WASHINGTON STATE HEALTH CARE AUTHORITY

Total Knee Arthroplasty

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TOTAL KNEE ARTHROPLASTY

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This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services.Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

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EXECUTIVE SUMMARY

Introduction

Arthritis of the knee often results in considerable loss of function, independence and quality of life. Total knee arthroplasty (TKA) has become the standard procedure for end stage knee arthritis. In 2005, over 555,000 TKA procedures were performed in the US, a 69% increase compared with 1997. The high prevalence of knee arthritis in the population is reflected in the high cost of treatment, which has been estimated at $6.3 billion per year.

TKA is a procedure in which articular surfaces of the medial and lateral compartments are replaced. The patellofemoral articular surface may or may not be replaced in TKA. The conventional method of achieving limb alignment in TKA includes use of anatomic landmarks and special jigs provided with the knee prosthesis. Conventional TKA (CONV-TKA) is the current standard for knee arthroplasty. Computer-navigated TKA (CN-TKA), a more expensive procedure, provides an alternative method of achieving correct limb alignment. More minimally invasive procedures that seek to treat only the diseased compartments of the knee have been recently developed and are now being advocated for younger more active patients. These procedures are referred to as partial knee arthroplasty and include the unicompartmental knee arthroplasty (UKA) or bicompartmental knee arthroplasty (BKA).

CONV-TKA for end stage knee arthritis is effective in improving short and long term outcomes and quality of life. However, questions remain about when the procedure is most appropriate and for whom, and whether certain types of procedures produce better results.

Key Questions

When used in adult patients:

1. What is the evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA? Outcomes to consider:
   a. Primary: Clinical outcomes, Revision rates
   b. Secondary: Radiographic, other reported outcomes

2. What is the evidence of efficacy and effectiveness of partial knee arthroplasty compared with conventional TKA? Include consideration of:
   a. Unicompartmental
   b. Bicompartmental
   c. Bi-unicompartmental

3. Whatis the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty? Including consideration of:
   a. Adverse events type and frequency (mortality, major morbidity, other)
   b. Deep venous thrombosis

4. What is the evidence that TKA or partial knee arthroplasty has differential efficacy or safety issues in sub populations? Including consideration of:
   a. Gender
   b. Age
   c. BMI
   d. Diagnosis, including osteoarthritis versus rheumatoid arthritis
   e. Psychological or psychosocial co-morbidities
   f. Other patient characteristics or evidence based patient selection criteria
   g. Provider type, setting or other provider characteristics
   h. Payor or beneficiary type, including worker's compensation, Medicaid, state employees
   i. Bilateral TKA (simultaneous or staged)

5. What is the evidence of cost implications and cost-effectiveness of computer-navigated TKA or partial knee arthroplasty compared with knee joint arthroplasty?

Methods for evaluating comparative effectiveness

We selected articles to summarize based on the inclusion and exclusion of the following table:

Study Component	Inclusion	Exclusion
Participants	Adults with knee: ◆ Non-inflammatory arthritis (osteoarthritis, traumatic arthritis, osteonecrosis) ◆ Inflammatory arthritis (rheumatoid arthritis)	◆ Age ≤18 years
Intervention	◆ Computer navigation knee arthroplasty ◆ Partial knee arthroplasty	◆ Revision of total knee arthroplasty ◆ Patellofemoral arthroplasty only
Comparators	◆ Standard total knee arthroplasty	
Outcomes	*Efficacy/Effectiveness* ◆ Revision Rate ◆ Time to revision ◆ Clinician reported and patient reported outcomes ◆ Radiographic alignment for computer navigation only (secondary outcome) *Safety*	◆ Non clinical outcomes

