A report on knee arthritis: surgical knee replacement versus conservative (non-surgical) therapy alone for Universitätsklinikum Schleswig-Holstein/Campus Kiel

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LIST OF ABBREVIATIONS

BKS	Bristol Knee Score
BMI	Body mass index
CDSR	Cochrane Database of Systematic Reviews
CI	Confidence interval
CPG	Clinical practice guideline
CRD	Centre for Reviews and Dissemination
DARE	Database of Abstracts of Reviews of Effects
EQ-5D	EuroQol-five dimensions questionnaire
FAQ	Frequently asked question
GRADE	The Grading of Recommendations Assessment, Development and Evaluation
JOAS	Japanese Orthopaedic Association Score
HR	Hazard ratio
HRQoL	Health-related quality of life
HTA	Health technology assessment
KOOS	Knee injury and Osteoarthritis Outcomes Score
KSR	Kleijnen Systematic Reviews
KSS	Knee Society Score
MA	Meta-analysis
MCID	Minimal clinically important difference
MD	Mean difference
N/A	Not applicable
NICE	National Institute for Health and Care Excellence
NR	Not reported
NST	Non-surgical treatment
OA	Osteoarthritis
OKS	Oxford Knee Score
OR	Odds ratio
PICOS	Participants, intervention, comparators, outcomes, and study design
PRISMA	Transparent Reporting of Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
RR	Risk ratio
SDM	Shared decision making
SD	Standard deviation
SMD	Standardised mean difference
SR	Systematic review
TKA	Total knee arthroplasty
TKR	Total knee replacement
UKR	Unicompartmental knee replacement
UKSH	Universitätsklinikum Schleswig-Holstein
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

1. PROJECT OBJECTIVES

An overarching aim of the research project "Making SDM a reality" is to inform patients as part of shared decision making (SDM).

Kleijnen Systematic Reviews Ltd (KSR) has prepared this evidence report with a synthesis of the relevant evidence of treatment options for surgical knee replacement versus conservative (non-surgical) therapies alone. This report is based on a previous report by EBSCO Information Services (2019), in which the comparison groups were limited to Total Knee Replacement (TKR) and conservative management alone.[1]

2. METHODS

2.1 INCLUSION CRITERIA

The frequently asked questions (FAQs) underpinning the literature searches were developed in collaboration with clinicians at the Universitätsklinikum Schleswig-Holstein (UKSH)/ Campus Kiel. These questions pertain to the relevant characteristics of participants, intervention, comparators, outcomes, and study design (PICOS), see Table 1. Systematic reviews (SRs), clinical practice guidelines (CPGs) evaluated herein aim to inform patients, clinicians, researchers, and health policy makers on relevant evidence relating to surgical knee replacement versus conservative (non-surgical) therapy alone.

It is worth stating that the PICOS and eligibility criteria listed herein (see Table 1) differ from the ones specified in the EBSCO report since the unicomparmental knee replacement (UKR) was only added after completion of the EBSCO report.[1]. This report can be considered to be an update to the EBSCO report, extended by the UKR treatment alternative.

Table 1: Inclusion and exclusion criteria

	Included	Excluded
Population	Adult patients with radiographically confirmed knee osteoarthritis; and considering or eligible for total or partial knee replacement	Adult patients with knee necrosis, rheumatoid arthritis
Intervention/ comparator	Surgical therapies a) Total knee replacement b) Unicompartmental knee replacement	N/A
Outcomes	• Resolution of symptoms • Improvement in function • Pain • Quality of life • Weight loss • Reoperation rates • Length of hospital stay • Time to recovery • Time to return to usual activities • Short and long-term risks/complications	N/A
Study design	Systematic reviews, clinical practice guidelines	Narrative reviews; expert opinions; letters' overviews of reviews
N/A = not applicable		

2.2 FREQUENTLY ASKED QUESTIONS

The following FAQs were identified:

1. What does the treatment involve?
2. Will my symptoms get better?
3. Will the treatment increase my overall well-being and improve my quality of life?

4. When will I recover?
5. What risks are associated with the treatments?
6. What are side effects of the treatments?
7. Will I be able to reduce my pain medication? Will the treatment help me lose weight?

2.3 LITERATURE SEARCHES

Literature searches were conducted to identify systematic reviews and guidelines on surgical knee replacement (followed by non-surgical therapy) versus conservative (non-surgical) therapy alone for osteoarthritis of the knee. The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Searches were not limited by language, publication date, or publication status. Of note, in the previous report, EBSCO used different search strategies including searches of the EBSCO databases.[1]

2.4 SEARCH SOURCES

2.4.1 Systematic reviews and guidelines

These searches comprise an update to a previous project conducted in May 2019, therefore the following systematic review/health technology assessment (HTA) specific databases were searched on 2 March 2021, from 2019 to the most recent date available:

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 3 of 12, March 2021
- INAHTA International HTA database (https://database.inahta.org/): to 2 March 2021
- KSR Evidence (Internet) (https://ksrevidence.com/): to 2 March 2021
- Epistemonikos (Internet) (https://www.epistemonikos.org/): to 2 March 2021

The following guidelines resources were searched on 2 March 2021, from 2019 to the most recent date available:

- NICE Guidance (Internet) (https://www.nice.org.uk/guidance): to 2 March 2021
- ECRI Guidelines Trust (Internet) (https://guidelines.ecri.org/): to 2 March 2021
- NICE Evidence (Internet) (www.evidence.nhs.uk/): to 2 March 2021
- Guidelines International Network (GIN) (Internet) (https://www.g-i-n.net/home): to 2 March 2021
- Trip Database (Internet) (https://www.tripdatabase.com/): to 2 March 2021

Full details of all search strategies are presented in Appendix 1.

2.4.2 Handling of citations

Identified references from the bibliographic database searches were downloaded into EndNote bibliographic management software for further assessment and handling.

2.4.3 Supplementary searches

Reviewers also conducted internet searches to identify other potentially relevant references. The bibliographies of included studies and review articles were also checked for additional relevant articles.

