Whittaker et al., Risk factors for knee osteoarthritis after knee trauma

Supplementary File: Extra Web Material

1. Database Search Strategies

MEDLINE (OVID)

(exp Knee Injuries/ OR ((Knee/ OR Patella/ OR Patellofemoral Joint/ OR Knee Joint/) AND (Athletic Injuries/ OR Joint Dislocations/ OR Rupture/ OR "Wounds and Injuries"/ OR Reconstructive Surgical Procedures/)) OR (((knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) ADJ3 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*)) OR meniscectom* OR patellectom*).ab,ti.) AND (Osteoarthritis/ OR Osteoarthritis, Knee/ OR (osteoarthrit* OR osteo-arthrit* OR Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR ((degenerat* OR arthrit* OR oa) ADJ3 (knee* OR joint*))).ab,ti.) AND (Systematic Review/ OR Meta-Analysis/ OR Randomized Controlled Trial/ OR exp Cohort Studies/ OR ((systematic* ADJ3 review*) OR meta-analy* OR ((random*) ADJ3 trial*) OR cohort* OR follow-up OR longitudinal* OR prospectiv* OR retrospectiv*).ab,ti.) AND (Risk Factors/ OR Risk/ OR Causality/ OR Prognosis/ OR (risk OR risks OR causa* OR prognos* OR consequence* OR history OR prior OR relationship* OR predict* OR subsequent*).ab,ti.) AND english.la.

EMBASE (OVID)

('knee injury'/exp OR 'knee surgery'/de OR 'knee ligament surgery'/exp OR 'meniscal surgery'/exp OR (('knee'/de OR 'patella'/de OR 'knee ligament'/exp OR 'patellofemoral joint'/de OR 'knee meniscus'/de) AND ('sport injury'/de OR 'joint dislocation'/de OR 'rupture'/de OR 'ligament rupture'/exp OR 'tendon rupture'/de OR 'injury'/de OR 'joint injury'/exp OR 'reconstructive surgery'/de)) OR (((knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) NEAR/3 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*)) OR meniscectom* OR patellectom*):ab,ti) AND ('osteoarthritis'/de OR 'knee osteoarthritis'/de OR 'knee arthritis'/de OR 'Knee Injury and Osteoarthritis Outcome Score'/de OR (osteoarthrit* OR osteo-arthrit* OR Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR ((degenerat* OR arthrit* OR oa) NEAR/3 (knee* OR joint*))):ab,ti) AND ('systematic review'/de OR 'meta analysis'/de OR 'randomized controlled trial'/de OR 'cohort analysis'/de OR 'longitudinal study'/de OR 'prospective study'/de OR 'follow up'/de OR 'retrospective study'/de OR ((systematic* NEAR/3 review*) OR meta-analy* OR ((random*) NEAR/3 trial*) OR cohort* OR follow-up OR longitudinal* OR prospectiv* OR retrospectiv*):ab,ti) AND ('risk factor'/de OR 'risk'/exp OR 'causality'/de OR 'prognosis'/de OR 'prognostic assessment'/de OR 'patient history of therapy'/de OR 'patient history of surgery'/de OR history/de OR 'medical history'/de OR prediction/de OR 'predictive value'/de OR (risk OR risks OR causa* OR prognos* OR consequence* OR history OR prior OR relationship* OR predict* OR subsequent*):ab,ti) NOT [conference abstract]/lim AND [English]/lim

CINAHL (EBSCO)

(MH Knee Injuries+ OR ((MH Knee OR MH Patella OR MH Knee Joint) AND (MH Athletic Injuries OR MH Dislocations OR MH Rupture OR MH "Wounds and Injuries" OR MH Surgery, Reconstructive)) OR TI(((knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) N2 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*)) OR meniscectom* OR patellectom*) OR AB(((knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) N2 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*)) OR meniscectom* OR patellectom*)) AND (MH Osteoarthritis OR MH Osteoarthritis, Knee OR TI(osteoarthrit* OR osteo-arthrit* OR Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR ((degenerat* OR arthrit* OR oa) N2 (knee* OR joint*))) OR AB(osteoarthrit* OR osteo-arthrit* OR

Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR ((degenerat* OR arthrit* OR oa) N2 (knee* OR joint*)))) AND (MH Systematic Review OR MH Meta-Analysis OR MH Randomized Controlled Trials OR MH Prospective Studies+ OR TI((systematic* N2 review*) OR meta-analy* OR ((random*) N2 trial*) OR cohort* OR follow-up OR longitudinal* OR prospectiv* OR retrospectiv*) OR AB((systematic* N2 review*) OR meta-analy* OR ((random*) N2 trial*) OR cohort* OR follow-up OR longitudinal* OR prospectiv* OR retrospectiv*)) AND (MH Risk Factors OR MH Causality OR MH Prognosis OR TI(risk OR risks OR causa* OR prognos* OR consequence* OR history OR prior OR relationship* OR predict* OR subsequent*) OR AB(risk OR risks OR causa* OR prognos* OR consequence* OR history OR prior OR relationship* OR predict* OR subsequent*)) AND LA(English)

SPORTdiscus (EBSCO)

(knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) n2 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*) OR meniscectom* OR patellectom*) AND osteoarthrit* OR osteo-arthrit* OR Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR (degenerat* OR arthrit* OR oa) n3 (knee* OR joint*) AND systematic review OR meta-analy* OR (random*) n2 (trial*) OR cohort OR longitudinal study OR prospective study OR follow-up OR retrospective study

Cochrane CENTRAL

((((knee* OR patell* OR tibiofemoral OR ACL OR PCL OR cruciate-ligament* OR MCL OR LCL OR menisc*) NEAR/3 (injur* OR tear* OR sprain* OR strain* OR dislocat* OR reconstruct* OR surg* OR repair* OR sublux* OR resect* OR repair* OR reconstruct* OR shav* OR lesion* OR defect* OR deficien* OR wound* OR damage* OR torn OR trauma* OR posttrauma* OR surger* OR reconstruct*)) OR meniscectom* OR patellectom*):ab,ti) AND ((osteoarthrit* OR osteo-arthrit* OR Arthrosis OR Arthroses OR Osteoarthros* OR gonarthr* OR ((degenerat* OR arthrit* OR oa) NEAR/3 (knee* OR joint*))):ab,ti) AND ((risk OR risks OR causa* OR prognos* OR consequence* OR history OR prior OR relationship* OR predict* OR subsequent*):ab,ti)

2. Quality in Prognostic Studies (QUIPS) Risk of Bias Tool Signaling Questions and Risk Definition Guidance

The Quality in Prognostic Studies (QUIPS) risk of bias tool requires research groups to establish definitions of risk level for each signaling question within each risk domain (e.g., selection bias) to match the context of their review.[1] Risk level definitions were operationalized based on QUIPS development,[1] and prognostic factor best practice recommendations.[2] Guidance pertaining to statistical analysis and regression model building, and results reporting, was sought from the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) checklist (statistical analysis and regression model building),[3] Prognosis Research Strategy (PROGRESS) 2,[4] and criteria for classifying and reporting osteoarthritis.[5] Finally, a comparable prognostic factor review assessing hip osteoarthritis,[6] a research report outlining the approach used to operationalize the QUIPS for a prognostic factor review of pain rehabilitation,[7] and foundational data imputation (i.e., missing data)[8] and epidemiologic principles were considered where applicable. Guidance within the context of post-traumatic knee osteoarthritis was provided from content matter experts within the authorship group (CBJ, SL). All team members approved the questions prior to study assessments.

SIGNALING QUESTION	DEFINITIONS
Section 1: Biases Related to Study Participation	
Adequate participation in the study by eligible persons	Low = Number of enrolled participants and number of eligible participants assessed are reported. Moderate = Number of eligible participants assessed are reported, but participation is low (<20%). High = Number of eligible participants assessed not reported.
Description of the source population	Low = Source population is reported in depth (e.g., pivoting athletes with ACL injuries, 10-20 years old). Moderate = Source population is reported in general (e.g., persons with ACL injuries). Low = When retrospective sufficient detail from the 'parent' study is reported (reference provided).
Description of the baseline study sample	Low = At least age, sex, BMI, and injury type(s) are reported. *If any information is missing, downgrade based on context and amount of missing information.*
Description of sampling frame and method of recruitment	Low = Clearly states who (e.g., persons with isolated ACL tear) was sampled and methods. Ideally methods minimize selection bias (e.g., consecutive cases, incident cases, randomized or probability-based sampling). When retrospective, selection criteria (i.e., one inclusion criteria) is reported.
Description of period and place of recruitment	Low = Clearly reports both recruitment period and site. High = Does not report recruitment period or site.
Inclusion and exclusion criteria	Low = Explicitly reports at least 1 inclusion criteria. High = No selection criteria information reported.
Section 2: Biases Related to Study Attrition	
Adequate response rate over study period	Low = ≥80%.
Attempts to collect information on dropouts	Low = One attempt and method reported (i.e., letters, phone calls, number of attempts). Moderate = No information on number of attempts or methods reported.
Reasons for loss to follow-up	Low = Number of participants and reasons for loss to follow-up reported. High = No reason(s) for participant loss to follow-up reported.

Description of participants lost to follow-up	Low = Demographic description (minimum age and sex) of participants lost to follow-up reported. Moderate = Only age OR sex of participants lost to follow-up is reported. High = No information about participants lost to follow-up is reported.
Differences between participants who completed the study vs those lost to follow-up	Low = Analysis comparing (at a minimum the age and sex) those retained in the study vs those lost to follow-up is performed, and no differences exist. High = Analysis comparing those retained in the study vs those lost to follow-up is not reported or clinically meaningful differences exist between the two groups.
Section 3: Biases Related to Prognostic Factor Measurement	
Clear, operationalized definition of the prognostic factor	Low = Clear description of how the prognostic factor was operationalized.
Methods of prognostic factor measurement	Low = Methods used to measure the prognostic factor are clearly detailed including at a minimum the system and its measurement properties (relevant reference). Moderate = The measurement properties of the measurement system are NOT reported. High = Methods used to measure the prognostic factor are not reported.
Methods of prognostic factor measurement the same for all participants	Low = Methods for measuring the prognostic factor(s) are the same for all participants, regardless of exposure status/demographics. Any deviations are noted and adequately justified. Moderate = Deviations in methods to measure the prognostic factor(s) reported but NOT justified. High = Methods for measuring the prognostic factor(s) differ based on exposure status.
How were variables treated	Low = Continuous variables are treated as continuous, or logical and pre-specified categories based on referenced literature (i.e., for dichotomous/categorical variables there is a pre-specified cut-off). Moderate = Information of how the prognostic variable was treated in NOT reported. High = Cut-offs for dichotomous/categorical variables are based on data distribution.
Proportion of sample with complete data	Low = Baseline prognostic factors are measured and reported for 100% of enrolled participants. Moderate = Baseline prognostic factors are measured and reported for 90-99% of participants. High = Baseline prognostic factors are measured and reported for <90% of enrolled participants.
How was missing prognostic factor data handled	Low = Missing prognostic factor data is reported and handled through appropriate imputation methods when necessary. Complete case analysis based on <11% missing data. Moderate = Complete case analysis performed with >10% missing data. High = Missing prognostic factor data is not reported.
Section 4: Biases Related to Outcome Measurement	
A clear, operationalized definition of the outcome (osteoarthritis)	Low = A clear definition of osteoarthritis (e.g., radiographic, MRI, diagnostic code) is reported. If a grading scale is used it must be described (reference). Moderate = A clear definition of osteoarthritis is NOT reported

Methods of outcome measurement	Low = Methods used to measure OA are clearly reported, including who the assessor was (blinding to exposure status is expected), when (time points) OA was assessed, how OA was measured and the properties of the measurement system (i.e., reliability and validity). Moderate = Methods reported but the measurement properties of the system are not provided OR multiple outcomes are used to assess OA without justification. High = Methods not reported OR no justification for not blinding reported.
Methods of outcome measurement were the same for all participants	Low = Methods used are the same for all participants, regardless of exposure status/demographics with any deviations noted and adequately justified. Moderate = Outcome measurement deviations occurred but not justified. High = Methods differed based on exposure status.
Section 5: Biases Related to Confounding	
Definitions and conceptual justification of important confounders	Low = Clear definition of potential confounder(s) with supporting evidence or conceptual rationale reported. Moderate = No mention of potential confounders.
Important confounders are measured and reported	Low = A minimum four confounding variable (i.e., age, sex, injury type, BMI) are measured and reported (unless age, sex, injury type or BMI are the primary prognostic factor). If confounding was not assessed or addressed, justification related to the relationship between prognostic factor and outcome is reported. High = No reporting of confounding, or justification of confounders considered.
Methods of confounder measurement	Low = Methods to measure confounders are clearly reported including measurement properties, AND the methods are the same for all participants, regardless of exposure status. Any deviations are reported and adequately justified. Moderate = Deviations occurred and were NOT justified. High = Methods differed based on exposure status.
How was missing confounder data handled	Low = Missing data was reported and handled through appropriate imputation methods when necessary. Moderate = Complete case analysis performed with >10% missing data. High = No mention of missing confounder data.
Methods of confounder adjustment	Low = Methods used to account for potential confounders are reported and include acceptable methods related to the study design (e.g., stratification, matching, randomization) or analysis (using stratification or adjustment). Moderate = Adjustments were performed, but continuous confounding variable data was categorized without an appropriate, pre-specified cut off. High = Known confounders were not adjusted for.
Section 6: Bias Related to Statistical Analysis and Reporting	
Data presentation and adequacy of analytic strategies	Low = Analytic strategy for the prognostic variable and outcome relationship is clearly stated, with statistical estimate and confidence intervals reported. Moderate = Analytic strategy is not clear, or not appropriate based on

	the hypothesis, OR no confidence intervals for the estimate are reported (when applicable). High = Analytic strategy is not reported in sufficient detail to enable replication.
Regression model building approach	Low = When regression was used, a clear description of the methods used to build the model (e.g., stepwise, adding in pre-specified confounders) was reported. Moderate = No description of the model building strategy is reported. High = Incorrect model was used based on outcome variable (i.e., linear for categorical outcome).
The selected regression model matches the study design	Low = The model selected matches the study hypothesis/aim, OR is performed according to a pre-published protocol.
Selective reporting	Low = All results related to prognostic factors and OA outcome are reported in text or in clearly interpretable figures/tables. All statistical models (or analyses) report an estimate, and error (SE, SD, range or CI). Moderate = Results for non-significant findings are not reported.