	◆ Complications and adverse effects ◆ Infection/fracture ◆ Blood loss ◆ Thromboembolic effect	
Study Design	◆ Meta-analyses ◆ RCTs ◆ Comparative observational studies ◆ Registry studies to assess long term revision rates and special populations	◆ Case reports ◆ Non-clinical studies ◆ Case series except for long term revision rates
Publication	◆ Studies published in English in peer reviewed journals, published HTAs or publically available FDA reports ◆ Full formal economic analyses (e.g. cost-utility studies) published in English in a HTA or in a peer-reviewed journal published after those represented in previous HTAs	◆ Abstracts, editorials, letters ◆ Duplicate publications of the same study which do not report on different outcomes ◆ Single reports from multicenter trials ◆ Studies reporting on the technical aspects total knee arthroplasty ◆ White papers ◆ Narrative reviews ◆ Articles identified as preliminary reports when results are published in later versions ◆ Incomplete economic evaluations such as costing studies ◆ Studies using administrative databases

We conducted a formal, structured systematic search of the peer-reviewed literature across a number of databases in addition to searches of pertinent databases related to clinical guidelines and previously performed assessments. Pertinent studies were critically appraised using our Level of Evidence (LoE) system which evaluates the methodological quality based on study design as well as factors which may bias studies. An overall Strength of Evidence combines the LoE with consideration of the number of studies and the consistency of the findings to describe an overall confidence regarding the stability of estimates as further research is available. Included economic studies were also formally appraised based on criteria for quality of economic studies and pertinent epidemiological precepts.

Results

KEY QUESTION 1

CN-TKA versus CONV-TKA, Efficacy

Knee pain, CN-TKA Efficacy

Four RCTs reported on pain outcomes following CN-TKA compared with CONV-TKA. One study reported that 58% and 61% of patients, respectively, were considered pain-free at 6 months follow-up. This same study reported VAS pain scores postoperatively only, and they were not

statistically different between groups (both < 2 cm out of 10 cm). Another study reported that 78% and 70% of patients in the CN-TKA and CONV-TKA groups, respectively, had no pain (any) at 2 years; 21% and 30% had mild pain, respectively; and 1% in the CN-TKA group was experiencing moderate pain. Anterior knee pain was reported in 8% of patients in each group in one RCT and in 44% and 47% of patients following CN-TKA and CONV-TKA, respectively, in another; however, only 16% and 7%, respectively, complained of moderate to severe pain in the latter trial. There was no statistically significant difference between the two groups in incidence of anterior knee pain in either RCT.

Knee Function, Patient Reported and Clinician Based, CN-TKA Efficacy

Oxford Knee Score

No significant differences were identified in Oxford Knee Scores between CN-TKA and CONV-TKA groups at 6 months as reported by one RCT or at 2 years as reported by two RCTs[51,148]. Across the three studies, follow-up Oxford Knee Scores in the computer-navigated group ranged from 20.0 to 26.7 and from 18.8 to 22.0 in the conventional group. None of the studies reported a significant difference in the preoperative scores between groups.

WOMAC

Four RCTs compared WOMAC scores between CN-TKA and CONV-TKA. No significant differences between treatment groups were reported in any study. Overall, total WOMAC scores ranged from 7 to 31 and from 7 to 32, respectively, across three RCTs[97,140,148] with follow-up times ranging from 6 weeks to 2 years. Pain scores ranged from 0.9 to 6.1 and 1.2 to 6.3, respectively, across three studies with follow-up times ranging from 6 weeks to 2 years. Stiffness scores ranged from 1 to 2.3 to 1 to 2.8, respectively, and physical function scores from 1.6 to 5 and 1.9 to 6, respectively, across two studies with follow-up times of 6 weeks and 1 year.

Knee Society Score

No significant differences were reported in KSS Knee or Function scores in six RCTscomparing CN-TKA with CONV-TKA. Follow-up times ranged from 6 weeks to 2 years after surgery. KSS Knee scores ranged from 65 to 93 and 66 to 94, respectively, and KSS Function scores ranged from 66 to 86 and 68 to 84, respectively. Four studies reported only a total KSS, assumed to be a sum of the Knee and Function scores, which also did not differ statistically between groups in any study at any of the follow-up periods (postoperative to 2 years). A KSS Pain score was also reported by one study at 2 years, also revealing no significant intergroup difference. None of the studies reported a significant difference in the preoperative scores or demographic data between groups.