2.5 STUDY SELECTION AND DATA EXTRACTION

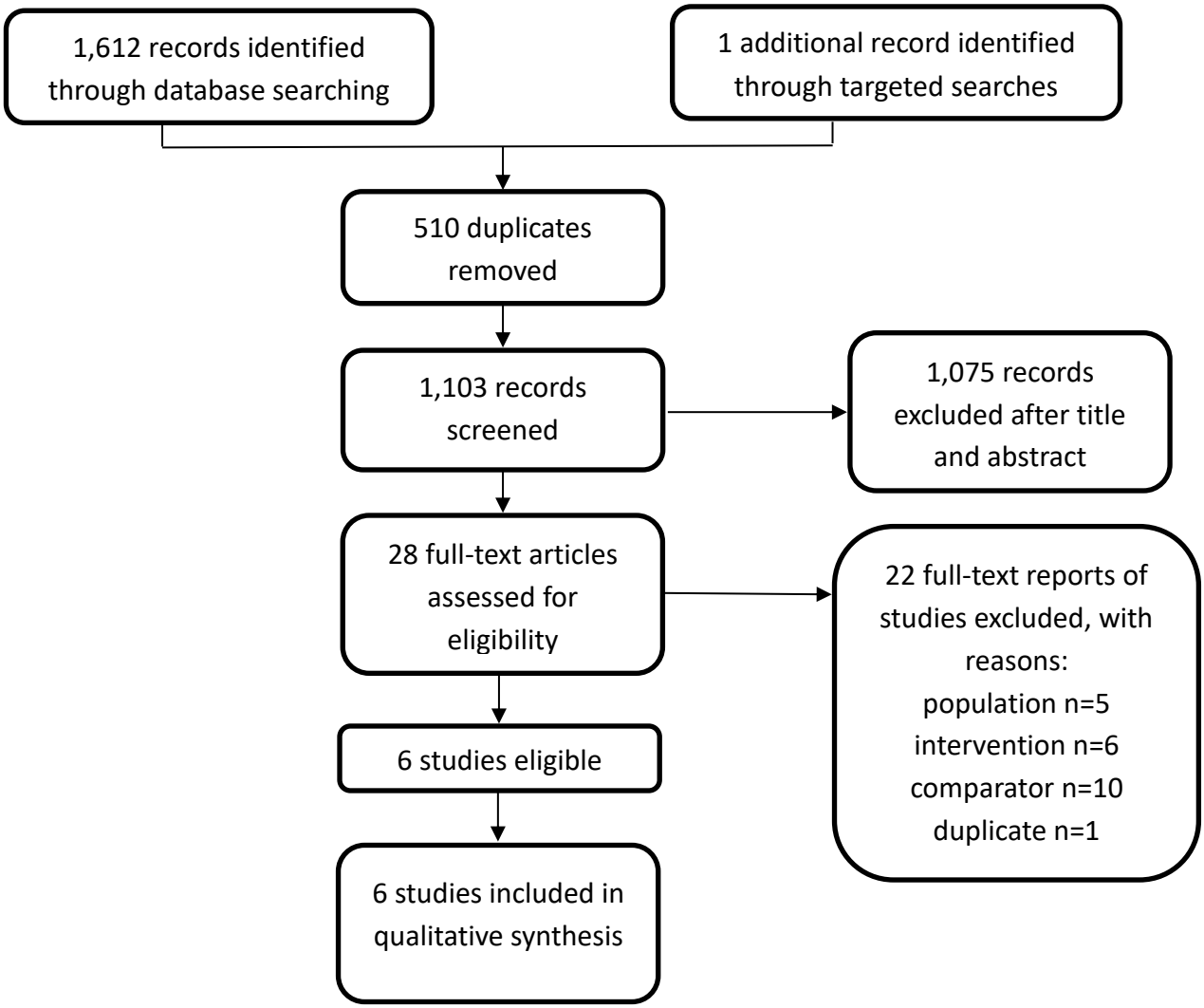
Two independent reviewers screened titles and abstracts of all records identified by the electronic searches and any disagreements were resolved through consensus. Full-text versions were obtained for all potentially eligible studies and screened by these same two reviewers independently against the pre-specified eligibility criteria. For each study, one reviewer extracted the data whereas another validated the entries. Any disagreements were settled through discussion.

3. RESULTS

3.1 LITERATURE SEARCHES AND INCLUSION ASSESSMENT

Searches were conducted in March 2021 to identify all relevant SRs or CPGs published in and after May 2019 (i.e. after EBSCO searches have been conducted). A total of 1,612 records were retrieved from the electronic literature searches; and one identified through targeted searches. One thousand one hundred and three titles and abstracts were screened by two reviewers after removing duplicate records. After screening of 28 full-text papers, six met the inclusion criteria. A summary of the study selection process according to modified PRISMA reporting guidelines is reported in Figure 1.[2] The EBSCO report included nine studies published before May 2019 of different designs (cohort study, SR, randomised controlled trial) with only one study overlapping with our findings.[1, 3]. Since the study by Wilson 2019, however, compare TKR to UKR and therefore at the time did not meet the PICO, it was limited to being used to identify data on complications of TKR in the EBSCO report.

Figure 1: Study selection process



3.2 OVERVIEW OF INCLUDED STUDIES

Five systematic reviews (SRs), and one clinical practice guideline (CPG) were eligible for inclusion. Table 2 below summarises the sources of evidence used to answer the respective

nine FAQs. These SRs and CPG included evidence from both randomised controlled trials (RCTs) and observational studies. Quantitative evidence was available to answer the FAQs 2 to 6. Qualitative evidence was available to answer FAQs 1 and 8. In the EBSCO report, which was limited to comparing TKR to conservative management (primarily consisting of physical therapy, pain management and dietary advice/treatment including exercise and lifestyle/dietary changes), the primary source of data used for FAQs 2-7 was the RCT by Skou et al. with publications reporting on outcomes for 1 and 2 years follow-up, respectively. [4, 5] Reported outcomes for treatment alternatives in this report regarding pain and function were primarily based on the KOOS score (Knee Injury and Osteoarthritis Outcome Score), with a 15% improvement in these scores being considered a response to treatment.[1] Also, the Skou trial reports on weight changes and side effects/complications of treatment alternatives. In this report, most function and pain-related outcomes were measured with other instruments than KOOS. Results of the EBSCO-report and this report have to therefore be compared and interpreted with caution.

