Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
eMethods

Search strategy and trial selection

The protocol for the systematic review is registered on PROSPERO (CRD42018089972). The PubMed, Cochrane Library, and Web of Science databases were systematically searched in September 2022. Using a search strategy for combined terms (((anterior cruciate ligament OR ACL) AND (reconstruction OR surgery OR repair)) AND (early OR acute)) AND (delayed OR chronic). The references in the included articles were further reviewed to identify additional studies.

The inclusion and exclusion criteria were reported in eTable 1 in Supplement. To ensure that the selected articles met the specified inclusion criteria, the titles and abstracts of the studies were independently reviewed by two authors (XYS and BC) in a blinded manner. Any disagreements on trial inclusion and data were resolved through discussion and consensus with the participation of a senior reviewer (JLX).

Data extraction

The extracted data included the following: study design, randomization, definition of surgery timing, inclusion/exclusion criteria, operative technique, rehabilitation protocols, and follow-up duration. The following participant and surgical characteristics were also collected: participants’ sample size, age, sex, graft type, associated lesions, injury mechanisms, injury-to-surgery time, and rehabilitation principle. The selected clinical outcomes took into account the most commonly used outcome measures in recent publications.

Statistical analysis

To evaluate the outcomes of early vs. elective delayed ACLR after different follow-up durations, we recorded the data given for all follow-up time points. The included trials were grouped according to their follow-up durations as follows: 6 months, 1 year, 2 years, and 5 years. If the relevant outcomes were reported at multiple follow-up time points, the data were analyzed separately for each time point. When same RCTs were included in subgroup analyses of different follow-up duration, only subtotals were calculated. All eligible studies were included in the meta-analyses and subgroup analyses, as applicable.

To estimate the standardized mean difference (sMD), we calculated the mean and standard deviation (SD) values. If the mean and SD data were not provided in the included studies, the sMD was calculated using the P value and sample size. The I² statistic was considered to evaluate the data.
for heterogeneity among studies and confirm the appropriateness of pooling among groups. Clinical heterogeneity was assumed present, a random-effects model was preferred.
### eTable 1. Study Inclusion and Exclusion Criteria

| Inclusion Criteria                                                                 | Exclusion Criteria                                                                 |
|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Randomized clinical Trial                                                         | Non-English articles                                                               |
| Clinical or functional outcomes and adverse complications associated with early and elective delayed ACLR | Case series and reviews                                                            |
|                                                                                  | Not compare clinical outcomes between early and delayed ACLR                        |
|                                                                                  | Not clearly define specific cutoff points for early and elective delayed surgery    |

Note: ACLR, anterior cruciate ligament reconstruction.

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**Table 2.** Risk of Bias of Assessment for the Included RCTs Using Cochrane Collaboration’s Tool

| Author (Year)       | Sequence generation | Allocation concealment | Blinding | Incomplete outcome data | Selective outcome report | Free of other bias |
|---------------------|---------------------|------------------------|----------|-------------------------|--------------------------|-------------------|
| Meighan et al.19 (2003) | ✓                   | ✓                      | ✓        | ?                       | ✓                        | ✓                 |
| Bottoni et al.20 (2008) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ✓                 |
| Raviraj et al.21 (2010) | ✓                   | ✓                      | ✓        | ×                       | ?                        | ?                 |
| Frobell et al.22 (2010) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ✓                 |
| Frobell et al.23 (2013) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ✓                 |
| Chen et al.24 (2015)   | ✓                   | ✓                      | ✓        | ✓                       | ?                        | ?                 |
| Manandhar et al.25 (2018) | ×                  | ×                      | ✓        | ✓                       | ✓                        | ?                 |
| Eriksson et al.26 (2018) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ?                 |
| von Essen et al.16 (2020) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ?                 |
| von Essen et al.27 (2020) | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ?                 |
| Reijman et al.17 (2021)  | ✓                   | ✓                      | ✓        | ✓                       | ✓                        | ✓                 |

Note: ✓ = Low risk of bias, ? = Unclear risk of bias, × = High risk of bias.
Table 3. Patient and Treatment Characteristics of Included Trials