Hospital for Special Surgery Knee Scale

Three RCTs compared HSS scores between CN-TKA and CONV-TKA. No statistically significant differences between groups were reported in total, pain, or function scores by any study with follow-up periods ranging from 7 months to 2 years. Total HSS scores ranged from 82 to 92 in the CN-TKA group and from 83 to 91 in the CONV-TKA group in three RCTs. In two RCTs HSS pain scores were 28.7 and 25 and 29.2 and 25, respectively. One study reported HSS function scores of 15 and 17, for the CN-TKA and the CONV-TKA groups, respectively. None of the studies reported a significant difference in the preoperative scores between groups.

*Bartlett Patellar Score*Only one study reported the Bartlett Patellar Score and found no difference between the CN-TKA and the CONV-TKA groups at 2 years (23.0 vs. 23.8, respectively).

Quality of Life, CN-TKA Efficacy

Two RCTs reported general health status and quality of life using the SF-36, one using the SF-12[33], and one using the EQ-5D. The only significant difference between the CN-TKA and the CONV-TKA groups was reported in the Role Emotional subscale of the SF-36 at 6 months in one study, 66.7 versus 83.3, respectively, $P = .024$; however, at 2 years follow-up this difference was no longer statistically significant. None of the studies reported a significant difference in the preoperative scores between groups.

Patient satisfaction, CN-TKA Efficacy

Two RCTs reported on patient satisfaction at 2 years follow-up. One study reported an average satisfaction score of 3.6 in both groups indicating that the majority of patients were either satisfied or very satisfied with the surgical outcome, regardless of the treatment type. Likewise, in the second RCT, 86.7% and 83.3% of patients in the CN-TKA and the CONV-TKA groups, respectively, indicated they were very satisfied or somewhat satisfied with their TKA.

Revision, CN-TKA Efficacy

Three studies reported the incidences of revision surgery following CN-TKA and CONV-TKA, however, none reported whether any differences between groups were significant. In one study, 3.7% and 8.0% of patients underwent revision surgery within 6 weeks following CN-TKA compared with CONV-TKA, respectively. Another study compared postoperative outcomes between the treatment groups and reported revision rates of 1.4% and 0%, respectively. In the third study, no patient in either group underwent a revision over a period of 2 years.

ROM, CN-TKA Efficacy

Range of motion was reported in six RCTs. No significant differences in total motion were found between groups across the five studies, either postoperatively or at 2 years, with ROM ranging from 102º to 129º in the CN-TKA group and from 100º to 129º in the CONV-TKA

group. At 1 year follow-up, one study reported significantly greater flexion following CN-TKA (131.9º vs. 125.4º, respectively, *P* = .001), while another found no difference between treatment groups. No differences in both extension and extension lag, as reported by two separate RCTs, were seen at 1 year.

Radiographic Alignment, CN-TKA Efficacy

We summarize two systematic reviews that report on limb axis alignment.

Bauwens et al summarized 28 studies (eight RCTs, seven quasi-RCTs, three prospective and five retrospective cohorts, and 5 matched-pair studies) for radiographic alignment of the mechanical limb axis following primary CN-TKA versus primary CONV-TKA. An Australian HTA calculated alignment using 43 studies (15 RCTs, seven quasi-RCTs and 21 cohort studies).

Bauwen et al reported no significant difference in the mean alignment achieved by navigated TKA (179.7°; 95% CI, 179.2°, 180.3°) compared with CONV-TKA (179.9°; 95% CI, 179.2°, 180.6°) with a weighted mean difference of 0.2° (95% CI, -0.2°, 0.5°; *P* = .308). Using data from 16 studies (four RCTs, three quasi-RCTs, and nine cohort studies), the Australian HTA calculated the mean of mean postoperative deformities and the pooled standard deviation and found it was slightly better following CN-TKA (n = 928) compared with CONV-TKA (n = 924) (0.79º ± 2.21º versus 0.90º ± 2.95º, respectively). Statistical significance was not calculated. Furthermore, the mean deviation from the mechanical axiswas evaluated by fixed-effects modeling using data from eight studies (1 RCT, 1 qRCT, and 6 cohort studies); it was reduced by a mean of -0.74º (95% CI, -0.89º, -0.59º; *P*< .0001) in patients treated with CN-TKA versus CONV-TKA. They concluded that CN-TKA yielded significantly lower mean deviations than CONV-TKA across all studies.