Table 2: Evidence sources

Study/year	Evidence source	Intervention	FAQ1: What does the treatment involve?	FAQ2: Will my symptoms get better?	FAQ3: Will the treatment increase my overall well-being and improve my quality of life?	FAQ4: When will I recover?	FAQ5: What risks are associated with the treatments?	FAQ6: What are side effects of the treatments?	FAQ7: Will I be able to reduce my pain medication? Will the treatment help me lose weight?
Deng 2021[6]	SR	TKR		✓	✓			✓	
		UKR							
Evans 2019[7]	SR	TKR					✓		
		UKR							
Han 2020[8]	SR	Medial UKR					✓		
		Lateral UKR							
Migliorini 2019[9]	SR	TKR	✓				✓		
		UKR							
NICE[10]	CPG	TKR	✓						
		UKR							
Wilson 2019[3]	SR	TKR		✓		✓	✓	✓	
		UKR							

CPG = clinical practice guideline; NICE = National Institute for Health and Care Excellence; SR = systematic review; TKR = total knee replacement; UKR = unicompartmental knee replacement

3.3 FAQ 1: What does the treatment involve?

This section describes the treatment options of knee osteoarthritis (OA), i.e. total knee replacement (TKR), unicompartmental knee replacement (UKR) and conservative (non-surgical) treatments. It is worth emphasising that the type of surgery e.g. UKR or TKR also depends on gender, knee deformity (varus or valgus), stage of the disease, body mass index (BMI), or the existing comorbidities. These options are briefly described in Table 3.

Table 3: Description of treatments

Total knee replacement (TKR)
During total knee replacement (TKR), the diseased and/or damaged joint surfaces of the knee joint are being surgically replaced with entirely artificial metal and plastic components to relieve the osteoarthritis-related pain and disability.[10] Typically, TKR is being carried out in people between the ages of 60 and 80 although the knee osteoarthritis (OA) also affects younger adults.[11] TKR can be offered if a person has severe pain, swelling and stiffness in the knee joint, reduced mobility, impaired quality of life (psychological or social) or activities of daily living, when other conservative treatments, e.g. physiotherapy or pharmacotherapy have failed.[3, 10] Preparing for the TKR might involve strengthening the muscles around the knee joint by swimming or cycling in the weeks (six to eight) before the operation.[11] Surgery time is about 2 hours. For TKR, the recovery time in a hospital ranges from three to five days.[10] Following a hospital discharge, a patient typically gets walking aids e.g. crutches and is prescribed strengthening exercises by a physiotherapist.
Unicompartmental knee replacement (UKR)
Unicompartmental or unicondylar knee replacement (UKR) is a very similar procedure to the above-described TKR but less invasive with potentially fewer surgical complications. UKR is suitable for the disease confined to one part of the tibiofemoral joint (the joint between the thigh bone and the shin bone) and only that worn compartment is replaced (the non-effected areas being left behind).[7, 10] UKR also preserves the cruciate ligaments, meniscus and tibia plateau of the healthy compartment.[9] Indications for UKR include having an efficient anterior cruciate ligament, varus deformity <5°, range of motion >90° without flexion contracture, body mass index (BMI) <30 kg/m^2.[9] Compared with TKR, UKR is shorter, results in reduced blood loss and length of hospital stay. However, these potential benefits have to be balanced against a greater failure rate and need for earlier revision surgery compared to TKR.
Conservative (non-surgical) treatments
Non-surgical treatments (NSTs) can be sub-divided into a) non-pharmacological i.e. strength training (resistance exercise), weight management (for overweight individuals), education (with or without lifestyle/dietary modifications), water-based exercise, physical therapy (e.g. medial or lateral wedge insoles, patellar taping, manual therapy), psychosocial interventions (Tai Chi, Qi Gong, meditation) or avocado-soybean unsaponifiables; and b) pharmacological i.e. paracetamol, topical non-steroidal anti-inflammatory drugs, glucosamine and chondroitin sulphate.[12, 13]

3.4 FAQ 2: WILL MY SYMPTOMS GET BETTER?

This section explains whether the patients' symptoms i.e. range of motion, pain and function will get better following different surgical techniques i.e. TKR or UKR. These symptoms are measured with a variety of instruments e.g. Knee Society Score (KSS) or Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS), Bristol Knee Score (BKS), Japanese Orthopaedic Association Score (JOAS), Knee injury and Osteoarthritis Outcomes Score (KOOS). These instruments are described in greater depth in the Appendix 3.

There is variability in the methods used to calculate the minimal clinically important difference (MCID) and different thresholds for it. For instance, MCIDs for the WOMAC in patients undergoing TKR can range from 13.3 to 36.0 for pain and 1.8 to 33.0 for function.[14] Three studies were included under this FAQ. The majority of the studies found no differences between TKR and UKR in reducing pain and improving function in patients with knee OA; and there was conflicting evidence for function and combined pain and function scores. Quality of the evidence ranged from low to moderate for this outcome (predominantly moderate). The details of their findings are summarised in Table 4.

3.4.1 Range of motion

One included study found that there were no differences between UKR and TKR in improving range of motion of the knee joint (Table 4).[3] The SR and MA by Wilson et al. 2019 searched three databases (MEDLINE, EMBASE and the Cochrane Library) and one trial registry (Clinical Trials.gov) for studies published between 1 January 1997 and 31 December 2018; and included RCTs, national joint registries/database studies, and cohort studies.[3] For this outcome, the authors found three randomised trials comparing UKR with TKR; and reported no difference between the techniques in improving range of motion in degrees (measured with goniometer on a scale from 0 to typically 135 degrees) (mean difference (MD) = -4.58; 95% confidence interval (CI) -10.75 to 1.59). The certainty of the evidence was ranked as low for this outcome due to data of unclear quality and imprecision.

3.4.2 Pain

Regarding pain, the SR by Wilson et al. 2019 found no differences between UKR and TKR in reducing pain standardised mean difference (SMD = -0.30; 95% CI -0.63 to 0.03; a standard deviation of 4.7 (on a 10 cm Visual Analogue scale, where lower score means less pain) was chosen from a representative study by Weale 1999, and this was used to convert the SMD to a familiar scale. -0.30 (SMD) x 4.7 (SD) = -1.41 points lower) based on low quality evidence (Table 4).[3]

3.4.3 Function

For this outcome, the SR by Wilson et al. 2019 found that no differences between UKR and TKR in improving function (SMD = -0.12; 95% CI -0.28 to 0.04; three studies; a standard deviation of 18.2 (on a 48 points Oxford Knee Score; where higher scores mean better function) was chosen from a representative study by Beard 2017, and this was used to convert the SMD to a familiar scale. -0.12 (SMD) x 18.2 (SD) = 2.18 points higher). The certainty of the evidence was ranked as low for this outcome due to highly biased data and imprecision (Table

4).[3] For this outcome, the SR and MA by Deng et al. 2021 found that compared with UKR, TKR may improve function mean difference (MD = 4.52; 95% CI 2.38 to 6.66) as measured with the Knee Society Score (KSS). The authors searched PubMed, Embase, Web of Science, and the Cochrane Library up to 1 April 2020 and included both experimental and observational studies. The certainty of the evidence was low for this outcome due to data being at high risk of bias and inconsistency,[6] see Table 4 for details.