BMI (body mass index), OA (osteoarthritis), SD (standard deviation), SE (Standard Error), CI (confidence interval), MRI (magnetic resonance imaging)

References

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6. Teirlinck CH, Dorleijn DMJ, Bos PK, et al. Prognostic factors for progression of osteoarthritis of the hip: a systematic review. *Arthritis Res Care* 2019;21(1):192. doi: 10.1186/s13075-019-1969-9 [published Online First: 2019/08/25]
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3: Semi-quantitative Synthesis Approach

Semi-quantitative syntheses[1] involved rating the quality and confidence of evidence for potential risk factors using a similar modified GRADE approach with adaptations to assess non-pooled data across all six domains. Specifically;

1. Phase of investigation (study design)[2] was rated as low-quality (Phase 1 exploratory design aimed at identifying associations), or high-quality (Phase 2 explanatory design testing an independent prognostic factor and outcome association, or Phase 3 explanatory design aimed at understanding or explaining a prognostic pathway).[2] Risk factors assessed with both Phase 2 and 3 studies were rated high-quality, while factors with Phase 1, 2 and 3 or Phase 1 and 2 were rated moderate-quality.
2. Methodological weakness (risk of bias) was rated based on QUIPS assessments as 'no serious limitations' (mostly low and no or minimal moderate ratings), 'serious limitations' (moderate and high ratings in ≥1 domain), and 'very serious limitations' (mostly moderate or high ratings). Consideration was given (no downgrading) when there were ≥2 Phase 3 or 2 studies for a given risk factor with no serious limitations regardless of Phase 1 studies with serious or very serious limitations.
3. Inconsistency was rated as present when estimates varied in direction, with minimal 95%CI overlap or, absent when estimates were similar in direction with 95%CI overlap.
4. Indirectness was considered in relation to this review's objective, risk factor definition, risk factor comparison, and sample characteristics. If a risk factor was only assessed in one knee injury type, it was considered indirect given the aim to broadly identify risk factors for OA after knee trauma.
5. Imprecision was rated as present if the sample size calculation for a risk factor and OA outcome relationship was not presented, or wide 95%CIs indicated important opposite directions of potential effect.[1] Imprecision was rated as absent if there was an adequate sample size and narrow 95%CIs.
6. Publication bias was rated present when a relationship between a risk factor and OA outcome was reported, and either 1) the estimate and p-value were not reported due to a lack of statistical significance[3] or, 2) a moderate to large effect was reported based on a reasonably small (n≤100) sample size.[4]

The quality of evidence was upgraded for a consistent moderate (OR≥2) or large (OR≥5) effect,[3] or consistent evidence of an exposure-gradient response.[3] All domain ratings were considered when assigning an overall judgement of high, moderate, low, or very-low quality of evidence[1] and a corresponding statement of confidence in the direction (considering consistency reported across studies) and magnitude of the risk factor and OA relationship was generated.

References

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4. Study Characteristics

Author, Year (Design, Phase)	Sample n (% female)	Primary Injury	Treatment	Injury to Baseline (months)[1,2]	Injury Age (years)[2,3]	Baseline BMI (kg/m²)[2]	Prognostic Factor(s)	Follow-up (years)[2]	OA Outcome	Joint
Aga, 2018 (RCT, 2)	113 (24)	ACL+	ACLRc	DB: 15.5±18.2 SB: 15.7±20.3	DB: 27.4±6.3 SB: 27.1±5.5	DB: 25.1±2.9 SB: 24.5±3.1	Graft bundle #	DB: 2.0±.1 SB: 2.1±.2	Radiograph[5]	TF
Ahlden, 2009 (RCT, 2)	44 (32)	ACL+	ACLRc	ST: 17 (3-240) BPTB: 11 (2-252)	ST: 29 (15-40)[14] BPTB: 26 (14-48)[14]	NR	Graft source	7.4 (5.8-9.2)	Radiograph[6,7]	TF, PFJ
Ahn, 2012 (RC, 1)	117 (25)	ACL+	ACLRc	42.7 (.5-360)	29.2 (17-51)	24.2±3.3	Age at Sx BMI at Sx Injury to Sx (time) Meniscal Tx Joint morphology	10.3 (8-13.1)	Radiograph[8]	TF, PFJ
Akelman, 2017 (RCT, 2)	T1: 85 (56) T2: 72 (NR)	ACL	ACLRc	<12	High Tension: 23 Low Tension: 24	NR	Graft tension	T1: 5 T2: 6.7	Radiograph,[9] MRI,[11] KOOS	TF, PFJ
Barenius, 2014 (RCT, 2)	134 (41)	ACL+	ACLRc	BPTB: 13.9±23 ST: 16.3±23	40.0±6.4[15]	NR	Sex Age at injury BMI at Sx Occupation Meniscal Tx Graft source TF joint laxity	14.1±.5	Radiograph[5]	TF, PFJ
Bjornsson, 2016 (RCT, 2)	147 (35)	ACL+	ACLRc	PT: 11.5 (2-252) HT: 14.0 (2-360)	PT: 26 (14- 52)[14] HT: 26 (15-59)[14]	NR	Graft source	PT: 16.9±.9 ST: 16.0±1.3	Radiograph[5,6,7]	TF, PFJ
Cantin, 2016 (RC, 1)	589 (41)	ACL+	ACLRc	22±41	29.7±9	23.9±3.3	Age at Sx Cartilage injury Meniscus Tx TF joint laxity	11.9±.8	Radiograph[8]	TF, PFJ
Castoldi, 2020 (RCT, 2)	45 (26)	ACL+	ACLRc	NR	26 (15-40)	NR	Graft augmentation	19.4 (19-20.2)	Radiograph[6,10]	TF, PFJ
Culvenor 2017 (RC, 2)	T1: 181 (42) T2: 142 (NR)	ACL+	ACLRc	NR	27 ± 8	26.5±3.7	Post-ACLRc pain	T1: ~15 T2: ~20	Radiograph,[5] pain	PFJ
Curado, 2019 (RC, 1)	182 (63)	ACL+	ACLRc	~16	26 ± 7	23.4±2.6	Age at Sx Return to sport Meniscus Tx TF joint laxity Post-ACLRc Sx	22±1	Radiograph[8]	TF, PFJ
Drogset, 2006 (RCT, 2)	103 (NR)	ACL+	ACLRc, ACLRp	NR	29 (16-50)	NR	Graft augmentation	~16	Radiograph[6]	TF
Drogset, 2002 (RCT, 2)	68 (55)	ACL+	ACLRc	42 (1-180)	26 (16-48)[14]	NR	Concomitant injury Graft augmentation	~8	Radiograph[6]	TF
Elveos, 2018 (RCT, 2)	56 (55)	ACL+	ACLRc	BPTB: 40 (1-180) LAD: 46 (3-168)	BPTB: 25 (16-42) LAD: 27 (17-48)	NR	Graft augmentation	25 (24-26)	Radiograph[6]	TF
Filbay, 2021 (PC, 1)	251 (NR)	ACL+	ACLRc, ACLnoSx	5±4[13]	23 (19-28)[4]	27 (24, 29)[15]	Sex Meniscal Tx ACL Tx at 4yr 4yr knee function 4yr joint ROM 4yr TF joint laxity 4yr activity level 4yr SR function	32-37	Radiograph[5], KOOS	TF, PFJ
Frobell, 2013 (RCT, 2)	113 (27)	ACL+	ACLRc, ACLnoSx	<1	Early: 26.4±5.1 Delay: 25.8±4.7	Early: 24.5±3.1 Delay: 23.8±2.6	Tx approach	~5	Radiograph[9]	TF, PFJ
Gifstad, 2013 (RC, 1)	108 (56)	ACL+	ACLRc	Revision: 14 (0-178) Primary: 14 (2-180)	Revision: 34 (20-57)[15] Primary: 36 (20-57)[15]	NR	ACLRc revision	7.5 (2.8-13.2)	Radiograph[5]	TF
Gudas, 2012 (RCT, 2)	57 (37)	Cartilage	OAT, MF	NR	OCD: 24.6±6.5[14] ACD: 24.3±6.8[14]	NR	Cartilage Sx	10.4 (9-11)	Radiograph[5]	TF

Haberfield, 2021 (PC, 1)	111 (36)	ACL+	ACLR	Pivot: 3.1 (4.3) + 12 No Pivot: 4.0 (6.8) + 12	Pivot: 22 (7)[14] No Pivot: 31(14)[14]	Pivot: 26.1 ± 3.7 No Pivot: 25.9 ± 3.8	Return to pivot sport	~5	Radiographs[9]	TF, PFJ
Hagmeijer, 2019 (RC, 1)	196 (36)	ACL+ meniscus	ACLRc, ACLnoSx	NR	28.9±9.6	NR	Age at injury Tx approach ACLRc timing Meniscus Sx	17.5 (3.9-26.3)	Radiograph[5], Diagnostic Code	TF
Holm, 2010 (RCT, 2)	57 (42)	ACL?	ACLRc	HT: 40.5± 41.6 PT: 41.3± 41.0	HT: 27±9[14] PT: 25±7[14]	HT: 25.2±2.8 PT: 26.5±3.5	Graft source	HT: 10.7±.4 PT: 10.2±.4	Radiograph[5]	TF
Holm, 2012 (RCT, 2)	53 (39)	ACL+	ACLRc	Open: 46±74 Endo: 41± 62	Open: 29.2±7.5 Endo: 27±9.4	Open: 26.6±3.6[15] Endo: 27±3.5[15]	ACLRc Sx technique	Open: 11.9±.5 Endo: 11.7±.5	Radiograph[5]	TF
Hoogeslag, 2019 (RCT, 2)	44 (23)	ACL+	ACLRc, ACLRp	ACLRp: 13 (12-16)[13] ACLRc: 47 (42-71)[13]	ACLRp: 21 (10-27) ACLRc: 22 (19.3-25)	ACLRp: 23 (21-24.5)[4] ACLRc: 23 (22.1-24.4)[4]	ACLRc Sx technique	~2	Radiograph[5]	TF
Hamrin Senorski, 2019 (RCT, 1)	124 (36)	ACL+	ACLRc	13 (2-360)	27.9±8.3	NR	Age at Sx Injury to Sx (time)	16.4 (15.4-17.1)	Radiographs[5]	TF, PFJ
Janssen, 2013 (PC, 1)	86 (34)	ACL+	ACLRc	60±57.6	31.2±8.0[14]	24.5±3.1	Age at Sx Cartilage injury Pre-Sx function Sx history	10±.7	Radiograph[5,6]	TF, PFJ
Johnson, 2016 (PC, 1)	T1: 119 (48) T2: 94 (NR) T3: 114 (NR) T4: 142 (NR)	ACL+	ACLRc	NR	Adolescent: 20.4±3.2 Adult: 29.2±2.5	NR	Age at Sx	T1: ~2 T2: ~5 T3: ~10 T4: ~15	Radiograph[8]	TF, PFJ
Jones, 2019 (RC, 2)	421 (51)	ACL+	ACLRc	NR	19.8±4.9	24.0±4.9	Sex Age at Sx BMI at Sx Pre-injury activity Cartilage injury Meniscus Tx Graft type	~2	Radiograph[9]	TF
Jonsson, 2004 (RC, 1)	63 (34)	ACL+	ACLRc	3.6 (0.5–15)	25 (15–40)	NR	TF joint laxity	6.6 (4.9–9.6)	Radiograph[7]	TF
Karikis, 2016 (RCT, 2)	87 (32)	ACL+	ACLRc	SB: 10 (3-240) DB: 9 (2-240)	SB: 25 (18-52) DB: 29 (18-52)	SB: 25.5±3.6 DB: 24.9±2.5	Graft bundle #	~5	Radiograph[5,6]	TF, PFJ
Kessler, 2008 (RC, 2)	109 (38)	ACL	ACLRc, ACLnoSx	NR	30.7 (12.5-54)	NR	Age at Sx BMI at Sx Tx approach	11.1 (7.5-16.3)	Radiograph[5]	TF, PFJ
Kvist, 2020 (PC, 1)	153 (30)	ACL+	ACLRc, ACLnoSx	NR	24±6	27±4[15]	Tx approach	32-37	Radiograph[5], pain, symptoms	TF, PFJ
Leys, 2012 (PC, 1)	109 (47)	ACL+	ACLRc	NR	PT: 25 (15-42) HT: 24 (13-52)	NR	Graft source Post-ACLRc Sx	~15	Radiograph[8]	TF, PFJ
Li, 2011 (RC, 1)	249 (39)	ACL+	ACLRc	18.8 (.1-307.8)	26.4±10.2	NR	BMI at Sx Length of follow-up Cartilage injury Meniscus Tx	7.86 (2.1-20.3)	Radiograph[5]	TF, PFJ
Lohmander, 2004 (RC, 2)	103 (100)	ACL+	ACLRc, ACLnoSx	~144	31 (26-40)[15]	23 (18-40)[15,18]	Tx approach Meniscus Tx	~12	Radiographs[5], KOOS	TF, PFJ
Mascarenhas, 2010 (RC, 1)	34 (37)	ACL+	ACLRc	NR	Auto: 27.9±8.1 Allo: 28.1±9.1	Auto: 25.7 ± 3.9 Allo: 27.7 ± 4.8	Graft type	Auto: 9.1±2.7 Allo: 10.3±2.6	Radiograph[5]	TF
Meuffels, 2008 (RC, 1)	50 (76)	ACL+	ACLRc, ACLnoSx	NR	Sx: 37.6±6.2[15] noSx: 37.8±6.8[15]	Sx: 25.3 (22.2-30.9)[4,15] noSx: 24.9 (20.9-28.7)[4,15]	Tx approach	~10	Radiograph[5]	?
Meunier, 2007 (RCT, 1)	93 (33)	ACL+	ACLRc, ACLnoSx, ACLRp	NR	Op: 22 (14-30) Non-op: 21 (14-30)	NR	Tx approach Meniscus Tx Meniscus Sx (future) Graft augmentation	15±1	Radiograph[6,7]	?
Neuman, 2017 (PC, 2)	69 (NR)	ACL+	ACLRc, ACLnoSx	0-18[13]	26±8	26.3±4.4	Serum biomarkers	~16	Radiograph[9]	TF, PFJ
Neuman, 2008 (PC, 1)	79 (42)	ACL+	ACLRc, ACLnoSx	<5[13]	26 (15-43)	23±3	Meniscus injury Tx approach	15.7±1.4	Radiograph[9]	TF, PFJ