The risk of unsatisfactory alignment by more than 3º was evaluatedby Bauwen et al using data from 22 studies (4 RCTs, 7 quasi-RCTs, 1 prospective and 6 retrospective cohorts, and 4 matched-pair studies). Patients who underwent primary CN-TKA had a significantly lower risk of misalignment by more than 3º than those who were treated with primary CONV-TKA, with a risk ratio of 0.79 (95% CI, 0.71, 0.87) (*P*< .001) and a risk difference of 19.2% (95% CI, 12.7%, 25.6%). The odds of achieving satisfactory alignment by the Australian HTA were calculated using data from 25 studies (5 RCTs, 6 quasi-RCTs, and 14 cohort studies). Of these, 10 studies were also reported in the Bauwen et al study (1 RCT, 1 qRCT, and 8 cohort studies). They reported that patients treated with navigated TKA had 4.14 times higher odds of achieving satisfactory alignment risk than those treated with CONV-TKA (odds ratio (OR): 4.14 (95% CI, 3.03, 5.66); *P*< .00001).

KEY QUESTION 2

UKA versus TKA, Efficacy

There was only one RCT that reported on this comparison.

Knee Function, UKA Efficacy

*Bristol knee scores*In the one RCT comparing UKA with TKA, the mean Bristol Knee Score was similar between the UKA and TKA groups 5 and 15 years following surgery: 91.1 (range, 32 to 100) and 92 (range 32 to 100) compared with 86.7 (range 48 to 98) and 88 (range 48 to 98). A larger percentage of the UKA group reported excellent Bristol scores at 5 and 15 year follow up (76% and 71% respectively) than in the TKA group (57% and 53%, respectively; though this did not reach statistical significance).

Revision or Failure, UKA Efficacy

Failure rate
Statistically significant differences in failure rate defined as revision or a Bristol Knee Score <60 were not reported; however, at 15 year follow up, 17% of the UKA group and 24% of the TKA group had experienced failure.

Revision rate
At the 15 year follow up, there were no statistically significant differences in revision. Thirteen percent of the UKA group and 16% of the TKA group had experienced revision.

Survival rate
There was no statistically significant differences in survival rate at 15 year follow up: 89.8% (95% CI, 74.3-100) for the UKA group and 78.7% (95% CI, 56.2-100) for the TKA group ($P > .05$).

Range of motion, UKA Efficacy
At five year follow up, a significantly greater percentage of the UKA group achieved $\geq$ 120° flexion than the UKA group (69% versus 17%, respectively, $P < .01$.)

UKA versus HTO, Efficacy

In the two RCTs providing data on the efficacy of UKA compared with TKA, there were no significant differences in knee pain, knee function, failure or revision, or ROM between the groups from 1 year to 10 years of follow-up.

Bi-UKA versus TKA, Effectiveness

There were no RCTs found making this comparison. One small retrospective cohort study compared bi-UKA with TKA. No difference was found in functional scores at a minimum of 4 years of follow-up. No revisions were recorded in either group.

Bicompartmental knee arthroplasty versus tricompartmentalTKA, Effectiveness

There were no RCTs found making this comparison. The two registry studies reported low revision rates in both the bi- and tri-compartmental groups: 3.2% and 2.8%, respectively, at 2 to 4 years follow-up and 1.5%.and 1.6%, respectively, at 2 years follow-up. No significant differences in overall revision rates between the two treatment groups were reported by either study.

KEY QUESTION 3

CN-TKA versus CONV-TKA, Safety

Thromboembolism, CN-TKA vs. TKA

Deep vein thrombosis (DVT)

Six RCTsand two prospective cohorts reported the incidence of DVT following CN-TKA and CONV-TKA. No statistically significant differences were reported in any of the studies with events ranging from 0% to 8% of patients in the CN-TKA groups compared with 0% to 10% of patients in the CONV-TKA groups.