3.4.4 Combined pain and function

For combined pain and function, the SR by Wilson et al. 2019 found that compared with TKR, UKR probably improves the outcome (SMD = -0.19; 95% CI -0.32 to -0.05; six studies; a standard deviation of 9.9 (on a 48 points Oxford Knee Score; where higher scores mean better function) was chosen from a representative study by Beard 2017, and this was used to convert the SMD to a familiar scale: -0.19 (SMD) x 9.9 (SD) = 1.88 points higher). The certainty of the evidence was ranked as moderate for this outcome due to mixed-quality data (Table 4).[3]

Table 4: FAQ 2 – Evidence synthesis

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CIs	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
Range of motion (measured on a scale from 0 to 135 degrees, higher = better)							
Wilson 2019[3]	3 RCTs	NR	UKR (N/A /128)	TKR (N/A/142)	MD = -4.58; 95% CI -10.75 to 1.59 degrees	Low (data of unclear quality, imprecision)	No difference shown ⇔
Pain							
Wilson 2019[3]	2 RCTs	NR	UKR (N/A /71)	TKR (N/A/71)	SMD = -0.30; 95% CI -0.63 to 0.03***	Low (high risk of bias; imprecision)	No difference shown ⇔
Function							
Wilson 2019[3]	2 RCTs	NR	UKR (N/A/302)	TKR (N/A/336)	SMD = -0.12; 95% CI -0.12 to 0.04[$]	Low (high risk of bias; imprecision)	No difference shown ⇔
Deng 2021[6]	6 (experimental and observational studies)	NR	UKR (N/A/496)	TKR (N/A/497)	MD = 4.52; 95% CI 2.38 to 6.66*	Low (data of low quality, inconsistency)	Benefit of TKR ⇗ but data of low quality
Combined pain and function							
Wilson 2019[3]	6 RCTs	NR	UKR (N/A/431)	TKR (N/A/437)	SMD = -0.19; 95% CI -0.32 to -0.05**	Moderate (data of mixed quality)	Benefit of UKR ⇗ but data of moderate quality

* = measured with Knee Society Score. ** = measured with Oxford Knee score, Bristol Knee score, Western Ontario and McMaster Universities index, Knee Society score, and the Japanese Orthopaedic Association score. *** = measured with Bristol Knee score. [$] measured with Oxford Knee Score and Knee Outcome Scale-Activities of Daily Living Scale. CI = confidence interval; MD = mean difference; NR = not reported; RCT = randomised controlled trial; SMD = standardised mean difference; TKR = total knee replacement; UKR = unicompartmental knee replacement

3.5 FAQ 3: Will the treatment increase my overall well-being and improve my quality of life?

This section explains whether the patients' quality of life will get better following either of the techniques. Only one study was included under this FAQ, and it favoured TKR.

For health-related quality of life (HRQoL), the SR and MA by Deng et al. 2021 found that compared with TKR, UKR may slightly improve HRQoL as measured with visual analogue scale of the EQ-5D questionnaire (on a 100 points scale, where a higher score means better life quality) (MD = 3.86; 95% CI 0.60 to 7.11; two studies). The certainty of the evidence was low for this outcome due to unclear quality data and imprecision – see Table 5.[6]

Table 5: FAQ 3 – Evidence synthesis

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CI	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
Health-related quality of life (on a 100 points scale: higher score means better quality of life)							
Deng 2021[6]	2 (experimental and observational)	NR	UKR (N/A/ 264)	TKR (N/A/ 253)	MD = 3.86; 95% CI 0.60 to 7.11*	Low (data of unclear quality, imprecision)	Benefit of UKR ⇗ but imprecise data of low quality

* = measured with visual analogue scale of the EQ-5D
CI = confidence interval; MD = mean difference; NR = not reported; TKR = total knee replacement; UKR = unicompartmental knee replacement.

3.6 FAQ 4: When will I recover?

This section explains how quickly the patients will recover following the two surgical techniques; length of hospital stay, return to work and return to sport are presented as outcomes. One study was included under this FAQ; and the quality of the evidence was low.[3] For all three outcomes, UKR showed benefits over TKR. The details of their findings are summarised in Table 6.

3.6.1 Length of hospital stay

For this outcome, the SR by Wilson et al. 2019 found that compared with TKR, UKR may reduce length of hospital stay in days (MD = 1.20; days shorter 95% CI −1.67 to −0.73; one study). The certainty of the evidence was ranked as low for this outcome due high risk of bias and imprecision (Table 6).[3]

3.6.2 Return to work

Similarly, the SR by Wilson et al. 2019 found that compared with TKR, UKR may reduce the time to return to work in weeks (MD = -0.96 weeks shorter; 95% CI -1.31 to -0.61; two studies). Analogically, the certainty of the evidence was low for due high risk of bias and imprecision (Table 6).[3]

3.6.3 Return to sport

The SR by Wilson et al. 2019 also found that compared with TKR, UKR may reduce the time to return to sport in weeks (MD = -5.24 weeks shorter; 95% CI -6.84 to -3.64; two studies). The certainty of the evidence was ranked as low for this outcome (high risk of bias and inconsistency). See Table 6 for more details.[3]

Table 6: FAQ 4 – Evidence synthesis

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CIs	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
Length of hospital stay							
Wilson 2019[3]	1 RCT	NR	UKR (N/A/36)	TKR (N/A/40)	MD = -1.20; 95% CI −1.67 to −0.73 days shorter	Low (high risk of bias, imprecision)	Benefit of UKR ⇗ but data of low quality
Return to work							
Wilson 2019[3]	2 cohort studies	NR	UKR (N/A/146)	TKR (N/A/156)	MD = -0.96; 95% CI -1.31 to -0.61	Low (low quality data, imprecision)	Benefit of UKR ⇗ but data of low quality
Return to sport							
Wilson 2019[3]	2 cohort studies	NR	UKR (N/A/151)	TKR (N/A/155)	MD = -5.24; 95% CI -6.84 to -3.64	Low (low quality data, inconsistency)	Benefit of UKR ⇗ but data of low quality
CI = confidence interval; MD = mean difference; NR = not reported; RCT = randomised controlled trial; TKR = total knee replacement; UKR = unicompartmental knee replacement.							

