction/about/pac-20384598.

MINZLAFF 2018
Minzlaff P, Heidt T, Feucht MJ, Plath JE, Hinterwimmer S, Imhoff AB, Saier T. Patient satisfaction with health is substantially improved following ACL reconstruction. Knee Surg Sports Traumatol Arthrosc. 2018 Feb;26(2):582-588. doi: 10.1007/s00167-017-4623-6. Epub 2017 Jun 26. PubMed

MONK 2016
Monk AP, Davies LJ, Hopewell S, Harris K, Beard DJ, Price AJ. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. Cochrane Database Syst Rev. 2016 Apr 3;4:CD011166. PubMed

NAWASREH 2018
Nawasreh Z, Adams G, Pryzbylkowski O, Logerstedt D. influence of patient demographics and graft types on acl second injury rates in ipsilateral versus contralateral knees: a systematic review and meta-analysis. Int J Sports Phys Ther. 2018 Aug;13(4):561-574. PubMed

NHS 2018
National Health Service. Knee ligament surgery: How it is performed. Last updated/reviewed June 14, 2018. Accessed March 26, 2018. Available at https://www.nhs.uk/conditions/knee-ligament-surgery/what-happens/.

National Health Service. Knee ligament surgery: Recovery. Last updated June 14, 2018. Accessed March 26, 2018. Available at https://www.nhs.uk/conditions/knee-ligament-surgery/recovery/.

NIH 2017
National Institute of Health, U.S. National Library of Medicine. ACL reconstruction. Last updated/reviewed April 18, 2018. Accessed March 26, 2019. Available at https://medlineplus.gov/ency/article/007208.htm.

OBERMEIER 2018
Obermeier MC, Sikka RS, Tompkins M, Nelson BJ, Hamilton A, Reams M, Chmielewski TL. Examination of Early Functional Recovery After ACL Reconstruction: Functional Milestone Achievement and Self-Reported Function. Sports Health. 2018 Jul/Aug;10(4):345-354. doi: 10.1177/1941738118779762. Epub 2018 Jun 4. PubMed

TIFTIKCI 2015
Tiftikci U, Serbest S, Kilinc CY, Karabicak GÖ, Vergili Ö. Return to work in miners following anterior cruciate ligament reconstruction. Pan Afr Med J. 2015 Oct 22;22:173. doi: 10.11604/pamj.2015.22.173.7979. eCollection 2015. PubMed

TSOUKAS 2016
Tsoukas D, Fotopoulos V, Basdekis G, Makridis KG. No difference in osteoarthritis after surgical and non surgical treatment of ACL-injured knees after 10 years. Knee Surg Sports Traumatol Arthrosc. 2016 Sep;24(9):2953-2959. Epub 2015 Apr 9. PubMed

UCSF HEALTH ND
University of California San Francisco. ACL reconstruction surgery. Date last reviewed/updated not provided. Accessed March 26, 2019. Available at https://www.ucsfhealth.org/education/acl_reconstruction_surgery/.