Nordenvall, 2014 (RC, 3)	64614 (37)	ACL+	ACLRc, ACLnoSx	NR	29 (15-60)	NR	Meniscus Tx Meniscus injury Tx approach	9 (2-25)	Diagnostic Code	TF
Oiestad,2018 (RC, 2)	210 (43)	ACL+	ACLRc	Pivot: 5 (0-260) No Pivot: 9 (0-278)	Pivot: 24.6 (13-48) No Pivot: 27.1 (13-61)	Pivot: 26.1±3.5[15] No Pivot: 26.5±3.8[15]	Sex Injury to Sx (time) Return to pivot sport Post-Sx function	~15	Radiograph[5], pain	TF, PFJ
Oiestad, 2010a (PC, 1)	181 (42)	ACL+	ACLRc	Isolated: 7.1±10.7 Combined: 42.4±63.0	Isolated: 37.5 (8.2)[15] Combined: 40.7 (8.7)[15]	NR	Concomitant injury	12.4±1.2	Radiograph[5], pain	TF
Oiested, 2010b (PC, 1)	164 (57)	ACL+	ACLRc	27.2 (53)	27.4 ± 8.5	NR	Sex Age at Sx Concomitant injury Graft source Post-Sx function	12.1±1.4	Radiograph[5], pain	TF
Persson, 2018 (RC, 3)	645967 (26[16])	Meniscus+	Meniscal Sx	NR	30.5 ± 8.6[16]	NR	Meniscus Sx	10 (0-18)	Diagnostic Code	TF, PFJ
Pinczewski, 2007 (RC, 1)	128 (47)	ACL+	ACLRc	NR	PT: 25 (15-42) HT: 24 (13-52)	NR	Graft source TF joint laxity Post-Sx joint ROM Post-Sx function	~10	Radiographs[8]	TF, PFJ
Pinczewski, 2002 (RC, 1)	T1: 142 (47) T2: 105 (NR)	ACL+	ACLRc	NR	PT: 25 (15-42) HT: 24 (13-52)	NR	Graft source	T1: ~2 T2: ~5	Radiographs[8]	TF, PFJ
Rhon, 2018 (RC, 2)	3605 (5)	Joint Injury	NR	NR	OA Dx: 31.1±8.9[15] No OA: 26±6.1[15]	NR	Injury type	8.5±3.3	Diagnostic Code	TF
Risberg, 2016 (PC, 1)	167 (43)	ACL+	ACLRc	26.4±51.6	45.2 ± 9.1**	26.7±4.0[15]	Injury type	17.8±1.8	Radiograph[5], pain	TF, PFJ
Rockborn, 2020 (RC, 1)	62 (16)	Meniscus	Meniscal Sx	0-25.5	~25	NR	Meniscus Sx	13.5 (11-19)	Radiograph[6,7]	TF
Roe, 2005 (RC, 1)	104 (47)	ACL+	ACLRc	NR	PT: 25 (15-42) HT: 24 (13-52)	NR	Sex Graft source TF joint laxity Post-Sx joint ROM	~7	Radiographs[8]	TF, PFJ
Sajovic, 2018 (RCT, 2)	48 (42)	ACL+	ACLRc	HT: 27.5±43.5 PT: 22.1±28.8	HT: 42.5±7.5[15] PT: 45.5±8.7[15]	HT: 24.5±3.1 PT: 24±3.5	Graft source Cartilage injury Meniscus Tx	~17	Radiographs[8]	TF, PFJ
Sajovic, 2011 (RCT, 2)	52 (42)	ACL+	ACLRc	HT: 25 (1-84) PT: 23 (1-60)	HT: 36 (25-54)[15] PT: 38 (27-58)[15]	NR	Graft source Meniscus Tx	~11	Radiographs[8]	TF, PFJ
Sajovic, 2006 (RCT, 2)	54 (50)	ACL+	ACLRc	HT: 25 (1-84) PT: 23 (1-60)	HT: 24 (14-42)[15] PT: 27 (16-46)[15]	NR	Graft source	~5	Radiographs[8]	TF, PFJ
Sanders, 2017 (RC, 2)	971 (54)	Patellar Dislocation	Sx, no-Sx	NR	Injury: 21.4±9.9 Control: 21.0±9.9	NR	Sex Age at injury Injury type Patellar Sx Joint morphology	Injury: 12.3±6.5 Control: 12.0±6.8	Radiographs[10], symptoms	PFJ
Sanders, 2016 (RC, 1)	1928 (39)	ACL+	ACLRc, ACLnoSx	NR	28.1±9.9[17]	NR	Sex Age at Sx Concomitant injury Tx approach Meniscus Tx Graft type	13.7±7.2	Diagnostic Code, TKA	NR
Shelbourne, 2017 (PC, 1)	423 (32)	ACL+	ACLRc	16.8 (0-246)	23.2±6.9	NR	Age at Sx Meniscus Tx Post-Sx joint ROM	22.5 (20-33.1)	Radiographs[8]	TF, PFJ
Shelbourne, 2015 (PC, 1)	391 (NR)	ACL+	ACLRc	NR	21.5±7.7	NR	Injury type	5.6 (2-15)	Radiographs[8]	TF, PFJ
Shelbourne, 2012 (PC, 2)	780 (NR)	ACL+	ACLRc	NR	25.4±9.2	NR	Cartilage lesion Meniscus Tx Post-Sx joint ROM	10.5 (5-21.2)	Radiographs[8]	TF, PFJ
Snoeker, 2020 (RC, 3)	148072 (54)	Joint Injury	NR	NR	Injury: 29.4±2.9 Control: 30.2±3.0	NR	Injury type	Injury: 14.5 (12.1-16.9) Control: 13.9 (11.7-16.8)	Diagnostic codes	TF
Sporsheim, 2019 (RCT, 2)	64 (44)	ACL+	ACLRc	<10[13]	60 (45-84)[15]	NR	Graft augmentation	30 (29-31)	Radiographs[6]	TF

Sun, 2015 (RCT, 2)	424 (29)	ACL?	ACLRc	NR	DB-AU: 27.5 (19-52) DB-AL: 27.1 (19-50) SB: 28.2 (19-52)	DB-AU: 23.5 DB-AL: 24.8 SB: 24.2	Graft bundle #	3 (.1-3.3)	Radiographs[8]	TF
Ulstein, 2017 (PC, 1)	41 (28)	ACL+	ACLRc	ACL+: 5.5±2.5 ACL: 5.5±2.6	ACL+: 34.9±6.8[15] ACL: 34.7±7.4[15]	ACL+: 25.1±2.7[15] ACL: 25.5±3.9[15]	Injury type	ACL+: 8.2 (6.4-9.8) ACL: 8.4 (6.7-9.8)	Radiographs[5]	TF
von Porat, 2004 (RC, 1)	122 (0)	ACL+	ACLRc, ACLnoSx	NR	38 (30-56)[15]	26 (2.3)	Tx approach Meniscus injury	~14	Radiographs[5]	TF
Webster, 2016 (RCT, 2)	38 (23)	ACL+	ACLRc	.75-12.0	HS: 26.1±5.9 PT: 26.6±6.7	NR	Graft source	HS: 15.2±.6 PT: 15.3±.4	Radiographs[5]	TF
Wellsandt, 2018 (PC, 1)	84 (38)	ACL+	ACLRc, ACLnoSx	No OA: 1.9±1.7 OA: 2.5±1.3	No OA: 28.8±11.3 OA: 28.3±11.5	No OA: 25.3±3.6 OA: 25.5±4.8	Second ACL tear Tx approach Post-rehab function	~5	Radiographs[5]	TF
Whittaker, 2018 (PC, 2)	146 (63)	Joint Injury	Sx, non-Sx	44.4-120	OA: 16 (14-18)[15] No OA: 15 (11-18)[15]	OA: 25.8 (21.3-38.9) No OA: 24.2 (18.5-36)	Injury type Bilateral knee injury ACLRc Bilateral Sx	OA: 6.8 (4-9.5) No OA: 7.0 (3.7-10)	MRI[12]	TF, PFJ
Yoo, 2017 (RCT, 2)	132 (9)	ACL+	ACLRc	Auto: 1.3 (.1-108.3) Allo: 1.7 (.1-50.1)	Auto: 30 (15-62) Allo: 24 (13-52)	NR	ACLRc graft type	Auto: 2.7 (2.4-4.3) Allo: 2.9 (2.1-5.0)	Radiographs[5]	TF

ACD (Articular cartilage defect), ACL (Anterior cruciate ligament tear, no concomitant injury), ACL+ (ACL tear+concomitant injury), ACL+? (ACL tear, concomitant injury unknown), ACLRc (ACL tear reconstruction), ACLRp (ACL tear repair), ACLnoSx (ACL tear no Sx), Allo (Allograft), Auto (Autograft), BMI (Body Mass Index), BPTB (Bone patellar tendon bone graft), DB (Double bundle ACL graft), DB-AU (Double Bundle autograft), DB-AL (Double Bundle allograft), Dx (Diagnosis), Endo (Endoscopic ACLR), HT (Hamstring tendon graft), KOOS (Knee Injury and Osteoarthritis Outcome Score), LAD (Kennedy Ligament Augmentation Device), Meniscus+ (meniscus injury+concomitant injury), MF (Microfracture), MRI (Magnetic Resonance Imaging), NR (Not reported), OA (Osteoarthritis), OAT (Osteochondral autologous transplantation), OCD (Osteochondral defect), PC (Prospective cohort study), PFJ (Patellofemoral joint), PT (Patellar tendon graft), RC (Retrospective cohort study), RCT (Randomized controlled trial), SB (Single bundle ACL graft), ST (Semitendinosus graft), Sx (Surgery), T (Follow-up time), TF (Tibiofemoral joint), TKA (Total knee arthroplasty), Tx (Treatment), US (United States), # (Number), ~ (Follow-up was broadly reported)

[1]If not available, time from injury to exposure was reported. [2]Mean±SD, median (min-max), or median (interquartile range). [3]If not availabe, age at Sx was reported. [4]Median (interquartile range). [5]Kellgren-Lawrence. [6]Ahlback. [7]Fairbanks. [8]IKDC. [9]OARSI Atlas (or modified OARSI Atlas). [10]Iwano. [11]Whole-Organ MRI Score. [12]MRI Osteoarthritis Knee Score. [13]Days. [14]at Sx. [15]at follow-up. [16]Only for exposed group, unexposed group not provided. [17]Only for knee injury group. [18]Mean (range).