Pulmonary embolism (PE)

Four RCTs and two cohort studies, one prospective and oneretrospective, reported the incidence of PE following CN-TKA and CONV-TKA. No statistically significant differences were reported in any of the studies with events ranging from 0% to 2% of patients in the CN-TKA groups compared with 0% to 3% of patients in the CONV-TKA groups. Of these six studies, two RCTs and the two cohort studies reported no instances of PE in either treatment group.

Venous thromboembolism (VTE)

One RCT was conducted specifically to investigate whether CN-TKA resulted in a lower rate of VTE compared with CONV-TKA, due to the elimination of intramedullary rodding. A significant difference was found in the Mayo Clinic score between the two treatment types, with a lower (better) score in the CN-TKA group as compared to the two CONV-TKA groups which consisted of patients who received TKA with an intramedullary femur guide and an extramedullary tibia guide, and those with intramedullary guides for both the tibia and the femur (4.2 vs. 5.1 and 5.4, respectively, P = .02, .04).

Number of detectable emboli

Two RCTs reported the mean number of detectable emboli between treatment groups and both found a significantly lower number in the CN-TKA group as compared with the CONV-TKA group, 4.89 versus 6.15 and 0.64 versus 10.7, P = .004 and .0003, respectively. One of these studies also reported the percentage of patients with greater than two detectable emboli, reporting an incidence of 0% in the CN-TKA group compared to 43% in the CONV-TKA group, P = .0003.

Ischemic events, CN-TKA vs. CONV-TKA

In one RCT, AMI was reported in 2% of patients in both the CN-TKA and the CONV-TKA groups. Transient ischemia was noted in 0% and 3% of patients, respectively, in another RCT.Acute post-operative confusion, attributed to transient hypoxia, was reported by these same RCTs, one of which found a much lower rate in the CN-TKA group compared with the CONV-TKA: 3% and 28%, respectively, and 0% and 4%, respectively.

Wound Complications, CN-TKA vs. CONV-TKA

Nine RCTs and seven cohort studies, five prospectiveand two retrospective,reported on infection rates following CN-TKA versus CONV-TKA. No significant differences were reported between the two treatment groups in any of the studies with respect to deep or superficial infection or delayed wound healing.

Other complications, CN-TKA vs. CONV-TKA

No statistically significant differences between treatment groups in frequency of other complications were reported by eight RCTs and seven cohort studies

UKA versus TKA, Safety

No deaths and few complications were reported in one RCT and nine cohort studies. No statistical significance between UKA and TKA was reported in the number of patients experiencing thromboembolic events, delayed wound healing, or a variety of other complications, (e.g., pneumonia, fracture, and knees requiring manipulation under anesthesia).

UKA versus HTO, Safety

Three studies reported complications after treatment. In two of the studies, the HTO groups experienced more total complications than the UKA group, 28.1% versus 6.7% (P = .044) and 24.3% versus 9.6% (P = .055), respectively. No statistically significant differences between treatment groups in mortality, thromboembolic events, wound complications, or various other complications were reported by any of the studies.

Bi-UKA versus TKA, Safety

No cases of radiological loosening or infection were seen in either the bi-UKA or TKA groups in the one retrospective cohort. Two cases (9%) of intraoperative fracture of the tibial spine block occurred in the bi-UKA group but did not have any adverse effect on the outcome at last follow-up in either case.

Bicompartmental knee arthroplasty versus tricompartmentalTKA, Safety

Complications were not reported for two registry studies comparing bi- and tri- compartmental TKA.

KEY QUESTION 4

Differential Characteristics, CONV-TKA

There is some evidence, based on data from one HTA, to suggest that patients with RA have slightly greater improvement in function compared with baseline after TKA than those with OA; however, this may be related to their lower function at baseline. Age, sex, obesity, comorbidities, and various other factors were found not to be associated with clinical or safety outcomes as reported by one HTA and studies published after the HTA. Likewise, hospital and surgeon volume were not found to be associated with decreased morbidity/mortality and length of hospital stay as reported by one systematic review.