| Author                  | Timing of ACLR | No. of Patients | Age           | M/F  | Graft type | Associated lesions | Mechanisms of injury | Injury to surgery | Operation time (min) |
|-------------------------|----------------|-----------------|---------------|------|------------|--------------------|---------------------|-------------------|---------------------|
| Meighan et al.19 (2003)| Early          | 13              | 21 (15-35)    | 28/3 | hamstring | 3                  | 18 football, 6 rugby, 4 basketball | NA                | 67                  |
|                         | Delayed        | 18              |               |      |            | 4                  | NA                  | NA                | 74                  |
| Bottini et al.20 (2008)| Early          | 35              | 26.4 (18-40)  | 29/6 | hamstring | 32                 | 49 sports, 13 falls, 4 training accidents, 4 vehicle accidents | 9.0 ± 4.4          | 64.0 ± 25.5          |
|                         | Delayed        | 35              | 27.5(19-43)   | 29/6 | hamstring | 24                 | NA                  | NA                | 84.8 ± 38.2         | 61.5 ± 23.9         |
| Raviraj et al.21 (2010)| Early          | 51              | 31.6 ± 5.3    | 25/26 | hamstring | 38                 | 23 fall, 21 sports injury, 7 traffic accidents | 7 (2-14)           | 64.9 ± 7.8           |
|                         | Delayed        | 48              | 31.2 ± 5.3    | 26/22 | hamstring | 35                 | 15 fall, 24 sports injury, 9 traffic accidents | 32 (29-42)         | 64.2 ± 7.8           |
| Frobell et al.22 (2010)| Early          | 62              | 26.3 ± 5.1    | 48/12 | 36 hamstring, 25 BPTB | 39 | 35 soccer, 9 Alphine skiing, 7 floor hockey, 11 others | 23.4 ± 9.5 | NA |
|                         | Delayed        | 23              | 25.8 ± 4.7    | 16/7  | 10 hamstring, 13 BPTB | 30 | 42 soccer, 7 Alphine skiing, 2 floor hockey, 8 others | 347 ± 124 | NA |
|                         | Rehabilitation | 36              |               | 23/13 | NA         | NA                 | NA                  | NA                | NA                  |
| Frobell et al.22 (2013)| Early          | 62              | 26.6 ± 5.1    | 47/12 | 36 hamstring, 25 BPTB | NA | 35 soccer, 9 Alphine skiing, 7 floor hockey, 11 others | 23.4 ± 9.5 | NA |
|                         | Delayed        | 30              | 25.2 ± 4.5    | 19/11 | 15 hamstring, 15 BPTB | NA | 42 soccer, 7 Alphine skiing, 2 floor hockey, 8 others | 867 (743-1695) | NA |
|                         | Rehabilitation | 29              | 26.4 ± 4.9    | 20/9  | NA         | NA                 | NA                  | NA                | NA                  |
| Chen et al.24 (2015)    | Acute          | 27              | 29.4 ± 5.8    | 15/12 | LARS graft | NA | NA | 5.4 w (3–7) | NA |
|                         | Chronic        | 28              | 31.9 ± 7.0    | 11/17 | LARS graft | NA | NA | 7.2 m (6–11) | NA |
| Manandhara             | Early          | 53              | 30 (18-55)    | 83/21 | hamstring | 22 | 73 sports injury, 26 road traffic | 11.20 (4-21) | NA |

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| Study                          | Timing          | Age (years) | Gender (M/F) | Activity | Days | Return to Normality (weeks) | Notes |
|-------------------------------|-----------------|-------------|--------------|----------|------|----------------------------|-------|
| **Eriksson et al.25 (2018)** | Early           | 33          | 27.7±6.5     | hamstring | 20   | 10                         | 13 soccer, 6 indoor floorball, 7 Alphine skiing, 1 handball, 3 wrestling, 2 gymnastics, 1 Dance | 5 ± 2 | 93 ± 20 |
|                              | Delayed         | 35          | 26.1±5.7     | hamstring | 12   | 4                          | 13 soccer, 10 indoor floorball, 3 Alphine skiing, 4 handball, 1 Ice hockey, 1 football, 1 badminton, 1 basketball, 1 tennis | 55 ± 8 | 83 ± 18 |
| **von Essen et al.16 (2020)** | Early           | 33          | 27.7±6.5     | hamstring | 20   | 10                         | 13 soccer, 6 indoor floorball, 7 Alphine skiing, 7 other sports activity | 5 ± 2 | 93 ± 20 |
|                              | Delayed         | 35          | 26.1±5.7     | hamstring | 12   | 4                          | 13 soccer, 10 indoor floorball, 3 Alphine skiing, 9 other sports activity | 55 ± 8 | 83 ± 18 |
| **von Essen et al.27 (2020)** | Early           | 34          | 27.7±6.5     | hamstring | 20   | 10                         | 14 soccer, 6 indoor floorball, 7 Alphine skiing, 7 other sports activity | 5 ± 2 | 93 ± 20 |
|                              | Delayed         | 35          | 26.1±5.7     | hamstring | 12   | 4                          | 13 soccer, 10 indoor floorball, 3 Alphine skiing, 9 other sports activity | 55 ± 8 | 83 ± 18 |
| **Reijman et al.17 (2021)**  | Early           | 85          | 31.2±10.3    | 78 hamstring, 4BPTB | 38   | 23                         | NA | 39.0 (25.5-53.0) | NA |
| Rehabilitation with optional delayed |               | 82          | 31.4±10.7    | 41 ACLR, (38 hamstring, 3BPTB) | 37   | 16                         | NA | 40.5 (29.8-52.5) | NA |