3.7 FAQ 5: What risks are associated with the treatments?

This section explains any risks associated with the treatments i.e., UKR versus TKR. The following outcomes are evaluated: revision rate, prosthesis survival, reoperation and early mortality. Four studies were included under this FAQ.[3, 7-9]

Three of the studies consistently favoured TKR over UKR in prosthesis survival and revision rates; and one study found reduced mortality rate following UKR compared with TKR. The quality of the evidence was low for all outcomes. For more details, please see Table 7.

3.7.1 Revision rate

Two studies evaluated this outcome.[3, 9] The study by Migliorini et al. 2019 searched Cochrane Systematic Reviews, Scopus, PubMed and Google Scholar. The authors pooled data from both controlled and uncontrolled studies; and reported no differences in revision rate between the two treatments after a (mean) follow-up of 42.6 months (RR = 0.97; 95% CI 0.94 to 1.01; 14 studies). The certainty of the evidence was ranked as low for this outcome (high risk of bias and inconsistency), see Table 7 for more details. The SR by Wilson et al. 2019 found that compared with UKR, TKR may reduce revision rate at five years follow-up risk ratio (RR = 0.17; 95% CI 0.04 to 0.78; three studies) but no differences were shown at 10 years follow-up (RR = 0.64; 95% CI 0.19 to 2.14; one study). The certainty of the evidence was low due to high risk of bias and imprecision (Table 7).[3]

3.7.2 Prosthesis survival

Two studies evaluated this outcome.[7, 8] The study by Evans et al. 2019 searched MEDLINE and Embase for case series and cohort studies published from databases inception until 21 July 2018.[7] The authors reported longer TKR prosthesis survival compared with UKR at 15 years follow-up (96.3%; 95% CI 95.7 to 96.9 versus 85.5%; 95% CI 82.2 to 88.7; 19 studies) based on low quality evidence (Table 7).[7] The study by Han et al. 2020 showed no differences in prosthesis survival between medial and lateral UKR (OR = 2.51; 95% CI 0.67 to 9.43; four studies).[8] The authors searched MEDLINE, Embase, Web of Science, Scopus and the Cochrane Library; and included mainly retrospective studies comparing implant survival rates. The certainty of the evidence was low (Table 7).

3.7.3 Reoperation

The SR by Wilson et al. 2019 found no differences in reoperation rates for TKR versus UKR (risk ratio (RR) = 0.73; 95% CI 0.27 to 2.02; two studies). The certainty of the evidence was ranked as low for this outcome (high risk of bias and imprecision). See Table 7 for more details.[3]

3.7.4 Early mortality

The SR by Wilson et al. 2019 found that compared with TKR, UKR may reduce early mortality rate (RR = 0.27; 95% CI 0.16 to 0.45; five studies). The certainty of the evidence was ranked as low for this outcome due to low-quality data (Table 7).[3]

Table 7: FAQ 5 – Evidence synthesis

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CIs	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
Revision rate							
Migliorini 2019[9]	14 (observational and experimental)*	42.6 months	UKR 458/8318 (5.5%)	TKR 115/2113 (5.4%)	RR = 0.97; 95% CI 0.94 to 1.01*	Low (data of low quality, inconsistency)	No difference shown ⇔
Wilson 2019[3]	3 (RCTs)	5 years	UKR 14/113 (12.3%)	TKR 1/114 (0.8%)	RR = 0.17; 95% CI 0.04 to 0.78*	Low (high risk of bias; imprecision)	Difference in favour of TKR; data of low quality ⇗
Wilson 2019[3]	1 (RCT)	10 years	UKR 4/52 (7.6%)	TKR 6/50 (12%)	RR = 0.64; 95% CI 0.19 to 2.14	Low (high risk of bias; imprecision)	No difference shown ⇔
Prosthesis survival							
Evans 2019[7]	19 (case series)	15 years	UKR (85.5%; 95% CI 82.2 to 88.7)^	TKR (96.3%; 95% CI 95.7 to 96.9)^	NR	Low (data of low quality)	Difference in favour of TKR; data of low quality ⇗
Han 2020[8]	4 (observational)	>10 years	Medial UKR 479/516 (92.8%)	Lateral UKR 110/127 (86.6%)	OR = 2.51; 95% CI 0.67 to 9.43	Low (data of low quality)	No difference shown ⇔
Reoperation							
Wilson 2019[3]	2 (RCTs)	NR	UKR 6/296 (2%)	TKR 9/300 (3%)	RR = 0.73; 95% CI 0.27 to 2.02	Low (high risk of bias; imprecision)	No difference shown ⇔
Mortality (early)							
Wilson 2019[3]	5 (national or large multicentre database or joint registry studies)	45 days	UKR 40/73,163 (0.05%)	TKR 1,755/696,356 (0.25%)	RR = 0.27; 95% CI 0.16 to 0.45	Low (data of low quality)	Difference in favour of UKR; data of low quality

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CIs	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
							⇗

* = own re-calculation, for more details, please refer to the appendix 2. ^ = pooled survival estimates form Kaplan-Meier and/or Armitage methods.
CI = confidence interval; NR = not reported; OR = odds ratio; RCT = randomised controlled trial; RR = risk ratio; SMD = standardised mean difference; TKR = total knee replacement; UKR = unicompartmental knee replacement

3.8 FAQ 6: What are the side effects of the treatments?

This section explains what the side effects of the treatments are. The following outcomes are evaluated: myocardial ischaemic events, cerebrovascular events, venous thromboembolism, total complications and deep infections. Two SRs were included under this FAQ.[3, 6] The two studies consistently showed lower rates of side effects following UKR compared with TKR. The quality of the evidence was low for all outcomes. For more details, please see the Table 8.