Differential Characteristics, CN-TKA

Obesity was tested in one study and found not be a factor for associated with complications in patients receiving CN-TKA.

Differential Characteristics, Partial Knee Arthroplasty

Younger age (<65 years) was consistently found as a factor for a greater risk of failure of TKA. No other characteristics to include obesity, sex, multicompartment or provider facility were associated with failure.

KEY QUESTION 5

We included one HTA that conducted a cost-effectiveness study on CN-TKA. They identified three other economic evaluations for this technology. Given the lack of long-term clinical trial data on CN-TKA, all three studies used modeling techniques to estimate cost-effectiveness. However, the lack of long-term data underscores this study as an early assessment of cost-effectiveness. Given the lack of clinical efficacy demonstrated by CN-TKA in the short term and no evidence available in the long term, there is insufficient data to make strong conclusions about the long-term cost effectiveness of CN-TKA.

We found three peer-reviewed economic evaluations; two conducted in US settings. All three studies found that total knee and unicompartmental knee arthroplasty have small differences in costs and outcomes; in the US studies this translated to incremental cost effectiveness ratios favoring UKA; in the Singapore favoring total knee replacement. All three studies highlight the lack of long-term data from randomized controlled trials, so each study's conclusions are subject to change s more evidence becomes available. We conclude that there is some evidence that unicompartmental knee arthroplasty (UKA) and conventional total knee arthroplasty (TKA) have similar cost and quality-adjusted outcome profiles from a health care perspective. However, lack of data precludes assessment of the cost effectiveness of UKA in people under age 65.

Summary by Key Question

Key Question 1: What is the evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA (CONV-TKA)?		
	Strength of evidence	**Conclusions/Comments**
Knee Pain, Function and Quality of Life	**High evidence (up to 2 years post surgery)**	• Several randomized controlled trials reported similar results in pain, function and quality of life outcomes when comparing patients receiving either CN-TKA or CONV-TKA at various follow-up times ranging from 3 months to 2 years . • The data are similar with respect to nonrandomized cohort studies with 1 to 3 year follow-up. • No comparative data are available for these outcomes past 2 to 3 years. *There is high evidence that CN-TKA results in similar clinical and functional outcomes as CONV-TKA in the short term.*
Revision	**Low evidence**	• Two RCTs and two cohort studies reported similar, low rates between CN-TKA AND CONV-TKA groups of less than 2%. A third RCT reported half as many revisions following CN-TKA (3.7% vs.8.0%) after 3 years though the study numbers were small. *The small sample sizes, short follow up, and inconsistent rate of revision among the RCTs renders low evidence concerning the relative short term revision rates between surgeries.Conclusions on whether CN-TKA affects long term revision rates are premature.*
Alignment	**High Evidence**	• Evidence from 2 metaanalyses of several RCTs and cohort studies demonstrate that the risk of unsatisfactory alignment by more than 3º is significantly less using CN-TKA compared with CONV-TKA. *There is high evidence that the risk of unsatisfactory alignment (> 3º) is significantly less following CN-TKA.However, this has not been shown to translate into better functional outcomes.*