Note: ACLR, anterior cruciate ligament reconstruction; BPTB, bone-patellar tendon-bone; NA, not available; LARS, ligament advanced reinforcement system.
| Author (Year) | Early ACLR | Elective delayed ACLR |
|--------------|------------|-----------------------|
| Meighan et al.19 (2003) | 2 deep vein thrombosis; 1 wound infection; 1 extension deficit; 1 painful tibial fixation screw; 1 knee stiffness | 1 knee stiffness; 1 subjective instability; 1 retear |
| Bottoni et al.20 (2008) | 1 intra-articular infection; 1 retear; one 5°-10° loss of extension; one > 10° loss of flexion; five 5°-10° loss of flexion | 1 retear; One >10° loss of extension; two 5°-10° loss of flexion; five 5°-10° loss of flexion |
| Raviraj et al.21 (2010) | 2 superficial wound infection | 1 pain |
| Frobell et al.22 (2010) | 2 subjective or clinical instability; 1 meniscal signs and symptoms; 6 pain, swelling, or both; 4 decreased ROM; 1 arthrofibrosis; 3 retear | 19 subjective or clinical instability; 13 meniscal signs and symptoms; 3 pain, swelling, or both; 1 decreased ROM; 1 retear |
| Frobell et al.23 (2013) | 19 radiographic osteoarthritis; 3 retear | 10 radiographic osteoarthritis; 1 retear |
| Chen et al.24 (2015) | 1 mild arthrofibrosis; 1 arthralgia due to loosen screw | 1 mild arthrofibrosis |
| Manandhara et al.25 (2018) | 1 infection | None |
| Eriksson et al.26 (2018) | Seven > 5° extension defects | Thirteen > 5° extension defects |
| von Essen et al.16 (2020) | 1 retear; four > 5° extension defects | 1 retear; five > 5° extension defects |
| von Essen et al.27 (2020) | NA | NA |
| MaxReij et al.17 (2021) | 4 retear; 3 ruptures of contralateral ACL; 1 tibial screw events; 4 meniscal tear; 2 extension deficit | 2 retear; 1 rupture of contralateral ACL; 2 tibial screw events; 3 meniscal tear; 4 extension deficit |

Note: ACLR, anterior cruciate ligament reconstruction; ROM, range of motion; NA, not available.

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**eFigure 1.** Forest Plot Depicting the Operative Time of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup | Early ACLR | Elective delayed ACLR | Mean Difference | Mean Difference |
|-------------------|------------|------------------------|----------------|----------------|
|                   | Mean      | SD         | Total | Mean   | SD   | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Bottoni 2008      | 64        | 25.5      | 34    | 61.5   | 23.9 | 35    | 15.7%  | 2.50 [-9.17, 14.17] |
| Eriksson 2018     | 93        | 20        | 33    | 83     | 18   | 35    | 21.3%  | 10.00 [0.94, 19.06] |
| Raviraj 2010      | 64.9      | 7.8       | 51    | 64.2   | 7.8  | 48    | 41.5%  | 0.70 [-2.37, 3.77]  |
| von Essen (12m) 2020 | 93    | 20        | 34    | 83     | 18   | 35    | 21.5%  | 10.00 [1.01, 18.99] |
| **Total (95% CI)** | 152       |           | 153   |        | 100.0% | 4.97 [-0.68, 10.61] |

Heterogeneity: Tau² = 17.52; Chi² = 6.62, df = 3 (P = 0.08); I² = 55%
Test for overall effect: Z = 1.72 (P = 0.08)

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eFigure 2. Forest Plots Depicting the Extension Deficit and Flexion Deficit of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup     | Early ACLR | Elective delayed ACLR | Mean Difference IV, Random, 95% CI |
|-----------------------|------------|------------------------|----------------------------------|
|                       | Mean       | SD                     | Total | Mean | SD | Total | Weight |
| 2.1.1 Follow-up 6 months |            |                        |       |      |    |       |        |
| Eriksson 2018         | 3          | 3                      | 33    | 4    | 3.5| 35    | 100.0% | -1.00 [-2.55, 0.55] |
| Subtotal (95% CI)     |            |                        |       |      |    |       |        | -1.00 [-2.55, 0.55] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.27 (P = 0.21) |
| 2.1.2 Follow-up 1 year |            |                        |       |      |    |       |        |
| Bottini 2008          | 0.6        | 1.6                    | 34    | 1.5  | 4.2| 35    | 43.9%  | -0.90 [-2.39, 0.59] |
| von Essen (12m) 2020  | 2          | 2.1                    | 31    | 3    | 3.3| 35    | 56.1%  | -1.00 [-2.32, 0.32] |
| Subtotal (95% CI)     |            |                        |       |      |    |       |        | -0.96 [-1.94, 0.03] |
| Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0% |
| Test for overall effect: Z = 1.90 (P = 0.06) |
| 2.1.3 Follow-up 2 years |            |                        |       |      |    |       |        |
| von Essen (24m) 2020  | 1.6        | 3                      | 28    | 1.3  | 2.5| 29    | 100.0% | 0.30 [-1.14, 1.74] |
| Subtotal (95% CI)     |            |                        |       |      |    |       |        | 0.30 [-1.14, 1.74] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.41 (P = 0.68) |
### Follow-up 6 months