3.8.1 Myocardial ischaemic events

The SR by Wilson et al. 2019 found no differences between TKR versus UKR in myocardial ischaemic events (RR = 0.33; 95% CI 0.01 to 8.14; one study). The certainty of the evidence was low for this outcome (high risk of bias and imprecision).[3]

3.8.2 Cerebrovascular events

The SR by Wilson et al. 2019 found that compared with TKR, UKR may reduce the rate of cerebrovascular events (RR = 0.34; 95% CI 0.15 to 0.74; two studies) based on low certainty evidence – see Table 8.[3]

3.8.3 Venous thromboembolism

The SR by Wilson et al. 2019 found no differences between TKR versus UKR in venous thromboembolism (RR = 0.24; 95% CI 0.04 to 1.37; two studies). The certainty of the evidence was low for this outcome.[3] The SR and MA by Deng et al. 2021 found that compared with TKR, UKR may reduce venous thromboembolism rates (OR = 0.39; 95% CI 0.16 to 0.93; six studies). The certainty of the evidence was low for this outcome due to low quality data – see Table 8.[6]

3.8.4 Total complications

The SR and MA by Deng et al. 2021 found that compared with TKR, UKR may reduce total complications rate (OR = 0.64; 95% CI 0.46 to 0.89; eight studies) based on low certainty of the evidence (low quality data) – see Table 8.[6]

3.8.5 Deep infection

The SR by Wilson et al. 2019 found that compared with TKR, UKR may result in lower rate of deep infections (RR = 0.59; 95% CI 0.43 to 0.82; two studies) based on low certainty evidence – see Table 8.[3]

Table 8: FAQ 6 – Evidence synthesis

Author	No. of studies (type of study)	Average follow up time	Intervention	Comparator	Effect estimates with 95% CIs	Certainty – quality of evidence (reason for downgrading)	Assessment for use in decision aid
			Proportion with event Intervention/control group event rate (n/N)				
Myocardial ischaemic events							
Wilson 2019[3]	1 (RCT)	NR	UKR 0/260 (0%)	TKR 1/260 (0.3%)	RR = 0.33; 95% CI 0.01 to 8.14	Low (high risk of bias, imprecision)	No difference shown ⇔
Cerebrovascular events							
Wilson 2019[3]	2 (national or large multicentre database or joint registry studies)	NR	UKR 7/26,922 (0.02%)	TKR 54/77,584 (0.06%)	RR = 0.34; 95% CI 0.15 to 0.74	Low (data of low quality)	Difference in favour of UKR; data of low quality ⇗
Venous thromboembolism							
Wilson 2019[3]	2 (RCTs)	NR	UKR 1/314 (0.31%)	TKR 6/300 (2%)	RR = 0.24; 95% CI 0.04 to 1.37	Low (data of low quality)	No difference shown ⇔
Deng 2021[6]	6 (experimental and observational)	NR	UKR 6/493 (1.2%)	TKR 17/526 (3.2%)	OR = 0.39; 95% CI 0.16 to 0.93	Low (data of low quality)	Difference in favour of UKR; data of low quality ⇗
Total complications							
Deng 2021[6]	8 (experimental and observational)	NR	UKR 72/643 (11.1%)	TKR 111/676 (16.4%)	OR = 0.64; 95% CI 0.46 to 0.89	Low (data of low quality)	Difference in favour of UKR; data of low quality ⇗
Deep infections							
Wilson 2019[3]	6 (national or large multicentre database or joint registry studies)	NR	UKR 113/20,675 (0.54%)	TKR 2,525/250,533 (1.0%)	RR = 0.59; 95% CI 0.43 to 0.82	Low (data of low quality)	Difference in favour of UKR; data of low quality ⇗

CI = confidence interval; NR = not reported; OR = odds ratio; RCT = randomised controlled trial; RR = risk ratio; TKR = total knee replacement; UKR = unicompartmental knee replacement

3.9 FAQ 7: Will I be able to reduce my pain medication? Will the treatment help me lose weight?

No quantitative evidence was found for the outcome of reduced pain medication.

4. DISCUSSION

4.1 SUMMARY OF MAIN FINDINGS

Overall, nine papers were included in this review; the certainty of the evidence varied from low to moderate (predominantly low); findings were inconsistent for a few FAQs/outcomes.

For instance, for FAQ 2 findings showed no differences between UKR and TKR in reducing pain intensity based on low quality of the evidence. The reasons for downgrading were high risk of bias and imprecision. However, when compared with placebo, all four NSTs i.e., intra-articular hyaluronic acid and triamcinolone, vitamin D, intra-articular hyaluronic acid, and prescription chondroitin sulphate showed benefits in reducing pain intensity at follow-ups less than (or equal to) six months based on moderate quality of the evidence.[15] For function, findings either showed no differences, or favoured TKR in improving function, when compared with UKR based on low quality of the evidence.[3, 6] When compared with placebo, all three NSTs i.e. prescription crystalline glucosamine sulphate, vitamin D or intra-articular hyaluronic acid showed beneficial effects at follow-ups less than (or equal to) six months. Analogically, the quality of the evidence was moderate.[15] For combined pain and function scores however, moderate quality evidence favoured UKR over TKR.[3]

Only one SR contributed low certainty evidence for this FAQ 3. Deng et al. 2021 found, UKR may improve slightly HRQoL measured with EQ-5D questionnaire when compared with TKR.[6] The certainty of the evidence was downgraded due to unclear quality of data and imprecision.

Findings were consistent for FAQ 4. The SR by Wilson et al. 2019 found that compared with TKR, UKR may reduce length of hospital stay, the time to return to work, or sport. For all three outcomes, the certainty of the evidence was low; with high risk of bias and imprecision being reasons for downgrading.[3]

Similarly, the results were rather inconsistent for FAQ 5. At five years follow-up, the findings showed lower revision rates following TKR, compared with UKR.[3] However no differences were shown between the two techniques at 3.5 and 10 years follow-ups.[3, 9] The findings also showed higher prosthesis survival following TKR, compared with UKR at 15 years follow-up.[7] Whereas no differences between the two techniques were found at follow-up of less than 10 years.[8] No differences were found for reoperation rates between TKR versus UKR.[3] Nevertheless, early mortality rate (up to 45 days post-surgery) was lower following UKR compared with TKR.[3] The certainty of the evidence was low for all outcomes under this FAQ.

Findings were consistent for FAQ 6. Compared with TKR, UKR may result in lower rates of cerebrovascular events, venous thromboembolism, total complications and deep infections.[3, 6] However, no differences were shown for myocardial ischaemic events.[3] For all four outcomes, the certainty of the evidence was low; with low quality data and imprecision being reasons for downgrading.[3]

For FAQ 7, no quantitative evidence was found for reduced pain medication outcome.