5. Summary of Symptomatic Osteoarthritis Estimates

Author Year	Primary Injury (Treatment)	Method of OA Identification	OA Definition	Persons with Clinical OA (n, %)	Comparison(s)	Statistical Estimate Reported HR (95%CI)	Re-calculated OR (95%CI)
Akelman, 2017	ACL (ACLRc)	KOOS	≤ threshold on KOOS-QOL + ≥2 other subscale thresholds	13 (18%)	High vs low graft tension[1]	KOA NR (NS)	KOA .56 (.19,1.92)
					High graft tension vs controls[1]	KOA p=.09	KOA 1.7 (.33,49.6)
					Low graft tension vs controls[1]	KOA p=.01	KOA 2.27 (.58,82.4)
Culvenor, 2017	ACL+ (ACLRc)	Radiograph (KL) Self-reported pain	KL ≥2 + knee pain in last 4-wks	15-yr 70 (39%) 20-yr 60 (42%)	AKP at 1-yr post-ACLRc (Y vs N[1])	KOA 15-yr RR .87 (.50,1.59)[2] KOA 20-yr RR 1.1 (.57,1.98)[2]	-
					AKP at 2-yr post-ACLRc (Y vs N[1])	KOA 15-yr RR 1.5 (.83,2.60)[2] KOA 20-yr RR .7 (.33,1.51)[2]	-
					AKP at 1 or 2-yr post-ACLRc (Y vs N[1])	KOA 15-yr RR 1.4 (.66,2.98) KOA 20-yr RR 1.2 (.51,2.87)	-
Filbay , 2021	ACL+ (ACLRp, ACLRc, ACLnoSx)	Radiograph (KL) KOOS	KL ≥2 +1-step decrease from best response on ≥50% of KOOS-pain or KOOS-symptoms subscale items	TF 61 (48%) PFJ 31 (24%)	Male vs female[2] sex	TF OA 2.1 (.8, 5.2) PFJ OA 2.2 (.7, 6.6)	
					Early ACLRc[2] vs delayed ACLRc	TF OA 1.2 (.2, 6.1) PFJOA .4 (.0, 3.7)	-
					Early ACLRc[2] vs rehabilitation	TF OA 1.0 (.4, 2.4) **PFJ OA .2 (.1, .7)**	-
					Meniscus tear (Y vs N[2])	TF OA 1.5 (.6, 4.1) PFJ OA 1.3 (.4, 4.5)	-
					Meniscal surgery (Y vs no tear[2])	TF OA 1.0 (.4, 2.6) PFJ OA 1.0 (.3, 3.3)	-
					Knee extension strength asymmetry at 4-yrs (Y vs N[2])	TF OA .6 (.2, 1.6) PFJ OA .3 (.1, 1.3)	-
					Knee flexion strength asymmetry at 4-yrs (Y vs N[2])	TF OA .6 (.2, 1.8) **PFJ OA 5.0 (1.3, 19.3)**	-
					Hop distance asymmetry at 4-yrs (Y vs N[2])	TF OA 2.6 (.8, 8.4) **PFJ OA 4.9 (1.2, 19.7)**	-
					Knee extension ROM loss at 4-yrs (Y vs N[2])	TF OA 1.4 (.4, 4.1) PFJ OA 1.4 (.3, 5.8)	-
					Knee flexion ROM loss at 4-yrs (Y vs N[2])	TF OA 1.8 (.7, 4.5) PFJ OA .7 (.2, 2.3)	-
					Anterior tibial translation at 4-yr >3 mm (Y vs N[2])	TF OA 1.2 (.5, 2.8) PFJ OA .8 (.3, 2.6)	-
					Tegner Score (0-5 vs. 6-10[2])	TF OA 1.2 (.5, 2.8) PFJ OA 1.1 (.4, 3.4)	-
					Lysholm Score (0-83 vs. 84-100[2])	TF OA 1.5 (.6, 3.8) PFJ OA 2.0 (.6, 6.6)	-
Hagmeijer, 2019	ACL+meniscus (ACLRc, ACLnoSx)	Radiograph Diagnostic Code	KL ≥2 + seek care for pain OR TKA	NR	Age at injury[2]	**KOA 1.1 (1.03,1.1)[2] TKA 1.1 (1.1,1.2)[2]**	-
					Meniscus Tx (meniscectomy vs untreated[1])[2]	KOA 1.3 (.7,2.2) TKA 6.6 (.7,64.8)	-
					Meniscus tear Tx (repair vs untreated[1])	KOA .47 (.1,2.4)[2] TKA UC	-
					Acute ACLRc vs ACLnoSx[1]	KOA .97 (.5,1.8)[2] TKA .2 (.02,2.7)[2]	-
					Delayed ACLRc vs ACLnoSx[1]	KOA .7 (.4,1.2) TKA .6 (.17,2.27)	-
Kvist, 2020	ACL+ (ACLRc, ACLnoSx)	Radiograph (KL) KOOS	KL ≥2 +1-step decrease from best response on ≥50% of KOOS-pain or KOOS-symptoms subscale items	76 (50%)	Allocated to ACLRc[1] vs ACLnoSx	NR	KOA 1.5 (.8,2.9)
					ACLnoSx vs ACLRc[1]	NR	KOA 1.2 (.7,2.4)
					ACLnoSx[1] vs delayed ACLRc	NR	KOA 1.1 (.5,2.6)
					Early[1] vs delayed ACLRc	NR	KOA 1.6 (.8,3.7)
Lohmander, 2004	ACL+ (ACLRc, ACLnoSx)	Radiograph (KL) KOOS	KL≥2 + ≤KOOS thresholds	28 (42%)	ACLRc vs ACLnoSx[1]	KOA OR 1.7 (0.5,5.3)[2]	-
					Meniscus Sx vs no meniscus injury[1]	**KOA OR 4.8 (1.5,16)[2]**	-

Nordenvall, 2014	ACL+ (ACLRc, ACLnoSx)	Diagnostic Code	Diagnostic Code	4314 (7%)	ACLRc vs ACLnoSx[1]	**KOA Overall 1.3 (1.2,1.3)[2]** KOA 2-5-yr 1.05 (0.95,1.2)[2] **KOA 5-10-yr 1.3 (1.2,1.4)[2]** **KOA >10-yr 1.4 (1.3,1.6)[2]**	-
					ACLRc + no meniscus injury vs ACLnoSx[1]	**KOA Overall 1.2 (1.1,1.3)[2]** KOA 2-4.9-yr 1.04 (0.9,1.2)[2] KOA 5-9.9-yr 1.1 (0.9,1.3)[2] **KOA >10-yr 1.4 (1.2,1.7)[2]**	-
					ACLRc + meniscus injury vs ACLnoSx[1]	**KOA Overall 1.2 (1.1,1.3)[2]** KOA 2-5-yr 1.01 (0.85,1.2)[2] KOA 5-10-yr 1.1 (0.94,1.3)[2] **KOA >10-yr 1.4 (1.2,1.6)[2]**	-
					ACLRc + meniscus injury (no Sx) vs ACLnoSx[1]	**KOA Overall 1.3 (1.1,1.6)[2]** KOA 2-5-yr 0.9 (0.7,1.3)[2] **KOA 5-10-yr 1.6 (1.1,2.2)[2]** **KOA >10-yr 1.6 (1.2,2.2)[2]**	-
					ACLRc + meniscus Sx vs ACLnoSx[1]	**KOA Overall 1.2 (1.1,1.3)[2]** KOA 2-5-yr 0.97 (0.8,1.1)[2] **KOA 5-10-yr 1.2 (1.04,1.4)[2]** **KOA >10-yr 1.4 (1.2,1.7)[2]**	-
					ACLRc (≤3-mo) vs ACLnoSx[1]	**KOA Overall 1.2 (1.2,1.3)[2]** KOA 2-5-yr 0.9 (0.8,1.0)[2] **KOA 5-10-yr 1.3 (1.2,1.5)[2]** **KOA >10-yr 1.44 (1.3,1.6)[2]**	-
					ACLRc (3-12-mo) vs ACLnoSx[1]	**KOA Overall 1.2 (1.1,1.4)[2]** KOA 2-5-yr 1.2 (0.99,1.3)[2] KOA 5-10yr 1.2 (0.98,1.5)[2] **KOA>10-yr 1.4 (1.02,1.9)[2]**	-
					ACLRc (>12-mo) vs ACLnoSx[1]	KOA Overall 1.1 (1.00,1.3)[2] KOA 2-5-yr 1.0 (0.9,1.2)[2] KOA 5-10-yr 1.1 (0.9,1.4)[2] KOA >10-yr 1.2 (0.9,1.6)[2]	-
Oiestad, 2018	ACL+ (ACLRc)	Radiograph (KL) Self-reported pain	KL≥2 + knee pain most days in last month	31 (15%)	Male vs female sex[1]	KOA OR 1.2 (.4,3.7)[2]	-
					Age at surgery	KOA OR 1.1 (.99,1.1)[2]	-
					Time from injury to sx	KOA OR .99 (.99,1.0)	-
					Isolated[1] vs combined Injury	**KOA OR 13.4 (1.7,107)[2]**	-
					Return, pivot sport (Y vs N1)	**KOA OR .3 (.1,.9)[2]**	-
					Cincinnati Knee Score 6-mo post-ACLRc[3]	KOA OR 1.0 (.99,1.1)[2]	-
Oiestad, 2010a	ACL+ (ACLRc)	Radiograph (KL) Self-reported pain	KL ≥2 + knee pain in last 4-wks	74 (41%)	Isolated vs combined Injury	KOA p=.053	-
Oiestad, 2010b	ACL+ (ACLRc)	Radiograph (KL) Self-reported pain	KL≥2 + knee pain in last 4-wks	58 (35%)	Male vs female sex[1]	KOA OR 2.2 (1.0,4.2)[2]	-
					Additional injury (Y vs N[1])	KOA OR 1.5 (.7,3.3)[2]	-
					ST[1] vs PT autograft	KOA OR 2.4 (.7,8.3)[2]	-
					Cincinnati Knee Score 2-yr post-ACLRc	**KOA OR .95 (.92,.98)[2]**	-
					Quadriceps strength change 2-15-yr post-ACLRc	KOA OR 1.0 (1.0,1.1)[2]	-
Persson, 2018	Meniscus Injury (Sx)	Diagnostic Code	Diagnostic Code	15042 (2%)	Meniscus repair vs partial meniscectomy[1]	KOA 0.7 (0.5,1.1)[2]	-
Rhon, 2018	Joint Injury (NR)	Diagnostic Code	Diagnostic Code	345 (10%)	Knee fracture vs mild knee injury[1]	**KOA OR 1.4 (1.0,1.8)[2]**	-
					Knee sprain vs mild knee injury[1]	**KOA OR 1.6 (1.2,2.0)[2]**	-
					Soft tissue vs mild knee injury[1]	**KOA OR 0.6 (0.4,0.8)[2]**	-
					Derangement vs mild knee injury[1]	**KOA OR 2.4 (1.3,4.3)[2]**	-
					Dislocation vs mild knee injury[1]	**KOA OR 3.7 (2.1,6.6)[2]**	-
Risberg, 2016	ACL+ (ACLRc)	Radiograph (KL) Self-reported pain	KL≥2 + knee pain in last 4-wks	TF 41 (25%) PFJ 24 (14%)	Isolated[1] vs combined Injury	TF OA p<0001 PFJ OA p=014	**TF OA 5.9 (1.6,15.9)** PFJ OA 4.7 (.91,16.5)

Sanders, 2017	Patellar Dislocation (Sx, no-Sx)	Radiograph (Iwano) Self-reported pain	Diagnostic Code + active PFJ pain in + PFJ radiographic changes	66 (7%)	Male vs female sex[1]	**KOA OR 1.8 (1.1,4.3)**	-
					Age at injury (<18 vs >18[1])	**KOA OR 4.0 (1.7,10.4)**	-
					Patellar dislocation vs no injury[1]	**KOA OR 7.8 (3.9,17.6)**	-
					Number of dislocations (≥ 2 vs 1[1])	**KOA OR 4.5 (1.6,12.6)**	-
					Patellar stabilization Sx (Y vs N[1])	NR (NS)	-
					Cartilage defect (Y vs N[1])	**KOA OR 11.3 (5.0,26.6)**	-
					Patella Alta (Y vs N[1])	NR (NS)	-
					Trochlear dysplasia (Y vs N[1])	**KOA OR 3.6 (1.3,10.0)**	-
Sanders, 2016	ACL+ (ACLRc, ACLnoSx)	Radiologist diagnosis Self-reported OA diagnosis	Radiographic changes + Care seeking pain	NR	Male vs female sex[1]	KOA 1.1 (.6,2.1) TKA .1 (.06,5.7)	-
					Age at injury (≤20[1] vs 21-40)	**KOA 3.1 (1.2,8.0)** TKA 2.1 (.04,116)	-
					Age at injury (≤20[1] vs >40)	**KOA 4.1 (1.2,14)** TKA 3.3 (.02,592)	-
					Early ACLRc vs no injury[1]	**KOA OA 3.5 (1.9,6.6)** TKA .3 (.0,2.2)	-
					Delayed ACLRc vs no injury[1]	**KOA OA 22.1 (13.3,36.8)** **TKA 6.5 (3.1,13.7)**	-
					Delayed vs early ACLRc[1]	**KOA 6.2 (3.4,11.4)** TKA 6.6 (.4,105.8)	-
					ACLRc[1] vs ACLnoSx	**KOA 6.0 (4.3,8.4)** **TKA 16.7 (5.0,55.2)**	-
					Meniscus tear (Y vs N[1])	KOA 1.7 (.84,3.47) TKA 2.3 (.06,95)	-
					Medial and lateral meniscus tear (Y vs N[1])	**KOA 4.3 (1.8,9.9)** TKA UC	-
					Medial meniscus tear (Y vs N[1])	KOA 1.5 (.67,3.4) TKA UC	-
					Lateral meniscus tear (Y vs N[1])	KOA 1.0 (.34,2.6) TKA UC	-
					Meniscectomy (Y vs N[1])	KOA 1.8 (.96,3.4) TKA 3.9 (.09,161)	-
					Cartilage injury at surgery (Y vs N[1])	**KOA 3.4 (1.4,8.0)** TKA 4.1 (.1,171)	-
					Autograft[1] vs Allograft	**KOA 4.9 (2.1,11.7)** TKA 5.2 (.12,224)	-
Snoeker, 2020	Joint Injury (NR)	Diagnostic Code	Diagnostic Code	3276 (2%)	Cruciate ligament tear (Y vs N[1])	**KOA 11-yr 8.2 (5.9,11.4)[2]** **KOA 12-19-yr 6.8 (5.0,9.2)[2]** **19-yr RD 19.6% (13.2,25.9)[2]**	-
					Meniscus tear (Y vs N[1])	**KOA 11-yr 7.6 (5.5,10.5)[2]** **KOA 12-19-yr 4.0 (2.7,5.9)[2]** **19-yr RD 10.5% (6.4,14.7)[2]**	-
					Fracture (Y vs N[1])	**KOA 11-yr 7.0 (4.2,11.7)[2]** KOA 12-19-yr 2.1 (0.9,5.1)[2] **19-yr RD 6.6% (1.1,12.2)[2]**	-
					Dislocation (Y vs N[1])	**KOA 11-yr 5.9 (3.4,10.1)[2]** **KOA 12-19-yr 3.0 (1.4,6.3)[2]** **19-yr RD 6.7% (1.8,11.5)[2]**	-
					Collateral ligament tear (Y vs N[1])	**KOA 11-yr 4.9 (3.3,7.3)[2]** **KOA 12-19-yr 2.1 (1.2,3.7)[2]** **19-yr RD 4.5% (1.3,7.8)[2]**	-
					Multiple structures injured (Y vs N[1])	**KOA 11-yr 6.5 (5.0,8.5)[2]** **KOA 12-19-yr 3.2 (2.3,4.6)[2]** **19-yr RD 8.0% (5.4,10.7)[2]**	-

Cartilage tear/other (Y vs N[1])	**KOA 11-yr 5.2 (3.8,7.0)[2]** **KOA 12-19-yr 2.4 (1.5,3.9)[2]** **19-yr RD 6.9 (3.5,10.2)[2]**	-
Knee injury (any; Y vs N[1])	**KOA 11-yr 5.7 (5.0,6.6)[2]** **KOA 12-19-yr 3.4 (2.9,4.0)[2]** **19-yr RD 8.1 (6.7,9.4)[2]**	-
Knee injury (men; Y vs N[1])	**KOA 11-yr 5.3 (4.5,6.3)[2]** **KOA 12-19-yr 2.9 (2.3,3.6)[2]** **19-yr RD 7.3 (5.7,8.9)[2]**	-
Knee injury (women; Y vs N[1])	**KOA 11-yr 6.5 (5.1,8.1)[2]** **KOA 12-19-yr 4.1 (3.2,5.3)[2]** **19-yr RD 9.5 (6.9,12.1)[2]**	-
Knee injury (≤30 years of age; Y vs N[1])	**KOA 11-yr 7.6 (6.2,9.3)[2]** **KOA 12-19-yr 4.8 (3.8,6.2)[2]** **19-yr RD 8.6 (6.9,10.4)[2]**	-
Knee injury (> 30 years of age Y vs N[1])	**KOA 11-yr 4.7 (3.9,5.7)[2]** **KOA 12-19-yr 2.6 (2.0,3.2)[2]** **19-yr RD 8.0 (5.9,10.1)[2]**	-

Bold (statistically significant). ACL (Anterior cruciate ligament tear, no concomitant injury), ACL+ (ACL tear+concomitant injury), ACL? (ACL tear, concomitant injury unknown), ACLRc (ACL tear reconstruction), ACLRp (ACL tear repair), ACLnoSx (ACL tear no Sx), AKP (anterior knee pain), CI (95% confidence interval), HR (hazard ratio), KL (Kellgren-Lawrence OA grade), KOA (knee OA inclusive of all compartments), mo (months), mm (millimeters), N (no), NR (not reported), NS (author reported not statistically significant), OA (osteoarthritis), PFJ (patellofemoral joint), PT (patellar tendon graft), RD (risk difference), RR (risk ratio), ST (semitendinosus graft), Sx (surgery), TF (tibiofemoral joint), UC (unable to calculate), Y (yes), yr (years).