| Study or Subgroup | Early ACLR Mean | SD | Total | Elective delayed ACLR Mean | SD | Total | Weight | Mean Difference | IV, Random, 95% CI |
|-------------------|----------------|----|-------|-----------------------------|----|-------|--------|-----------------|-------------------|
| Eriksson 2018     | 4.0            | 5.4| 33    | 5.4                         | 5.4| 35    | 100.0% | -1.00           | [-3.57, 1.57]     |
| Subtotal (95% CI) | 33             |    |       | 35                          | 100.0% | -1.00 | [-3.57, 1.57] |

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

### Follow-up 1 year

| Study or Subgroup | Early ACLR Mean | SD | Total | Elective delayed ACLR Mean | SD | Total | Weight | Mean Difference | IV, Random, 95% CI |
|-------------------|----------------|----|-------|-----------------------------|----|-------|--------|-----------------|-------------------|
| Bottoni 2008      | 2.1            | 3.9| 34    | 2.6                         | 4.8| 35    | 30.6%  | -0.50           | [-2.56, 1.56]     |
| von Essen (12m) 2020 | 1.8          | 2.2| 31    | 3.2                         | 3.4| 35    | 69.4%  | -1.40           | [-2.77, -0.03]    |
| Subtotal (95% CI) | 65             |    |       | 70                          | 100.0% | -1.13 | [-2.26, 0.01] |

Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.48); I² = 0%

Test for overall effect: Z = 1.94 (P = 0.05)

### Follow-up 2 years

| Study or Subgroup | Early ACLR Mean | SD | Total | Elective delayed ACLR Mean | SD | Total | Weight | Mean Difference | IV, Random, 95% CI |
|-------------------|----------------|----|-------|-----------------------------|----|-------|--------|-----------------|-------------------|
| von Essen (24m) 2020 | 1.75          | 2.8| 28    | 2.8                         | 4.1| 29    | 100.0% | -1.05           | [-2.87, 0.77]     |
| Subtotal (95% CI) | 28             |    |       | 29                          | 100.0% | -1.05 | [-2.87, 0.77] |

Heterogeneity: Not applicable

Test for overall effect: Z = 1.13 (P = 0.26)
eFigure 3. Forest Plot Depicting the Tegner Score of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup | Elective delayed ACLR | Early ACLR | Mean Difference | Mean Difference |
|------------------|-----------------------|------------|----------------|----------------|
|                  | Mean     | SD        | Weight   | IV, Random, 95% CI | IV, Random, 95% CI |
| 3.1.1 Follow-up 6 months |          |           |          | | |
| Mananandhar 2018     | 4.15     | 1.45      | 53       | 54 100.0% | 0.43 [-0.10, 0.96] |
| Subtotal (95% CI)    | 53       |           | 54       | 100.0% | 0.43 [-0.10, 0.96] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.59 (P = 0.11) |

| 3.1.2 Follow-up 1 year |          |           |          | | |
| Chen 2015            | 6.3      | 1.1       | 27       | 28 100.0% | 0.20 [-0.33, 0.73] |
| Subtotal (95% CI)    | 27       |           | 28       | 100.0% | 0.20 [-0.33, 0.73] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.74 (P = 0.46) |

| 3.1.3 Follow-up 5 years |          |           |          | | |
| Chen 2015            | 6.3      | 1.3       | 27       | 28 100.0% | 0.00 [-0.66, 0.66] |
| Subtotal (95% CI)    | 27       |           | 28       | 100.0% | 0.00 [-0.66, 0.66] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.00 (P = 1.00) |
**eFigure 4.** Forest Plots Depicting the IKDC Score and IDKC Rating Scale of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup | Early ACLR | Elective delayed ACLR | Mean Difference | Mean Difference |
|-------------------|------------|-----------------------|----------------|----------------|
|                   | Mean  | SD    | Total | Mean | SD   | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 4.1.1 Follow-up 6 months | | | | | | | | |
| Mananandhar 2018 | 69.68  | 8.14  | 53   | 67.14 | 6.08 | 51   | 10.4% | 2.54 [-0.21, 5.29] | |
| Reijman 2021     | 69.6  | 3.1   | 83   | 66.8 | 3   | 80   | 89.6% | 2.80 [1.86, 3.74] | |
| Subtotal (95% CI)| 136   |       | 131  | 100.0% | 2.77 [1.89, 3.66] | |

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%

Test for overall effect: Z = 6.13 (P < 0.00001)

Total (95% CI) 136 131 100.0% 2.77 [1.89, 3.66]

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%

Test for overall effect: Z = 6.13 (P < 0.00001)