4.2 STRENGTH, LIMITATIONS AND UNCERTAINTIES

This report has several strengths including comprehensive and most up-to-date searches, as well as broad coverage of FAQs/outcomes of interest. Evidence from high quality SRs, NMAs and CPGs was utilised when preparing this report. This report has several limitations too. These include an unequal distribution of results for FAQs 2, 4 to 6 compared with FAQs 3 and 7. Several uncertainties exist in the area, as the quality of the evidence was predominantly low. Additionally, heterogeneity of populations, diversity of surgeries, comparators and study designs further limit applicability of the findings. For conservative/NSTs, the list is not comprehensive i.e., we only chose those modalities that showed benefit when compared with placebo (and did not include treatments showing no effect). Some of these NSTs non-pharmacological treatments (e.g. physical activity, diet, education, manual therapy, physiotherapy, etc.) were covered in the EBSCO report.[1]

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APPENDIX 1: SEARCH STRATEGIES

Systematic reviews and guideline search results

Database	Date searched	Dates	Results
CDSR	02.03.21	Issue 3/12, Mar 2021	10
INAHTA	02.03.21	2019 -02.03.21	5
KSR Evidence	02.03.21	2019 -02.03.21	607
Epistemonikos	02.03.21	2019 -02.03.21	813
NICE Guidance	02.03.21	2019 -02.03.21	2
ECRI Guidelines	02.03.21	2019 -02.03.21	11
NICE Evidence	02.03.21	2019 -02.03.21	154
GIN	02.03.21	2019 -02.03.21	1
Trip	02.03.21	2019 -02.03.21	9
Total			**1612**
Total after de-duplication			**1103**

SEARCH STRATEGIES

Cochrane Library (Wiley): Cochrane Database of Systematic Reviews (CDSR) – 2019 to Issue 3 of 12, March 2021
Date searched: 2.3.21
Records found: 10

#1 MeSH descriptor: [Arthroplasty, Replacement, Knee] this term only 2540
#2 MeSH descriptor: [Knee Prosthesis] this term only 717
#3 (knee* near (replace* or arthroplast* or implant* or prosthe* or endoprosthe* or total or unicompartmental or "uni compartmental")):ti,ab 8863
#4 (TKR or TKA or UKA or UKR):ti,ab 3558
#5 #1 or #2 or #3 or #4 with Cochrane Library publication date Between Jan 2019 and Mar 2021, in Cochrane Reviews, Cochrane Protocols 10

International HTA Database: 2019-2.3.21
https://database.inahta.org/
Date searched: 2.3.21
Records found: 5

1 "Arthroplasty, Replacement, Knee"[mh] 40 March 02 2021 12:03 PM
2 "Knee Prosthesis"[mh] 16 March 02 2021 12:03 PM
3 knee* and (replace* or arthroplast* or implant* or prosthe* or endoprosthe* or total or unicompartmental or "uni compartmental") 130 March 02 2021 12:03 PM

4 TKR or TKA or UKR or UKA 30 March 02 2021 12:03 PM
5 #4 OR #3 OR #2 OR #1137 March 02 2021 12:04 PM

Limit: YEAR 2019-2020
6 #4 OR #3 OR #2 OR #1 5 March 02 2021 12:04 PM

KSR Evidence: 2019-2.3.21
https://ksrevidence.com/
2019-2.3.21
Date searched: 2.3.21
Records found: 607
1 knee* near (replace* or arthroplast* or implant* or prosthe* or endoprosthe* or total or unicompartmental or "uni compartmental") in All text 1370 results
2 TKR or TKA or UKR or UKA in All text 739 results

Filtered by: PUBLICATION DATE 2021, 2020, 2019
3 #1 or #2 in All text 607 results

Epistemonikos: 2019-2.3.21
https://www.epistemonikos.org/
Date searched: 02.03.21
Records found: 813
Limits:
Years: 2019-2021
Publication Type: Systematic review
(title:(knee* AND (replace* OR arthroplast* OR implant* OR prosthe* OR endoprosthe* OR total OR unicompartmental OR "uni compartmental")) OR abstract:(knee* AND (replace* OR arthroplast* OR implant* OR prosthe* OR endoprosthe* OR total OR unicompartmental OR "uni compartmental"))) OR (title:(TKR OR TKA OR UKR OR UKA) OR abstract:(TKR OR TKA OR UKR OR UKA))

National Institute for Health and Care Excellence (NICE) Guidance: 2019-2.3.21
https://www.nice.org.uk/guidance
Date searched: 2.3.21
Records found: 2
Limits:
Last updated: January 2019 – March 2021
Type: Guidance

Search term	**Results**
knee	2
knees	0
TKR	0
TKA	0
UKR	0
UKA	0
Total before deduplication	**2**
Total after deduplication	**2**

ECRI Guidelines Trust: 2019-2.3.21
https://guidelines.ecri.org/
Date searched: 2.3.21
Records found: 11
Limits:
Publication year: 2019 –2021

Search term	Results
knee	11
knees	11
TKR	0
TKA	2
UKR	0
UKA	0
Total before deduplication	**24**
Total after deduplication	**11**

NICE Evidence Search: 2019-2.3.21
https://www.evidence.nhs.uk/
Date searched: 2.3.21
Records found:
Limits:
Date: January 2019 – March 2021
Type: Guidance

Search term	Results
knee	109
knees	61
TKR	0
TKA	4
UKR	0
UKA	0
Total before deduplication	**174**
Total after deduplication	**154**

Guidelines International Network (GIN)
https://g-i-n.net/
Date searched: 2.3.21
Records found: 1
Limits:
Date: 2019 –2021