[1]reference group. [2]multivariable analysis.

6. Summary of Structural Osteoarthritis Estimates

Author	Primary Injury (Treatment)	Method of OA Identification	OA Definition	Participants with Structural OA (n, %)	Comparison(s)	Statistical Estimate Reported OR (95%CI, p-value)	Re-calculated OR (95%CI)
Aga, 2018	ACL+ (ACLRc)	Radiograph (KL)	NR[1]	2 (2%)	Double vs single bundle[2]	NR (NS)	KOA 1.2 (.07,18.9)
Ahlden, 2009	ACL+ (ACLRc)	Radiograph (Ahlback)	NR[1]	5 (11%)	ST[2] vs PT autograft	Medial TF OA p=.69 Lateral OA p=.54	Medial TF OA .7 (.13,4.7) Lateral TF .3 (.05,3.2)
Ahn, 2012	ACL+ (ACLRc)	Radiograph (IKDC)	C or D	Medial TF 36 (31%) Lateral TF 11 (9%) PFJ 9 (8%)	Age at surgery[3]	Medial TF OA 1.1 (1.0,1.2)[3] Lateral TF OA .8 (.24,2.8)[3]	-
					BMI at surgery	Medial TF OA 1.0 (.8,1.2)[3] Lateral TF OA 1.6 (1.0, 2.3)[3]	-
					Injury to surgery	Medial TF OA 1.0 (.99,1.0)[3] Lateral TF OA 1.0 (.98,1.0)[3]	-
					Partial meniscectomy (Y vs N[2])	**Medial TF OA 20.7 (2.3,177)[3,4]** Lateral TF OA .8 (.04,17.5)[3,4]	-
					Sub-total meniscectomy (Y vs N[2])	Medial TF OA 8.9 (.67,119)[3] Lateral TF OA 2.0 (.9, 87)[3]	-
					Medial proximal tibial angle	Medial TF OA 1.0 (.84,1.4)[3] Lateral TF OA 1.5 (.70,3.2)[3]	-
					Anatomic axis angle	Medial TF OA 1.0 (.84,1.4)[3] Lateral TF OA .73 (.5,2.3)[3]	-
Barenius, 2014	ACL+ (ACLRc)	Radiograph (KL)	≥2	81 (60%)	Age at injury	Medial OA 1.0 (.97, 1.1)[3] Lateral OA 1.0 (.97, 1.1) PFJ OA 1.0 (.96, 1.1)	-
					Male sex vs female sex[2]	Medial OA 1.2 (.5,3.1)[3] Lateral OA 1.4 (.6,3.1) PFJ OA 2.2 (.94,5.3)	-
					BMI ≥25, 2-yr post-ACLRc (Y vs N[2])	**Medial OA 3.1 (1.2,7.9)[3]** Lateral OA 1.7 (.73,3.8) **PFJ OA 3.5 (1.5,7.8)**	-
					Injury to surgery (<6 vs ≥6 mo)	Lateral TF OA 1.0 (.4,2.3) PFJ OA .9 (.4,2.0)	-
					Injury to surgery (<12 vs ≥12 mo)	Lateral TF OA 1.5 (.6,3.7) PFJ OA 1.1 (.48,2.6)	-
					Manual occupation at injury (Y vs N[2])	Medial TF OA 2.0 (.5,7.4)[3] Lateral TF OA 1.2 (.4, 3.5) PFJ OA 1.4 (.5,4.1)	-
					Pivot Shift ≥1, 2-yr post-ACLRc (Y vs N[2])	Medial TF OA 2.1 (.8,5.4)[3] Lateral TF OA .7 (.3,1.8) PFJ OA .6 (.2,1.6)	-
					Medial meniscus resection (Y vs N[2])	**Medial TF OA 3.6 (1.4,9.3)[3]** Lateral TF OA 1.5 (.7,3.6) **PFJ OA 2.3 (1.01,5.2)**	-
					Lateral meniscus resection (Y vs N[2])	**Lateral OA 5.1 (2.1,12.3)** PFJ OA 1.7 (.7,4.0)	-
					Medial meniscus suture (Y vs N[2])	Medial OA .5 (.1,2.5) PFJ OA .8 (.2,3.1)	-
					Lateral meniscus suture (Y vs N[2])	Lateral OA .5 (.06,4.6) PFJ OA .5 (.1,4.2)	-
					ST vs PT autograft[2]	Medial TF OA 1.7 (.7,3.9)[3] Lateral TF OA 2.3 (1.0,5.4) PFJ OA 1.2 (.5,2.6)	-
Bjornsson, 2016	ACL+ (ACLRc)	Radiograph (KL)	NR[1]	TF 65 (39%) PFJ 67 (47%)	ST[2] vs PT autograft	TF OA p=.53 PFJ OA p=.67	TF OA 0.9 (.4,1.7) PFJ OA 1.14(.6,2.2)

Cantin, 2016	ACL+ (ACLRc)	Radiograph (IKDC)	C or D	112 (19%)	Age at surgery (>34 yr)	NR	UC
					Residual laxity (Y vs N)	NR	UC
					Stage 3 or 4 cartilage lesion (Y vs N)	NR	UC
					Medial and lateral meniscectomy (Y vs N)	NR	UC
Castoldi, 2020	ACL+ (ACLRc)	Radiograph (Ahlback, Iwano)	≥1	Medial TF 32 (71%) Lateral TF 18 (40%) PFJ 30 (67%)	PT[2] vs PT with LET	Medial TF OA p=.7 Lateral TF OA p<.02 PFJ OA p=.4	Medial TF OA .8 (.2,2.8) **Lateral TF OA 5.2 (1.3,19.2)** PFJ OA 1.7 (.5,6.0)
					ACLRc vs uninjured knee[2]	Medial TF OA p=.6 Lateral TF OA p<.0001 PFJ OA p=.09	Medial TF OA 1.2 (.5,3.0) **Lateral TF OA 14.3 (1.9,66.7)** PFJ OA 2.1 (.9,4.9)
Culvenor, 2017	ACL+ (ACLRc)	Radiograph (KL)	≥2 or osteophytes	15-yr 130 (72%) 20-yr 115 (81%)	AKP 1-yr post-ACLRc (Y vs N[2])	KOA 15-yr RR .9 (.6,1.4)[3] KOA 20-yr RR .9 (.6,1.5)[3]	-
					AKP 2-yr post-ACLRc (Y vs N[2])	KOA 15-yr RR .98 (.6,1.6)[3] KOA 20-yr RR .9 (.6,1.5)[3]	-
					AKP 1 or 2-yr post-ACLRc (Y vs N[2])	KOA 15-yr RR 1.1 (.6,2.1)[3] KOA 20-yr RR 1.0 (.5,2.1)[3]	-
Curado, 2019	ACL+ (ACLRc)	Radiograph (IKDC)	C or D	53 (29%)	Age >30 at surgery (Y vs N)	NR	UC
					Return to pivot sport (Y vs N)	NR	UC
					Meniscectomy (present or future; Y vs N)	NR	UC
					Residual Laxity (IKDC C or D, Y vs N[2])	NR	UC
Drogset, 2006	ACL+ (ACLRc, ACLRp)	Radiograph (Ahlback)	NR[1]	9 (9%)	Primary repair vs PT autograft[2]	NR	KOA 1.4 (.3,6.3)
					PT[2] vs PT with augmentation	NR	KOA .3 (.1,2.4)
Drogest, 2002	ACL+ (ACLRc)	Radiograph (Ahlback)	NR[1]	34 (50%)	PT[2] vs PT with augmentation	NR	KOA 1.23 (.8,5.4)
					Meniscus tear (Y vs N)	NR (NS)	UC
					Cartilage Injury (Y vs N)	KOA p=0.005	**KOA 4.4 (1.7,12.2)**
Elveos 2018	ACL+ (ACLRc)	Radiograph (Ahlback)	≥3	15 (27%)	PT[2] vs PT with augmentation	KOA p=0.37	KOA .6 (.2,1.9)
FIlbay 2021	ACL+ (ACLRp, ACLRc, ACLnoSx)	Radiograph (KL)	≥2	TF 79 (62%) PF 41 (32%)	Male vs female[2] sex	TF OA 1.3 (.5,3.4) PFJ OA 1.8 (.6,4.8)	-
					Early ACLRc[2] vs delayed ACLRc	TF OA 4.1 (.6,27.0) PFJ OA 1.1 (.2,6.8)	-
					Early ACLRc[2] vs rehabilitation	TF OA 2.0 (.8,5.0) PFJ OA .4 (.2,1.3)	-
					Meniscus tear (Y vs N[2])	TF OA 2.7 (1.0,7.6) PFJ OA 1.0 (.3,3.1)	-
					Meniscal surgery (Y vs no tear[2])	**TF OA 3.0 (1.2,7.8)** PFJ OA 1.2 (.4,3.6)	-
					Knee extension strength asymmetry at 4-yrs (Y vs N[2])	TF OA .7 (.3,1.8) PFJ OA .4 (.1, 1.2)	-
					Knee flexion strength asymmetry at 4-yrs (Y vs N[2])	TF OA 1.2 (.4,3.7) PFJ OA 2.6 (.8,8.8)	-
					Hop distance asymmetry at 4-yrs (Y vs N[2])	TF OA 1.0 (.3,3.2) **PFJ OA 5.1 (1.4,18.7)**	-
					Knee extension ROM loss at 4-yrs (Y vs N[2])	TF OA 1.3 (.4,4.1), PFJ OA 3.6 (1.0,13.5)	-
					Knee flexion ROM loss at 4-yrs (Y vs N[2])	TF OA 1.8 (.7,4.6) PFJ OA 1.0 (.4,2.9)	-
					Anterior tibial translation at 4-yr >3 mm (Y vs N[2])	TF OA 1.0 (.4,2.4) PFJ OA 1.7 (.6,4.4)	-
					Tegner Score (0-5 vs. 6-10[2])	TF OA .8 (.3,2.0) PFJ OA .5 (.2,1.4)	-
					Lysholm Score (0-83 vs. 84-100[2])	TF OA 1.6 (.6,4.6) PFJ OA 1.5 (.5,4.6)	-