Test for subuous differences: Not applicable

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Early ACLR Elective delayed ACLR Odds Ratio

| Study or Subgroup       | Early ACLR | Elective delayed ACLR | Odds Ratio          |
|-------------------------|------------|-----------------------|---------------------|
|                         | Events     | Total     | Events     | Total     | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| 4.2.1 Follow-up 6 months|            |           |            |           |        |                    |                    |
| Eriksson 2018           | 27         | 33        | 24         | 34        | 100.0% | 1.88 [0.59, 5.93]   |                    |
| Subtotal (95% CI)       |            |           |            |           |        |                    |                    |
| Total events            | 27         | 24        |            |           |        |                    |                    |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.07 (P = 0.28) |
| 4.2.2 Follow-up 1 year  |            |           |            |           |        |                    |                    |
| Meighan 2003            | 11         | 13        | 15         | 18        | 29.7%  | 1.10 [0.16, 7.74]   |                    |
| von Essen (12m) 2020    | 26         | 31        | 27         | 34        | 70.3%  | 1.35 [0.38, 4.79]   |                    |
| Subtotal (95% CI)       | 44         | 52        |            |           | 100.0% | 1.27 [0.44, 3.67]   |                    |
| Total events            | 37         | 42        |            |           | 100.0% |                    |                    |
| Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0% |
| Test for overall effect: Z = 0.44 (P = 0.66) |
| 4.2.3 Follow-up 2 year  |            |           |            |           |        |                    |                    |
| von Essen (24m) 2020    | 24         | 27        | 28         | 28        | 100.0% | 0.12 [0.01, 2.50]   |                    |
| Subtotal (95% CI)       | 27         | 28        |            |           | 100.0% | 0.12 [0.01, 2.50]   |                    |
| Total events            | 24         | 28        |            |           | 100.0% |                    |                    |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.36 (P = 0.17) |
| 4.2.4 Follow-up 5 year  |            |           |            |           |        |                    |                    |
| Chen 2015               | 26         | 27        | 26         | 28        | 100.0% | 2.00 [0.17, 23.44]  |                    |
| Subtotal (95% CI)       | 27         | 28        |            |           | 100.0% | 2.00 [0.17, 23.44]  |                    |
| Total events            | 26         | 26        |            |           | 100.0% |                    |                    |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.55 (P = 0.58) |

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eFigure 5. KOOS Subscales for Early ACLR and Elective Delayed ACLR Cohorts From Four Included Studies

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eFigure 6. Forest Plot of the Results of Re-Tear of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup       | Early ACLR | Elective delayed ACLR | Odds Ratio | M-H, Random, 95% CI Year |
|-------------------------|------------|------------------------|------------|----------------------------|
| Meighan 2003            | 0 13       | 1                      | 0.43 [0.02, 11.47] 2003 |
| Bottoni 2008            | 1 34       | 1                      | 1.03 [0.06, 17.16] 2008 |
| Frobell 2010            | 3 62       | 1                      | 2.95 [0.30, 29.18] 2010 |
| Chen 2015               | 0 27       | 0                      | Not estimable 2015 |
| von Essen (12m) 2020    | 1 34       | 1                      | 1.03 [0.06, 17.16] 2020 |
| Reijman 2021            | 4 85       | 2                      | 1.98 [0.35, 11.09] 2021 |
| Total (95% CI)          | 255        | 257 100.0%             | 1.52 [0.52, 4.43]   |
| Total events            | 9          | 6                      |

Heterogeneity: Tau² = 0.00; Ch² = 1.12, df = 4 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.44)
eFigure 7. Forest Plot of the Results Infection of Early ACLR Versus Elective Delayed ACLR

| Study or Subgroup | Early ACLR | Elective Delayed ACLR | Odds Ratio | Year |
|-------------------|------------|------------------------|------------|------|
| Meighan 2003      | 1          | 13                     | 4.44 [0.17, 118.00] | 2003 |
| Bottoni 2008      | 1          | 34                     | 3.18 [0.13, 30.79]  | 2008 |
| Raviraj 2010      | 2          | 51                     | 4.90 [0.23, 104.70] | 2010 |
| Chen 2015         | 0          | 27                     | Not estimable | 2015 |
| Mananandhar 2018  | 1          | 53                     | 2.94 [0.12, 73.92]  | 2018 |
| **Total (95% CI)**| **178**    | **180**                | **3.80 [0.77, 18.79]** |      |
| Total events      | 5          | 0                      |            |      |

Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 3 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.64 (P = 0.10)
**eFigure 8.** Forest Plots Depicting the Extension Deficit and Flexion Deficit of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup | Early ACLR | Delayed ACLR | Mean Difference |
|-------------------|------------|--------------|----------------|
|                   | Mean       | SD           | Total          | Mean | SD       | Total | Weight | IV, Random, 95% CI |
| 8.1.1 Follow-up 6 months |           |              |                |      |          |       |        |                    |
| Eriksson 2018     | 3          | 3            | 33             | 4    | 3.5      | 35    | 100.0% | -1.00 [-2.55, 0.55] |
| Subtotal (95% CI) | 33         |              |                |      |          | 35    | 100.0% | -1.00 [-2.55, 0.55] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.27 (P = 0.21) |

| 8.1.2 Follow-up 1 year |           |              |                |      |          |       |        |                    |
| Bottoni 2008        | 0.6       | 1.6          | 34              | 1.5  | 4.2      | 35    | 43.9%  | -0.90 [-2.39, 0.59] |
| von Essen (12m) 2020 | 2          | 2.1          | 34              | 3    | 3.3      | 35    | 56.1%  | -1.00 [-2.32, 0.32] |
| Subtotal (95% CI)   | 65         |              |                |      |          | 70    | 100.0% | -0.96 [-1.94, 0.03] |
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.01, df = 1 (P = 0.92); I^2 = 0% |
| Test for overall effect: Z = 1.90 (P = 0.06) |

| 8.1.3 Follow-up 2 years |           |              |                |      |          |       |        |                    |
| von Essen (24m) 2020   | 1.6       | 3            | 28              | 1.3  | 2.5      | 29    | 100.0% | 0.30 [-1.14, 1.74] |
| Subtotal (95% CI)      | 28         |              |                |      |          | 29    | 100.0% | 0.30 [-1.14, 1.74] |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.41 (P = 0.68) |
### 8.2.1 Follow-up 6 months

| Study or Subgroup | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-------------------|------------|--------------|-----------------|----------------|
|                   | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Eriksson 2018     | 4    | 5.4 | 33    | 5    | 5.4 | 35    | 100.0% | -1.00 [-3.57, 1.57] |                      |
| Subtotal (95% CI) |     |    |       |      |    |       |        | -1.00 [-3.57, 1.57] |                      |

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

### 8.2.2 Follow-up 1 year

| Study or Subgroup | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-------------------|------------|--------------|-----------------|----------------|
|                   | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Bottoni 2008      | 2.1  | 3.9 | 34    | 2.6  | 4.8 | 35    | 30.6%  | -0.50 [-2.56, 1.56] |                      |
| von Essen (12m) 2020 | 1.8  | 2.2 | 31    | 3.2  | 3.4 | 35    | 69.4%  | -1.40 [-2.77, -0.03] |                      |
| Subtotal (95% CI) |     |    |       |      |    |       |        | -1.13 [-2.26, 0.01] |                      |

Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.48); I² = 0%

Test for overall effect: Z = 1.94 (P = 0.05)

### 8.2.3 Follow-up 2 years

| Study or Subgroup | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-------------------|------------|--------------|-----------------|----------------|
|                   | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| von Essen (24m) 2020 | 1.75 | 2.8 | 28    | 2.8  | 4.1 | 29    | 100.0% | -1.05 [-2.87, 0.77] |                      |
| Subtotal (95% CI) |     |    |       |      |    |       |        | -1.05 [-2.87, 0.77] |                      |

Heterogeneity: Not applicable

Test for overall effect: Z = 1.13 (P = 0.26)

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eFigure 9. Forest Plot Depicting the Knee Laxity of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup | Early ACLR | Delayed ACLR | Std. Mean Difference |
|-------------------|------------|--------------|---------------------|
|                   | Mean  | SD  | Total | Mean  | SD  | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 9.1.1 Follow-up 6 months | | | | | | | | | |
| Eriksson 2018 | 2.3  | 1.4 | 32 | 1.8  | 1.2 | 33 | 100.0% | 0.38 [-0.11, 0.87] |
| Subtotal (95% CI) | 32 | | 33 | 100.0% | 0.38 [-0.11, 0.87] |
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z = 1.51 (P = 0.13) | | | | | |
| 9.1.2 Follow-up 1 year | | | | | | | | | |
| Bottini 2008 | 1.2  | 1.8 | 34 | 0.88 | 1.1 | 34 | 49.5% | 0.21 [-0.26, 0.69] |
| von Essen (24m) 2020 | 2  | 1.4 | 34 | 1.9 | 1.2 | 35 | 50.5% | 0.08 [-0.40, 0.55] |
| Subtotal (95% CI) | 68 | | 69 | 100.0% | 0.14 [-0.19, 0.48] |
| Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0% | | | | | |
| Test for overall effect: Z = 0.84 (P = 0.40) | | | | | |
| 9.1.3 Follow-up 2 year | | | | | | | | | |
| von Essen (24m) 2020 | 1.8 | 1.5 | 28 | 2 | 1.5 | 29 | 100.0% | -0.13 [-0.65, 0.39] |
| Subtotal (95% CI) | 28 | | 29 | 100.0% | -0.13 [-0.65, 0.39] |
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z = 0.50 (P = 0.62) | | | | | |
**eFigure 10.** Forest Plot Depicting the Lysholm Score of Early ACLR Versus Elective Delayed ACL After Redefinition