Search term	Results
knee	1
knees	1
TKR	0

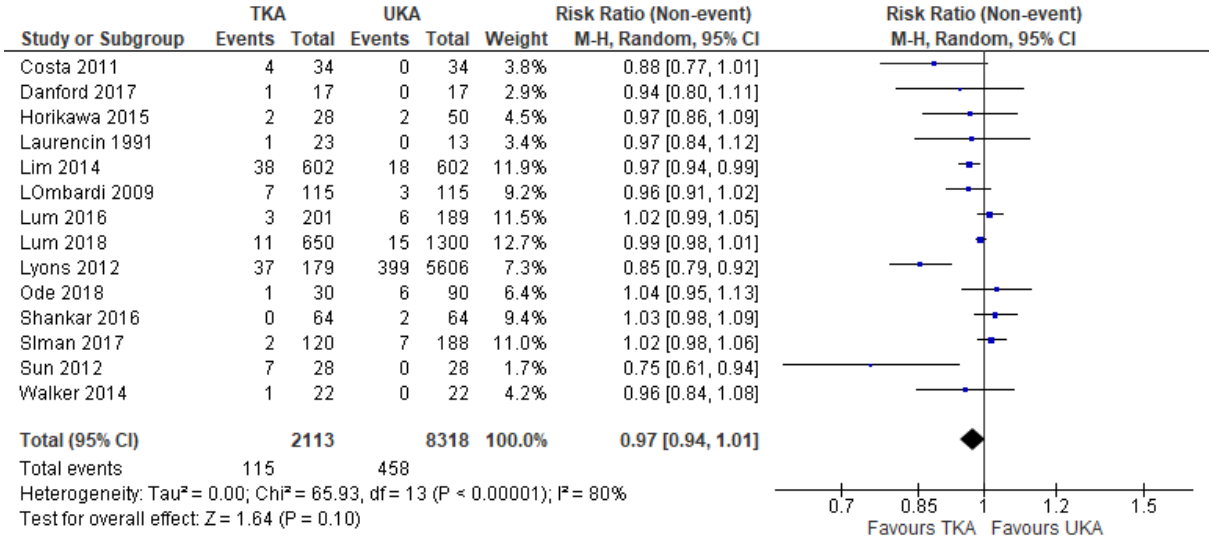
TKA	0
UKR	0
UKA	0
Total before deduplication	**2**
Total after deduplication	**1**

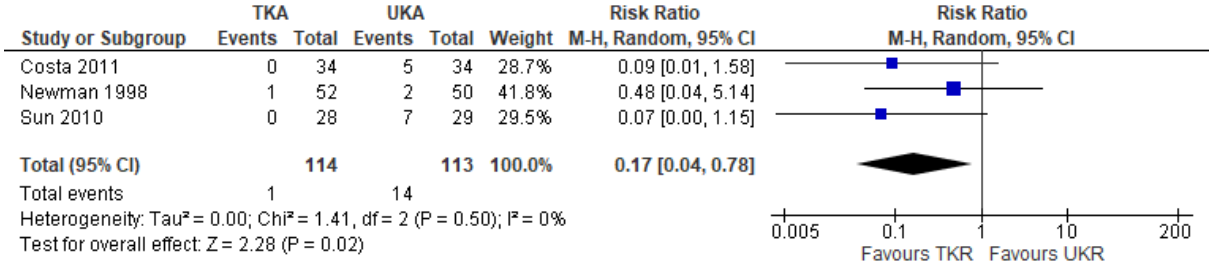
TRIP Database
https://www.tripdatabase.com/
Date searched: 2.3.20
Records found: 130 (9 after screening for relevance)
Limits:
Guidelines
Published since 2019

knee* and (replace* or arthroplast* or implant* or prosthe* or endoprosthe* or total or unicompartmental or "uni compartmental") 111

tkr or tka or ukr or uka 19

APPENDIX 2: OWN CALCULATIONS WITH REVIEW MANAGER 5.4.1





Figures footnotes: Outcome: revision rate (refer to Table 7)

APPENDIX 3: DESCRIPTION OF OUTCOME MEASURE/INSTRUMENTS

The Oxford Knee Score (OKS)

The Oxford Knee Score (OKS) is a questionnaire to assess the patient's perspective of outcome following TKR. [16] The tool consists of twelve questions covering an individual's activities of daily living such as pain, self-care, transport, walking, rising from chair, limping, kneeling, sleep, work, buckling, shopping, stairs; and how these have been affected by pain over the preceding four weeks.[17] Each question can be scored as 1 = least difficult to 5 = most difficult with a total score ranging from 12-60 (the higher score meaning better results). The questionnaire is completed for each knee independently. The tool has good evidence for reliability, content validity and construct validity.[18] Minimal detectable change at the 95% confidence level is 4.15 points. It takes approximately 5-10 minutes to complete.

Bristol Knee Score (BKS)

Bristol knee score (BKS) is a clinical scoring system which has been used in patients following TKR. It is a 50-point score that assesses joint pain, function, movement, deformity and laxity.[19] The total grade/score falls into four categories (Excellent = 41-50; Good = 36-40; Fair = 30-35; Poor = <30).[20] It has a very high reliability, content validity and construct validity with interobserver correlation coefficients alpha ranging from 0.22 to 0.88.[21]

Western Ontario and McMaster Universities index (WOMAC)

Western Ontario and McMaster Universities index is a self-administered questionnaire that measures pain, physical function, stiffness of patients following TKR or UKR.[22] The tool measures five items for pain, two for stiffness, and 17 for functional limitation; and there two scaling versions for WOMAC items: one applies a 100 mm visual analogue scale (VAS); the other uses a five-point Likert scale.[23] The tool has an excellent reliability, content validity and construct validity.[18] Minimal detectable change at the 95% confidence level is 0.5-1.3 points.[18] It takes approximately 5-10 minutes to complete.

Knee Society Score (KSS)

Knee Society Score (KSS) is an interview and examination-based measurement instrument that assesses pain, expectation, satisfaction, and physical function of patients with knee OA. The tool consists of four scales measuring 34 items.[18] Scores range from 0-100 for pain, 0-40 for satisfaction, 0-15 for expectations and 0-100 for function. It has good internal consistency but doubtful construct and content validity. It takes approximately 15 minutes to complete.

Japanese Orthopaedic Association Score (JOAS)

The tool consists of four main items assessing: pain and stiffness (a total of eight questions, 0–32 points), activities of daily living (a total of 10 questions, 0–40 points), participation in social activities (a total of five questions, 0–20 points), and general health conditions (a total of two questions, 0–8 points).[24] The highest possible score is 100 points with the higher scores, meaning better the recovery of knee joint function. JOAS has acceptable psychometric properties of reliability and construct validity.[25]

Knee Injury and Osteoarthritis Outcomes Score (KOOS)

This is a self-administered tool that has five scales measuring 42 items such as pain, disease-specific symptoms, activities of daily living, sport and recreation, function, knee related QoL. The score has good evidence for reliability, content validity and construct validity.[18] It takes approximately 10 minutes to complete.