Frobell 2013	ACL+ (ACLRc, ACLnoSx)	Radiograph (mOARSI)	JSN grade ≥2 (TF only), OR sum of compartment specific marginal osteophyte(s) grade ≥2, OR compartment specific JSN grade 1 + osteophyte grade 1	TF 13 (12%) PFJ 22 (19%)	Early ACLRc[2] vs delayed(optional) ACLRc	TF OA p=0.17 PFJ OA p=0.20	TF OA .4 (.2,1.5) PFJ OA .5 (.2,1.4)
					Early ACLRc[2] vs delayed ACLRc	TF OA p=0.25 PFJ OA p=0.21	TF OA .2 (.1, 1.6) PFJ OA .8 (.4, 2.4)
					Early ACLRc[2] vs rehabilitation	TF OA p=0.25 PFJ OA p=0.21	TF OA .7 (.3 2.9) PFJ OA .3 (.1, 1.3)
Gifstad, 2013	ACL+ (ACLRc)	Radiograph (KL)	≥2	NR	Primary ACLRc vs ACLRc Revision	KOA p=0.45	UC
Gudas, 2012	Cartilage (OCD, ACD)	Radiograph (KL)	NR[1]	21 (37%)	OAT vs MF[2]	KOA p=.083	KOA .4 (.23,1.1)
Haberfield, 2021	ACL+ (ACLRc)	Radiograph (OARSI)	JSN grade ≥2 OR osteophyte grade ≥2 OR grade 1 JSN + grade 1 osteophyte	15 (19%)	Return to pivot sport at 1 yr (Y vs N[2])	KOA 5-yr RR .5 (.1,2.4)[3]	-
					Return to pivot sport (Y vs N[2])	KOA 5-yr RR .6 (.2,2.2)[3]	-
Hamrin Senorski, 2019	ACL+ (ACLRc)	Radiograph (KL)	≥2	53 (43%)	Age at surgery	**KOA 2.3 (1.3,3.9)[3]**	-
					Injury to surgery	KOA 2.3 (1.0,5.0)[3]	-
Holm, 2012	ACL+ (ACLRc)	Radiograph (KL)	≥2	TF 42 (79%) PFJ 15 (28%)	Open vs endoscopic[2] ACLRc	TF OA p=1.0 PFJ OA p=.09	TF OA 1.1 (.3,4.1) PFJ OA .5 (.2,1.6)
Holm, 2010	ACL? (ACLRc)	Radiograph (KL)	≥2	34 (60%)	ST[2] vs PT autograft	KOA p=.27	KOA 1.5 (.5,4.2)
Hoogeslag, 2019	ACL+ (ACLRc, ACLRp)	Radiograph (KL)	NR[1]	0 (0%)	ACLRc vs ACLRp	NR	KOA 1
Janssen, 2013	ACL+ (ACLRc)	Radiograph (KL, Ahlback)	KL ≥3 Ahlback ≥1	46 (53%)	Age at surgery	NR (NS)[3]	UC
					Medial meniscectomy (past or current; Y vs N[2])	**KOA 4.0 (1.4, 11.5)[3]**	-
					ICRS grade ≥3 (Y vs N[2])	**KOA 5.2 (1.1, 24.8)[3]**	-
					Pre-ACLRc hop distance (IKDC ≥C vs A or B[2])	NR (NS)[3]	UC
Johnson, 2016	ACL+ (ACLRc)	Radiograph (IKDC)	B, C or D	2-yr 5 (4%) 5-yr 12 (13%) 10-yr 17 (15%) 15-yr 89 (63%)	Age at surgery (≤25[2] vs 26-34)	KOA 2-yr p=0.004 KOA 5-yr p=0.04 KOA 10-yr p>.999 KOA 15-yr p=0.65	KOA 2-yr UC KOA 5-yr 2.8 (.7,10.2) **KOA 10-yr 19.7, (1.2,155)** KOA 15-yr 1.1 (.6,2.3)
Jones 2019	ACL+ (ACLRc)	Radiograph (mOARSI)	Sum of osteophytes, JSN, femoral sclerosis, and attrition (Medial TF only to a maximum of 11 (Medial TF) and 10 (Lateral TF)	NR	Male vs female[2] sex	Lateral TF OA 1.3 (.9,1.9)[3] Medial TF OA 1.2 (.9,1.8)[3] KOA 1.3 (.9,1.8)[3]	-
					Age at surgery	Lateral TF OA 0.98 (0.9,1.02)[3] **Medial TF OA 1.1 (1.02,1.10)[3]** KOA 1.0 (0.98,1.1)[3]	-
					BMI at surgery	Lateral TF OA 1.0 (0.97,1.1)[3] Medial TF OA 1.1 (1.0,1.1)[3] KOA 1.04 (0.99,1.1)[3]	-
					Marx Activity Score at ACLRc	Lateral TF OA 0.99 (0.95,1.0)[3] Medial TF OA 1.0 (0.98,1.1)[3] KOA 1.0 (0.96,1.1)[3]	-
					PT autograft[2] vs allograft	Lateral TF OA 1.3 (0.6,2.9)[3] Medial TF OA 1.11(0.5,2.4)[3] KOA 1.3 (0.6,2.8)[3]	-
					ST vs PT autograft[2]	Lateral TF OA 1.2 (0.8,1.7)[3] Medial TF OA 0.9 (0.6,1.4)[3] KOA 1.1 (0.7,1.6)[3]	-
					Lateral cartilage status (Grade 1[2] vs 2-4)	Lateral TF OA 0.9 (0.5,1.5)[3] KOA 1.5 (0.9,2.6)[3]	-
					Lateral meniscus (no tear[2] vs repair)	Lateral TF OA 2.0 (1.0,3.8)[3] KOA 1.3 (0.7,2.7)[3]	-
					Lateral meniscus (no tear[2] vs partial meniscectomy)	Lateral TF OA 3.0 (2.0,4.5)[3] **KOA 2.2 (1.5,3.3)[3]**	-

Jones 2019 cont.					Lateral meniscus (no tear[2] vs untreated tear)	Lateral TF OA 1.1 (0.7,1.8)[3] KOA 1.1 (0.6,1.7)[3]	-
					Medial cartilage status (Grade 1[2] vs Grade 2-4)	Medial TF OA 1.6 (0.8,3.0)[3] KOA 1.0 (0.5,2.0)[3]	-
					Medial meniscus (no tear[2] vs repair)	**Medial TF OA 1.9 (1.2,3.0)[3]** **KOA 1.8 (1.2,2.9)[3]**	-
					Medial meniscus (no tear[2] vs partial meniscectomy)	**Medial TF OA 2.1 (1.1,3.9)[3]** KOA 1.7 (0.9,3.2)[3]	-
					Medial meniscus (no tear[2] vs untreated tear)	Medial TF OA: 0.9 (0.5,1.7)[3] KOA 0.0 (0.5,1.5)[3]	-
Jonsson, 2004	ACL+ (ACLRc)	Radiograph (Fairbanks)	NR[1]	12 (19%)	Pivot shift (present vs absent[2])	KOA p=0.1	UC
					Anterior tibial translation at 2-yr >2.5 mm (Y vs N[2])	KOA p=.09	KOA .3 (.1,1.1)
Karikis, 2016	ACL+ (ACLRc)	Radiograph (KL)	NR[1]	19 (23%)	Double vs single bundle[2]	TF OA p=.64 PFJ OA p=.35	TF OA 1.2 (.4,3.4) PFJ OA .5 (.2,1.4)
Kessler, 2008	ACL (ACLRc, ACLnoSx)	Radiograph (KL)	≥2	29 (27%)	Age at surgery (10-yr units)	KOA 1.7 (1.0,2.9)[3]	-
					BMI at surgery	KOA 1.2 (1.0,1.3)[3]	-
					ACLRc vs ACLNoSx[2]	**KOA 2.8 (1.1,7.5)[3]**	-
Kvist, 2020	ACL+ (ACLRc, ACLnoSx)	Radiograph (KL)	≥2	TF 95 (62%) PFJ 48 (35%)	Allocation to ACLRc[2] vs ACLnoSx	NR	**TF OA 2.4 (1.2,4.7)** PFJ OA .6 (.3,1.2)
					ACLnoSx vs ACL surgery[2]	NR	**TF OA 2.5 (1.4,5.3)** PFJ OA .9 (.5,1.9)
					ACLnoSx[2] vs Delayed ACLRc	NR	TF OA .6 (.2,1.5) PFJ OA .7 (.3,1.8)
					Early ACLRc[2] vs Delayed ACLRc	NR	TF OA 1.8 (.9,4.1) PFJ OA .5 (.2,1.2)
Leys, 2012	ACL+ (ACLRc)	Radiograph (IKDC)	NR[1]	54 (50%)	Future surgery (Y vs N)	KOA p=0.73	UC
					ST[2] vs PT autograft	**KOA 2.8 (1.2,6.2)**	KOA 2.2 (.99,4.7)
Li, 2011	ACL+ (ACLRc)	Radiograph (KL)	≥2- grade bilateral difference in 1 compartment OR ≥1-grade bilateral difference in 2 compartments	NR	BMI >25 at surgery (Y vs N[2])	**KOA 2.0 (1.1,3.8)[3]**	-
					BMI >30 at surgery (Y vs N[2])	**KOA 3.2 (1.3,7.8)[3]**	-
					Length of follow-up	**KOA 1.2 (1.1,1.2)[3]**	-
					Medial meniscectomy (yes vs no[2])	**KOA 3.1 (1.4,6.9)[3]**	-
					Grade ≥2 medial cartilage chondrolysis (Y vs N[2])	**KOA 2.9 (1.3,6.7)[3]**	-
Lohmander, 2004	ACL+ (ACLRc, ACLnoSx)	Radiograph (KL)	≥2	34 (51%)	ACLRc vs ACLNoSx[2]	KOA 1.7 (.6,5.0)[3] TF OA 1.3 (.5,3.9)[3] PFJ OA 14 (.9,224)[3]	-
					Meniscus surgery vs no injury[2]	**KOA 3.6 (1.2,11)**	-
Mascarenhas, 2010	ACL+ (ACLRc)	Radiograph (KL)	≥2	18 (53%)	Autograft vs allograft[2]	KOA p=0.99	KOA 1.0 (.3,3.8)
Meuffels, 2008	ACL+ (ACLRc, ACLnoSx)	Radiograph (KL)	≥2	19 (38%)	ACLRc vs ACLnoSx[2]	KOA p=0.145	KOA 2.4 (.7,7.7)[6]
Meunier, 2007	ACL+ (ACLRc, ACLnoSx, ACLRp)	Radiograph (mAhlback, Fairbank)	NR[1]	48 (52%)	Meniscectomy (Y vs N)	KOA p=0.02	UC
					ACLRp[2] vs ACLnoSx	NR (NS)	KOA .38 (.1,1.7)
					ACLRp[2] vs ACLRp with augmentation	NR (NS)	KOA .35 (.1,1.6)
					ACLRp[2] vs Delayed ACLRc	NR (NS)	KOA .7 (.1,3.9)
Neuman, 2017	ACL+ (ACLRc, ACLnoSx)	Radiograph (mOARSI)	JSN grade ≥2 in any 2 TF or PF compartments OR osteophyte score ≥2 in any 2 TF or PF compartments OR compartment specific JSN grade 1 + osteophyte grade 1	NR	Acute Aggrecan	KOA 1.0 (.995,1.0)	-
					Chronic Aggrecan	KOA 1.0 (.99,1.0)	-
					Acute COMP	KOA 1.0 (.98,1.0)	-
					Chronic COMP	KOA 1.1 (.99,1.1)	-
					Acute MMP-3	KOA 1.0 (.99,1.0)	-
					Chronic MMP-3	KOA 1.0 (.98,1.1)	-
					Acute TIMP-1	KOA .99 (.95,1.0)	-
					Chronic TIMP-1	KOA 1.3 (.98,1.7)	-
Neuman, 2008	ACL+ (ACLRc, ACLnoSx)	Radiograph (mOARSI)		13 (16%)	Meniscus tear (Y vs N)	KOA p<0.0001	UC
					Delayed ACLRc vs no-surgery[2]	KOA p=0.03	**KOA 4.8 (1.6,17.1)**
					Delayed ACLRc + meniscus tear (Y vs N[2])	NR	KOA 1.57 (.4,6.9)

Bold (statistically significant). ACL (Anterior cruciate ligament tear, no concomitant injury), ACL+ (ACL tear+concomitant injury), ACL? (ACL tear, concomitant injury unknown), ACLRc (ACL tear reconstruction), ACLRp (ACL tear repair), ACLnoSx (ACL tear no Sx), AKP (anterior knee pain), BMI (Body Mass Index), CI (95% confidence interval), COMP (Cartilage Oligomeric Matrix Protein), ICRS (International Cartilage Repair Society Cartilage Rating), IKDC (International Knee Documentation Committee OA scoring system), JSN (joint space narrowing), KL (Kellgren-Lawrence OA grade), KOA (knee OA inclusive of all compartments), KOS-ADL (Knee Outcome Survey Activities of Daily Living subscale), LET (Lateral Extraarticular Tenodesis), LSI (lower limb symmetry index), m (meter), MF (Microfracture), MOAKS (MRI OA knee score), mo (months), mm (millimeters), MMP-3 (Matrix metalloproteinase-3), mOARSI (modified Osteoarthritis Research Society International Atlas score), N (no), NR (not reported), NS (author reported not statistically significant), OA (osteoarthritis), OAT (Osteochondral autologous transplantation), PFJ (patellofemoral joint), PT (patellar tendon graft), ROM (range of motion), RR (risk ratio), RTS (return to sport), ST (semitendinosus graft), Sx (surgery), TF (tibiofemoral joint), TIMP-1 (), UC (unable to calculate), Y (yes), yr (years).

[1]Recalculated (IKDC OA = Grade B, C or D; KL OA = ≥2; Ahlback OA = ≥1, PFJ OA = Grade ≥1 osteophyte, [2]Reference group, [3]Multivariable analyses, [4]Medial compartment assessed with medial meniscectomy only, and lateral compartment assessed with lateral meniscectomy only, [5]Odds ratio (95%CI) not provided, OA (95%CI) does not account for matching.