| Study or Subgroup     | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-----------------------|------------|--------------|-----------------|-----------------|
|                       | Mean       | SD           | Total           | IV, Random, 95% CI | IV, Random, 95% CI |
| 10.1.1 Follow-up 6 months |            |              |                 |                 |
| Eriksson 2018         | 76         | 16.2         | 33              | 79              | 15.2           | 35              | 39.3%           | -3.00 [-10.48, 4.48] |
| Reijman 2021          | 86.6       | 3.5          | 83              | 81.4            | 1.3            | 80              | 60.7%           | 5.20 [4.39, 6.01]   |
| Subtotal (95% CI)     | 116        | 115          | 100.0%          |                 |                |                 | 1.98 [-5.87, 9.83] |
| Heterogeneity: Tau² = 26.26; Chi² = 4.57, df = 1 (P = 0.03); I² = 78% |
| Test for overall effect: Z = 0.49 (P = 0.62) |

10.1.2 Follow-up 1 year

| Study or Subgroup     | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-----------------------|------------|--------------|-----------------|-----------------|
|                       | Mean       | SD           | Total           | IV, Random, 95% CI | IV, Random, 95% CI |
| Reijman 2021          | 90.3       | 1.3          | 85              | 86.2            | 1.4            | 82              | 50.3%           | 4.10 [3.69, 4.51]   |
| von Essen (24m) 2020  | 87         | 1.8          | 34              | 88              | 1.7            | 35              | 49.7%           | -1.00 [-1.83, -0.17] |
| Subtotal (95% CI)     | 119        | 117          | 100.0%          |                 |                |                 | 1.56 [-3.43, 6.56] |
| Heterogeneity: Tau² = 12.89; Chi² = 117.35, df = 1 (P < 0.00001); I² = 99% |
| Test for overall effect: Z = 0.61 (P = 0.54) |

10.1.3 Follow-up 2 years

| Study or Subgroup     | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|-----------------------|------------|--------------|-----------------|-----------------|
|                       | Mean       | SD           | Total           | IV, Random, 95% CI | IV, Random, 95% CI |
| Reijman 2021          | 90.6       | 2.7          | 83              | 87.1            | 2.7            | 80              | 53.3%           | 3.50 [2.67, 4.33]   |
| von Essen (24m) 2020  | 88.05      | 2.4          | 28              | 86.46           | 2.5            | 29              | 46.7%           | 1.59 [0.32, 2.86]   |
| Subtotal (95% CI)     | 111        | 109          | 100.0%          |                 |                |                 | 2.61 [0.74, 4.48] |
| Heterogeneity: Tau² = 1.52; Chi² = 6.08, df = 1 (P = 0.01); I² = 84% |
| Test for overall effect: Z = 2.74 (P = 0.006) |

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**Figure 11.** Forest Plot Depicting the Tegner Score of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup          | Early ACLR | Delayed ACLR | Mean Difference | Mean Difference |
|---------------------------|------------|--------------|-----------------|-----------------|
|                           | Mean       | SD           | Total           | Mean            | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 11.1.1 Follow-up 6 months | 4.15       | 1.45         | 53              | 3.72            | 54      | 100.0%             | 0.43 [-0.10, 0.96]  |
| Mananandhar 2018          | 53         |              |                 | 54              | 100.0%             | 0.43 [-0.10, 0.96]  |
| Subtotal (95% CI)         | 53         |              |                 | 54              | 100.0%             | 0.43 [-0.10, 0.96]  |
| Heterogeneity: Not applicable |           |              |                 |                 |                     |                     |
| Test for overall effect: Z = 1.59 (P = 0.11) | | | | | |
| Total (95% CI)            | 53         |              |                 | 54              | 100.0%             | 0.43 [-0.10, 0.96]  |
| Heterogeneity: Not applicable |           |              |                 |                 |                     |                     |
| Test for overall effect: Z = 1.59 (P = 0.11) | | | | | |
| Test for subroous differences: Not appicable | | | | | |
**eFigure 12.** Forest Plots Depicting the IKDC Score and IKDC Rating Scale of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup | Early ACLR Mean | Early ACLR SD | Early ACLR Total | Delayed ACLR Mean | Delayed ACLR SD | Delayed ACLR Total | Mean Difference IV, Random, 95% CI | Weight |
|-------------------|-----------------|---------------|------------------|------------------|----------------|-------------------|----------------------------------|--------|
| 12.1.1 Follow-up 6 months |
| Mananandhar 2018   | 69.63           | 8.14          | 53               | 67.14            | 6.08           | 51                | 2.54 [-0.21, 5.29]               | 10.1%  |
| Reijman 2021       | 69.63           | 3.1           | 85               | 66.68            | 3             | 82                | 2.80 [1.87, 3.73]                | 89.9%  |
| Subtotal (95% CI)  | 138             | 133           | 100.0%           |                  |                |                   | 2.77 [1.90, 3.65]                |        |
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.03, df = 1 (P = 0.86); I^2 = 0% |
| Test for overall effect: Z = 6.20 (P < 0.00001) |