Key Question 2: What is the evidence of efficacy and effectiveness of using partial knee arthroplasty compared with TKA?		
	Strength of evidence	**Conclusions/Comments**
UKA vs. TKA *Knee Pain and Function*	**Moderate evidence**	• Knee pain and function were comparable between UKA and TKA in one RCT and 14 cohort studies over a variety of follow up times ranging from 3 months to 15 years. • Range of motion was consistently higher in the UKA group in the studies comparing mean motion and the proportion of patients achieving ≥120º of flexion at a variety of follow up times. *The low quality of studies renders the evidence for function between UKA and TKA moderate.*
Revision, prosthesis survival	**Low evidence**	• Revision rates were comparable between UKA and TKA in one RCT at 5 and 15 year follow up. • In 9 cohort studies the rates of revision were slightly higher in the UKA compared with TKA group in 8, mean follow up between 2 and 10 years. Survival of the arthroplasty in two large studies at 10 and 14-15 years slightly favored TKA. *It is unclear whether long term revision risks differ between UKA and TKA. This evidence is low.*
UKA vs. HTO *Knee Pain, Function and Revision*	**Moderate evidence**	• Knee pain, function and revision rates were comparable in 3 small RCTs assessing UKA and HTO for patients with isolated medial compartment arthritis. Follow up ranged from 1 to 10 years. *This evidence is moderate.*
Bi-UKA vs. TKA *Knee Pain, Function and Revision*	**Very low evidence**	• Only one small retrospective cohort study compared bi-UKA with TKA. No difference was found in functional scores at a minimum of 4 year follow up. No revisions were recorded in either group. *Lack of the number of studies renders this evidence very low.*
Bicompartmental knee arthroplasty vs. TKA *Revision*	**Very low evidence**	• Two large registry studies comparing revision between bicompartmental knee arthroplasty and tricompartmental TKA found similar revision rates and 2 to 4 year implant survival. *Lack of the number of studies renders this evidence very low.*

Key Question 3: What is the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty?		
	Strength of evidence	**Conclusions/Comments**
CN-TKA *Thromboembolic events, wound and other complications*	**High evidence**	•Several RCTs and cohort studies report no significant differences between CN-TKA and CONV-TKA with respect to thromboembolic events, infection or all other complications other than ischemic events (see below). *The evidence is high that CN-TKA is as safe as CONV-TKA when considering these safety parameters.*
Ischemic events	**Low evidence**	•One RCT reported no significant differences in acute myocardial infarction and one reported no difference in transient ischemia following CN-TKA vs. CONV-TKA. Confusion was reported by two RCTs at different rates (0% in the CN-TKA group, 4% in the CONV-TKA group in one, and 3% in the CN-TKA group vs. 28% in the CONV-TKA group.) *The infrequent reporting of these outcomes renders the evidence for ischemic events low.*
UKA vs. TKA	**Low evidence**	•Complications were infrequent, and the risk of complications was similar between UKA and TKA in one RCT and nine cohort studies. *The paucity of higher quality studies renders the evidence for the safety of UKA compared with TKA as low.*
UKA vs. HTO	**Very low evidenece**	•The incidence of total complications was similar between UKA and HTO in two studies (1 RCT, 1 cohort) and slightly higher in the HTO group in another RCT. *Few higher quality studies and the inconsistency of the findings render the evidence that UKA is similar to HTO with respect to safety as very low.*
Bi-UKA vs. TKA	**Very low evidence**	•One small cohort study reported 2 cases (9%) of intraoperative fracture of the tibial spine in the bi-UKA group. No other complications reported. *The lack of literature in general render the evidence for the safety of bi-UKA compared with TKA as very low.*
Bi- vs. tricompartmental TKA	**No evidence**	•Complications not addressed in two registry studies.
Simultaneous vs. staged bilateral TKA *Mortality*	**Low evidence**	•Four cohort studies reported 30 day mortality rates following either staged or simultaneous TKA. Three of the four report significantly higher rates in the simultaneous group. *Despite the consistency of the findings, the potential for bias due to study design renders this evidence low.*
Thromboembolic events, wound and other complications	**Low evidence**	•From nine cohort studies, there are no significant differences in thromboembolic events, wound complications, or other complications between simultaneous and staged bilateral TKA. *The lack of higher quality studies renders the evidence for safety following simultaneous compared with staged bilateral TKA as low.*