7. Meta-analysis Forest Plots

Male Sex

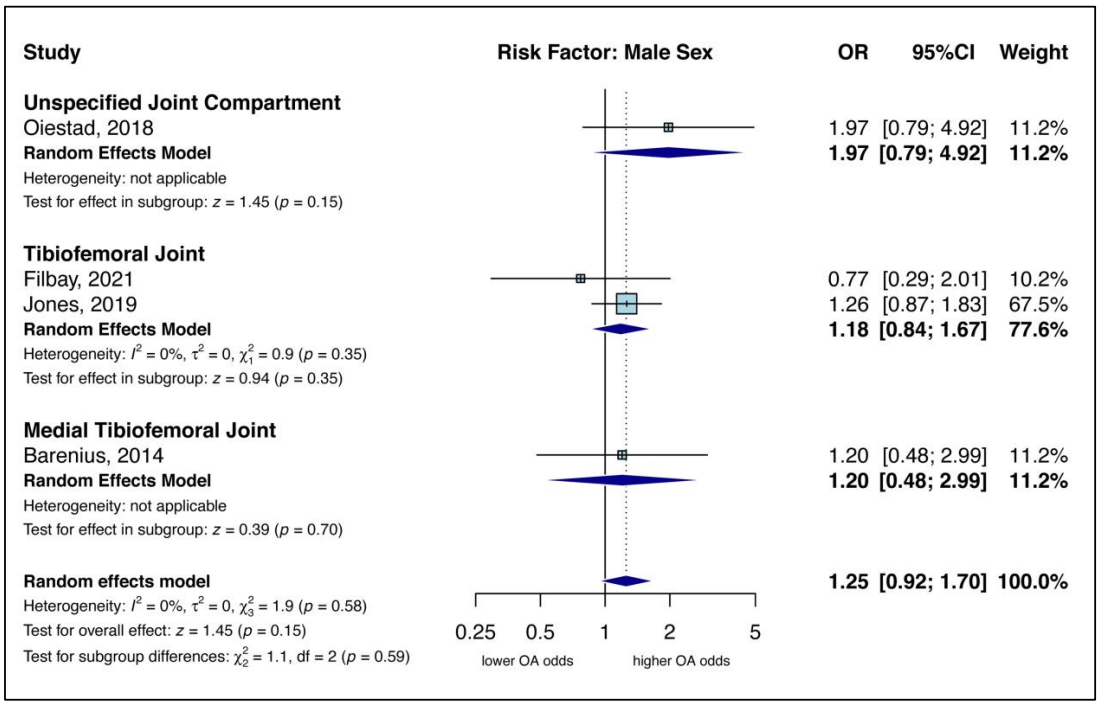

Figure 1: Odds (OR; 95% CI) of structural knee osteoarthritis (OA) by sex at Anterior Cruciate Ligament (ACL) tear, stratified by joint compartment. *There is very low-quality evidence that male sex may increase the odds of OA after an ACL tear 1.25 times (not statistically significant).*

Rehabilitation for Anterior Cruciate Ligament Tear

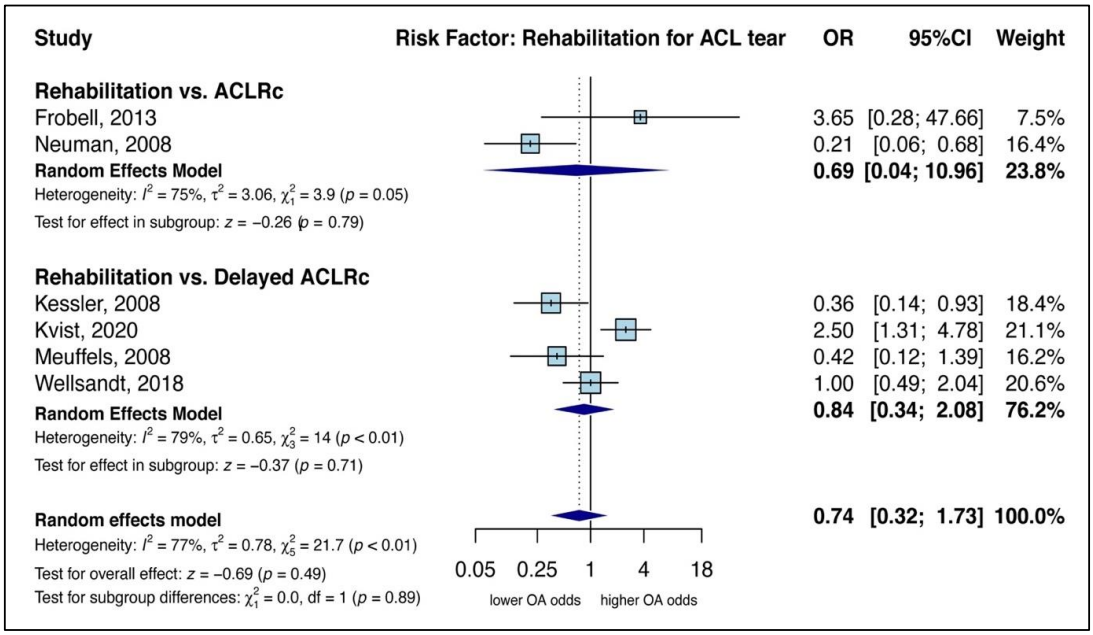

Figure 2: Odds (OR; 95% CI) of structural knee OA for management of an ACL tear with rehabilitation stratified by comparison condition (i.e., rehabilitation or delayed ACL reconstruction; ACLRc). Frobell et al 2013, Kvist 2020 and Neuman 2008 assessed tibiofemoral and patellofemoral OA with the tibiofemoral estimates included in the meta-analyses, Meuffels et al 2008 assessed tibiofemoral OA (based on radiographic views reported), Wellsandt et al 2018 assessed tibiofemoral OA but only reported medial tibiofemoral compartment OA estimates, while Kessler et al 2008 did not specify joint compartment. *There is very low-quality evidence of no difference in the odds of OA between ACL tear management with rehabilitation vs ACLRc or delayed ACLRc.*

Anterior Cruciate Ligament Reconstruction for Anterior Cruciate Ligament Tear

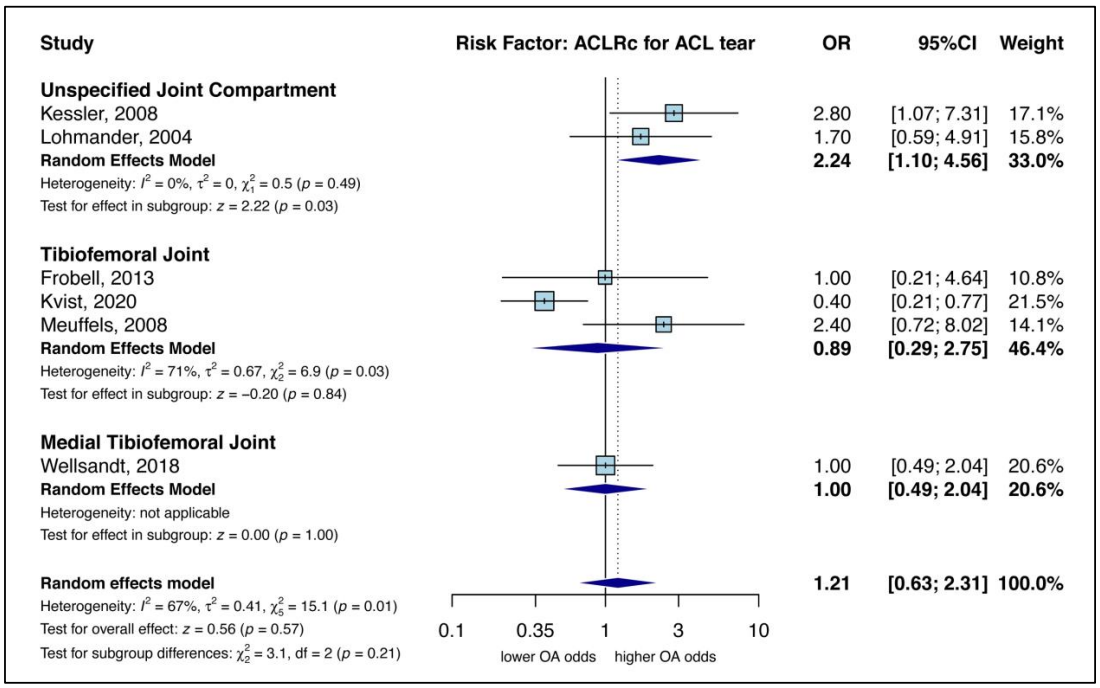

Figure 3: Odds (OR; 95% CI) of structural knee OA for management of an ACL tear with an ACLRc stratified by joint compartment. *There is very low-quality evidence of no difference in odds of structural knee OA between ACL tear management with ACLRc or non-operative management.*

Age at Anterior Cruciate Ligament Reconstruction

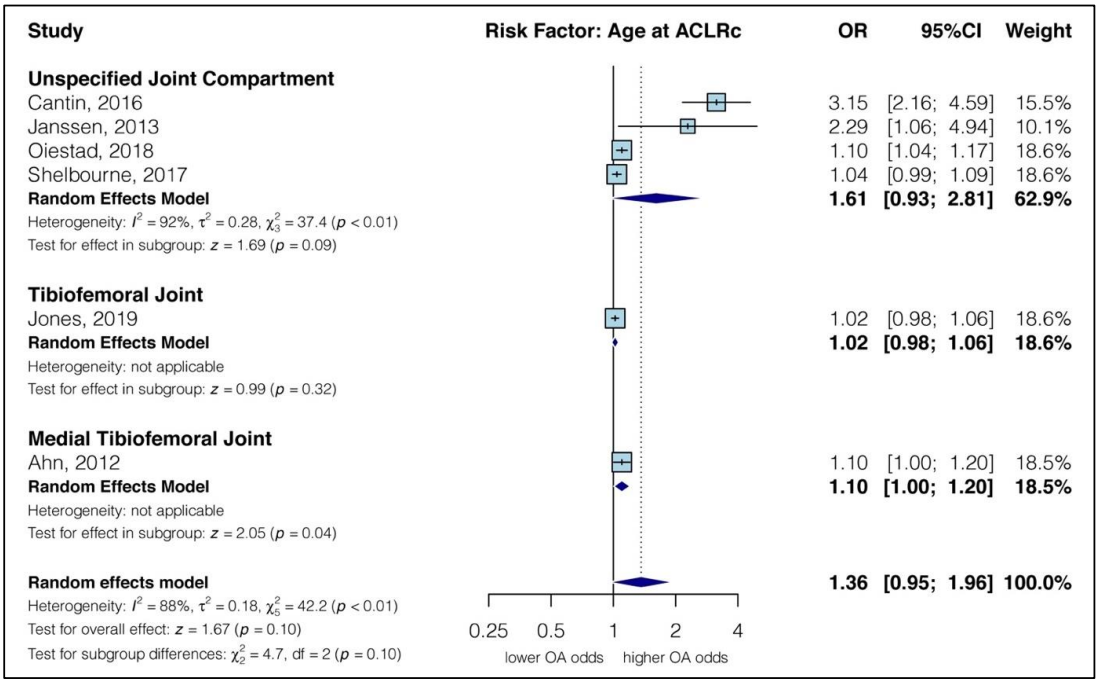

Figure 4: Odds (OR; 95%CI) of structural knee OA for every one-year increase in age at ACLRc, stratified by joint compartment. *There is very-low quality evidence that the odds of structural knee OA may increase 1.36 times for every one-year increase in age at ACLRc (not statistically significant).*

Body Mass Index at Anterior Cruciate Ligament Reconstruction

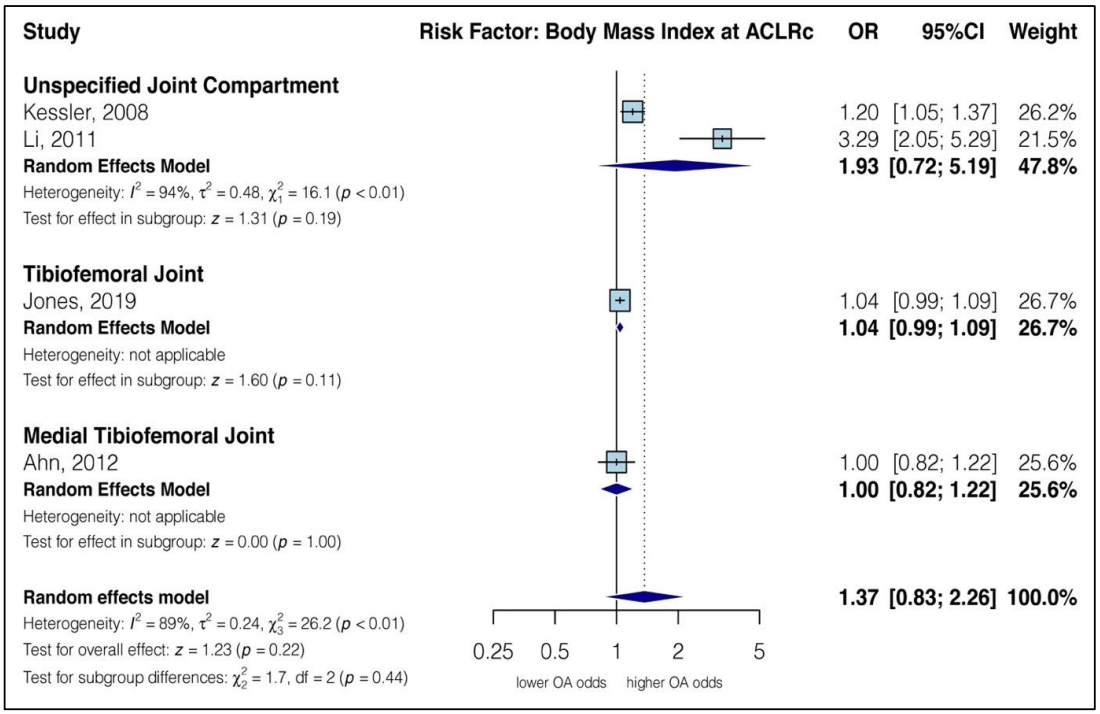

Figure 5: Odds (OR; 95% CI) of structural knee OA for every one kg/m^2 increase in body mass index (BMI) at ACLRc, stratified by joint compartment. *There is very low-quality evidence of no difference in odds of structural knee OA with a one kg/m^2 change in BMI at ACLRc.*