| 12.1.2 Follow-up 1 year |
| Reijman 2021           | 81.63           | 1.9           | 85               | 74.43            | 1.9           | 82                | 7.20 [6.62, 7.78]                | 100.0% |
| Subtotal (95% CI)      | 85              | 82            | 100.0%           |                  |                |                   | 7.20 [6.62, 7.78]                |        |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 24.48 (P < 0.00001) |

| 12.1.3 Follow-up 2 years |
| Reijman 2021           | 84.73           | 3             | 85               | 79.43            | 3             | 82                | 5.30 [4.39, 6.21]                | 100.0% |
| Subtotal (95% CI)      | 85              | 82            | 100.0%           |                  |                |                   | 5.30 [4.39, 6.21]                |        |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 11.41 (P < 0.00001) |
| Study or Subgroup | Early ACLR Events | Total Events | Delayed ACLR Events | Total Events | Weight | Odds Ratio M-H | Random | 95% CI |
|-------------------|------------------|--------------|---------------------|--------------|--------|----------------|---------|--------|
| 12.2.1 Follow-up 6 months |                |              |                     |              |        |                |         |        |
| Eriksson 2018     | 27              | 33           | 24                  | 34           | 100.0% | 1.88           |         | [0.59, 5.93] |
| Subtotal (95% CI) | 33              | 34           | 100.0%              |              | 1.88   | [0.59, 5.93]   |         |        |
| Total events      | 27              | 24           |                      |              |        |                |         |        |

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.28)

| 12.2.2 Follow-up 1 year |                |              |                     |              |        |                |         |        |
|-------------------------|                |              |                     |              |        |                |         |        |
| Meighan 2003            | 11              | 13           | 15                  | 18           | 29.7%  | 1.10           |         | [0.16, 7.74] |
| von Essen (12m) 2020    | 26              | 31           | 27                  | 34           | 70.3%  | 1.35           |         | [0.38, 4.79] |
| Subtotal (95% CI)       | 44              | 52           | 100.0%              |              | 1.27   | [0.44, 3.67]   |         |        |
| Total events            | 37              | 42           |                      |              |        |                |         |        |

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)

| 12.2.3 Follow-up 2 years |                |              |                     |              |        |                |         |        |
|--------------------------|                |              |                     |              |        |                |         |        |
| von Essen (24m) 2020     | 24              | 27           | 28                  | 28           | 100.0% | 0.12           |         | [0.01, 2.50] |
| Subtotal (95% CI)        | 27              | 28           | 100.0%              |              | 0.12   | [0.01, 2.50]   |         |        |
| Total events             | 24              | 28           |                      |              |        |                |         |        |

Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.17)
**eFigure 13.** Forest Plot of the Results of Re-Tear of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup     | Early ACLR Events | Total | Delayed ACLR Events | Total | Weight | Odds Ratio | M-H, Random, 95% CI | Year |
|-----------------------|-------------------|-------|---------------------|-------|--------|------------|---------------------|------|
| Meighan 2003          | 0                 | 13    | 1                   | 18    | 13.6%  | 0.43 [0.02, 11.47] | 2003 |
| Bottoni 2008          | 1                 | 34    | 1                   | 35    | 18.5%  | 1.03 [0.06, 17.16] | 2008 |
| von Essen (12m) 2020  | 1                 | 34    | 1                   | 35    | 18.5%  | 1.03 [0.06, 17.16] | 2020 |
| Reijman 2021          | 4                 | 85    | 2                   | 82    | 49.3%  | 1.98 [0.35, 11.09] | 2021 |
| Total (95% CI)        | 166               | 170   | 100.0%              |       |        | 1.26 [0.38, 4.23]  |      |

Total events 6

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 0.71, df = 3 (P = 0.87); I^2 = 0\%$

Test for overall effect: $Z = 0.38 (P = 0.71)$

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**eFigure 14.** Forest Plot of the Results Infection of Early ACLR Versus Elective Delayed ACLR After Redefinition

| Study or Subgroup   | Early ACLR | Delayed ACLR | Odds Ratio M-H, Random, 95% CI | Year |
|---------------------|------------|--------------|-------------------------------|------|
| Meighan 2003        | 1          | 13           | 4.44 [0.17, 118.00]            | 2003 |
| Bottini 2008        | 1          | 34           | 3.18 [0.13, 80.79]             | 2008 |
| Mananandhar 2018    | 1          | 53           | 2.94 [0.12, 73.92]             | 2018 |
| Total (95% CI)      | 100        | 104          | 3.45 [0.53, 22.50]             |      |
| Total events        | 3          | 0            |                               |      |

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.30 (P = 0.19)