Patellar Tendon Autograft

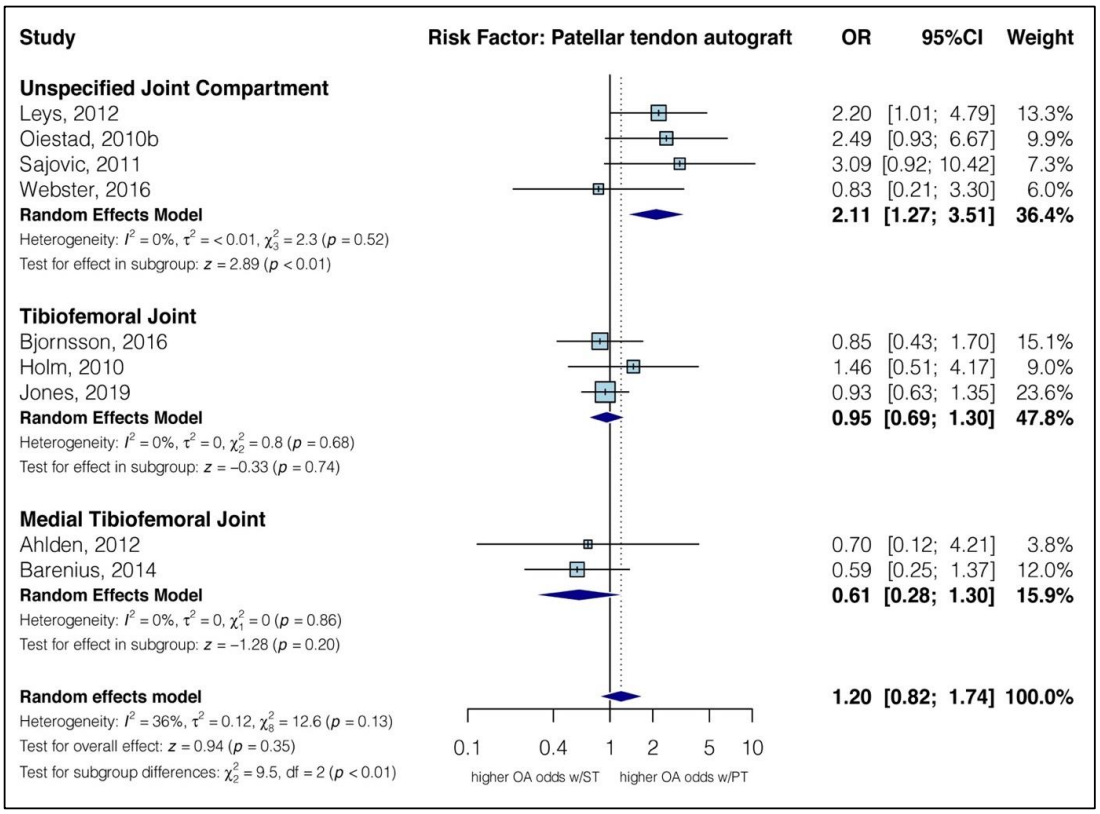

Figure 6: Odds (OR; 95% CI) of structural knee OA for patellar tendon autograft for ACLRc, stratified by joint compartment. *There is very low-quality evidence of no difference in odds of structural knee OA between a patellar tendon autograft and a semitendinosus tendon autograft.*

Anterior Cruciate Ligament Reconstruction with Augmentation

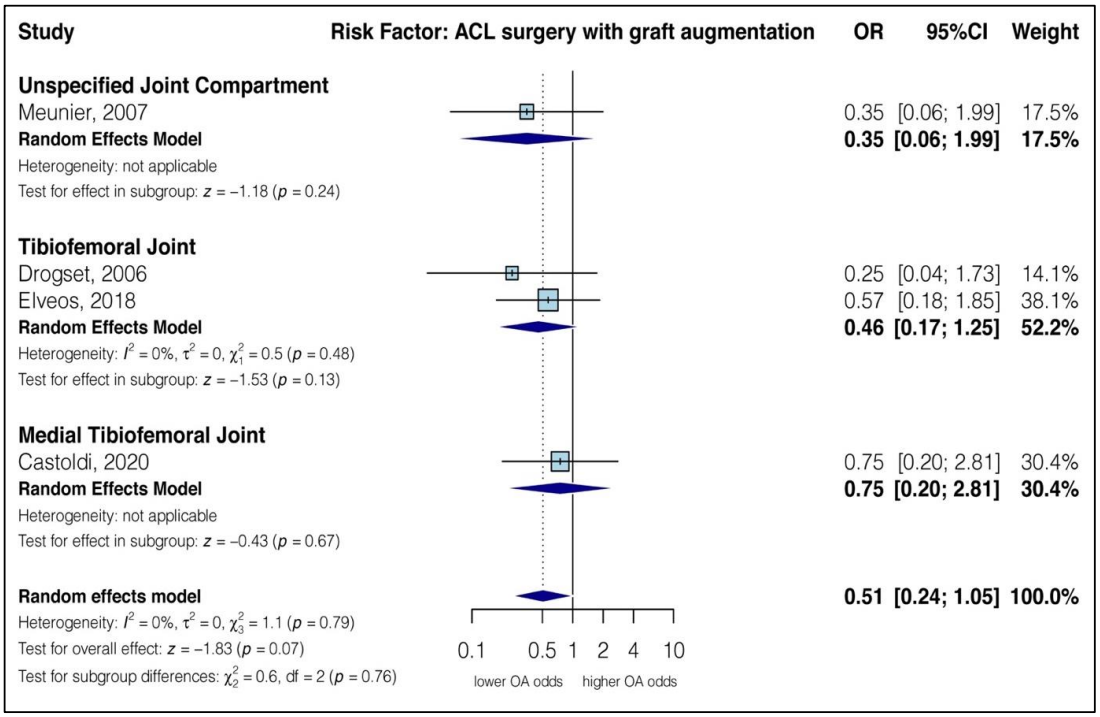

Figure 7: Odds (OR; 95% CI) of structural knee OA for ACLRc or ACL Repair with ACL graft augmentation, stratified by joint compartment. *There is very low-quality evidence that ACLRc (Castoldi et al 2020, Drogset et al 2006, Elveos et al 2018) or ACL Repair (Meunier et al 2007) with graft augmentation may decrease the odds of structural knee OA 0.51 times compared to ACL surgery with no augmentation (not statistically significant).*

Cartilage Injury at Anterior Cruciate Ligament Reconstruction

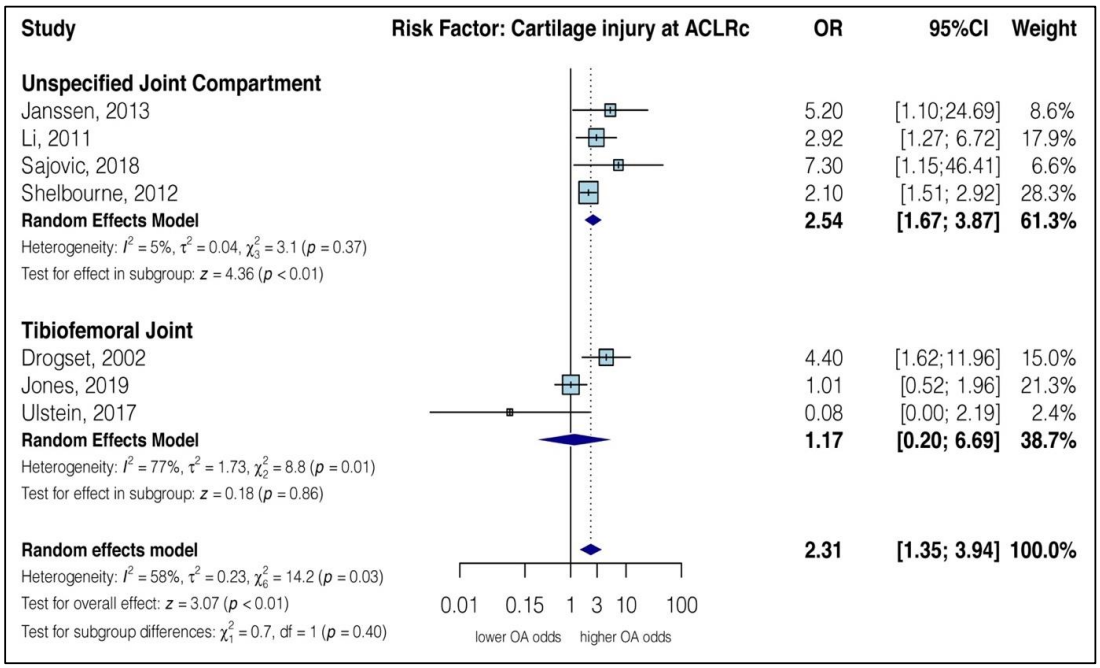

Figure 8: Odds (OR; 95% CI) of structural knee OA for cartilage injury at the time of ACLRc, stratified by joint compartment. *There is very low-quality evidence that cartilage injury at ACLRc increases the odds of structural knee OA 2.31 times compared to no cartilage injury (Drogset et al 2002, Sajovic et al 2018, Shelbourne et al 2012, Ulstein et al 2017) or less severe cartilage injury [Janssen et al 2013 (International Cartilage Repair Society Grade 3-4 vs 0-2), Jones et al 2019 (Modified Outerbridge classification Grade 2-4 vs. Grade 1), Li et al 2011 (unspecified classification system Grade 2-4 vs. grade 0-1)].*

Anterior Cruciate Ligament Reconstruction with Partial Meniscectomy

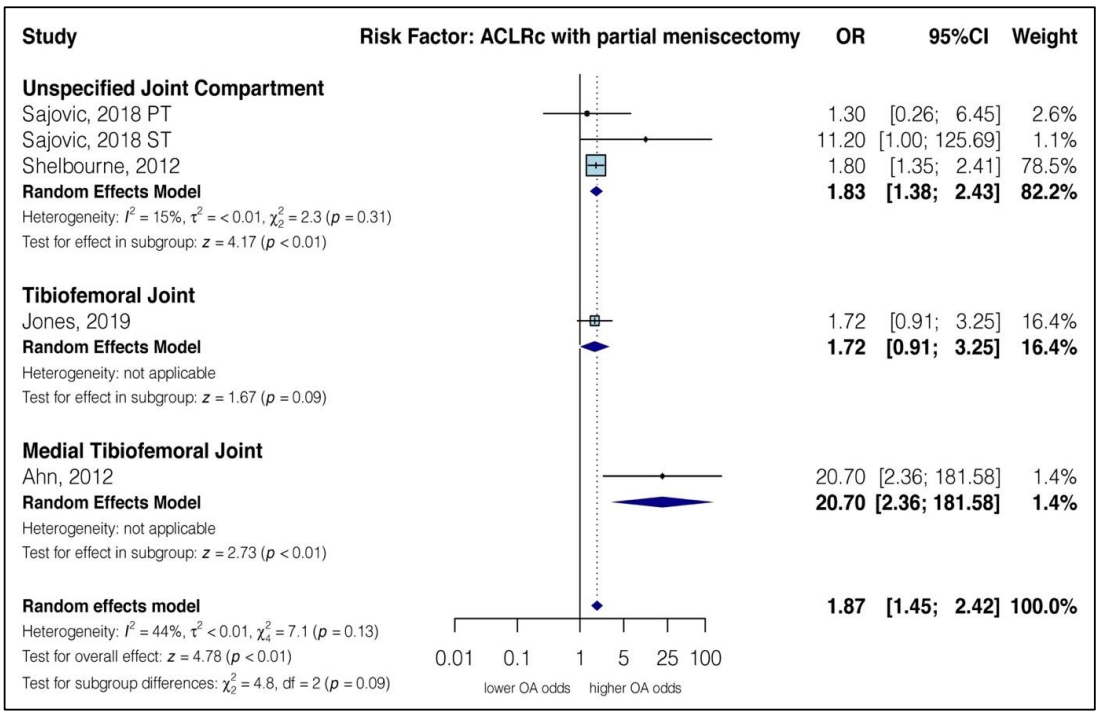

Figure 9: Odds (OR; 95% CI) of structural knee OA for ACLRc with concomitant partial meniscectomy, stratified by joint compartment. *There is very low-quality evidence that ACLRc with a concomitant partial meniscectomy increases the odds of structural knee OA 1.87 times compared to ACLRc with no concomitant partial meniscectomy.*

Anterior Cruciate Ligament Reconstruction with Total Medial Meniscectomy

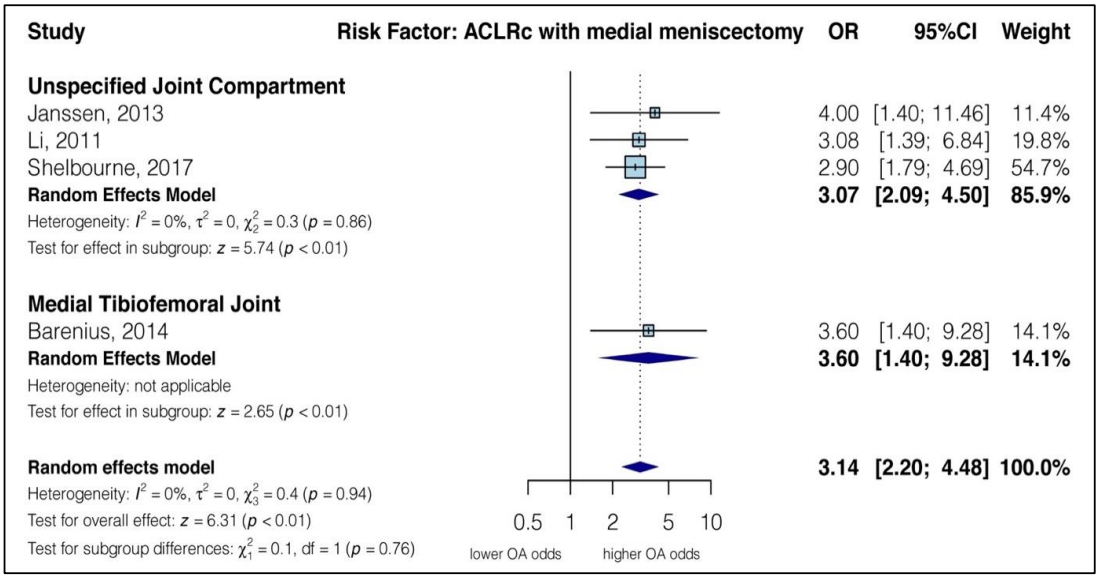

Figure 10: Odds (OR; 95% CI) of structural knee OA for ACLRc with concomitant total medial meniscectomy, stratified by joint compartment. *There is very low-quality evidence that ACLRc with a concomitant total medial meniscectomy increases the odds of structural knee OA 3.14 times compared to ACLRc without a concomitant total medial meniscectomy.*