Question 4: What is the evidence that TKA or partial KA has differential efficacy or safety issues in sub populations?		
	Strength of Evidence	**Conclusions/Comments**
CONV-TKA		
Age, sex, obesity, comorbidity	**Very low evidence**	• Evidence from one HTA and studies published after the HTA reported inconsistent results as to whether age, sex, obesity or comorbidity significantly affected outcomes. *The low quality and inconsistency render very low evidence for or against age, sex, obesity or comorbidity as factors affecting success or failure of TKA.*
Type of arthritis	**Moderate evidence**	• One HTA reported greater improvement in baseline functional scores among RA patients compared with OA patients. One prospective study published after the HTA no difference in function/quality of life outcomes based on type arthritis type. *There is some evidence to suggest that patients with RA have greater improvement in function after TKA than those with OA; however, this may be related to their lower function at baseline. Given that and this difference and the lack of consistency, this evidence is moderate.*
Hospital and surgeon volume	**Very low evidence**	• One systematic review of several studies reported mixed results with respect to morbidity, mortality and length of hospital stay *Low study quality and inconsistency render very low evidence for a trend towards increased hospital volume and lower morbidity and length of hospital stay.*
Other characteristics	**Very low evidence**	• One study each either in the HTA or published after the HTA reported on possible associations between preoperative pain levels, length of hospital stay, waiting time, year of follow-up, education, SF-36 mental health scores and ethnicity and outcomes. *The low quality and/or the small number of studies render very low evidence for or against these other characteristics as factors influencing outcomes.*
CN-TKA		
Obesity	**Very low evidence**	• One retrospective study reported that morbidly obese patients experienced a significantly greater mean total blood loss, mean hemoglobin loss, and superficial infection rate compared with those of normal weight. *The low quality, low number of studies and inconsistency render very low evidence for or against obesity as a risk facture for increased complications following CN-TKA.*
UKA		
Age	**High evidence**	• Five of six registry studies reported a statistically significant higher revision rate among patients < 65 years of age versus those >65 years of age. . *The higher quality studies consistently found a greater risk among patients < 65 years of age; therefore, there is high evidence that younger patients are at greater risk of failure after UKA than older patients.*
Obesity	**Very low evidence**	• Among three retrospective cohort studies evaluating obesity as a risk factor, one found higher rates among obese, one found lower rates among obese, and the 3rd found no statistically significant difference. *The low quality and inconsistency render low evidence for or against obesity as a risk factor for UKA failure.*
Sex	**High evidence**	• Five of seven published studies found no association between sex and UKA failure. Among the two that found an association, both were LoE III retrospective cohort studies. One reported a higher revision rate among males, the other a higher revision rate among females. *The higher quality studies consistently found no association between sex and revision*

Question 4: What is the evidence that TKA or partial KA has differential efficacy or safety issues in sub populations?		
	Strength of Evidence	**Conclusions/Comments**
		rates; therefore, there is high evidence that sex is not a risk factor for UKA failure.
Multi-compartment	**Very** low evidence	• One LoE II registry study reported higher rates of revision among patients with RA compared to those with OA *There is very low evidence that patients with RA are at greater risk of UKA failure than patients with OA.*
Provider facility	**Low evidence**	• Two LoE II studies found no statistically significant difference in revision rates among caseloads ≤10 or >10 UKAs per year; and one study did not find an association between different surgeons or different hospitals on revision rates. *The limited quantity of reports evaluating these factors renders low evidence for or against different surgeons or hospitals as risk factors for UKA failure.*

Question 5: What is the evidence of cost implications and cost effectiveness of CN-TKA or partial knee arthroplasty?		
	Strength of evidence	**Conclusions/Comments**
CN-TKA	**Low evidence**	• There is insufficient data to make strong conclusions about the long-term cost effectiveness of CN-TKA. • Modeling suggests that CN-TKA is potentially a cost effective intervention compared with CONV-TKA if the 10-year revision rate is reduced by between 33 to 50%.
UKA vs. TKA	**Moderate**	• There is some evidence that UKA and TKA have similar cost and quality-adjusted outcome profiles from a health care perspective • Lack of data precludes assessment of the cost effectiveness of UKA in people under age 65.

1. Appraisal

1.1. Rationale

Arthritis is a significant public health issue affecting a large number of people and causing significant functional limitation. An estimated 48 million people in the US in 2005 reported being told by a doctor that they have some form of arthritis[70]. Of these, 38% describe activity limitation, 31% work limitation and 26% report severe pain[18]. By 2030 25 million or 9.3% of the adult population are projected to report activity limitations attributable to arthritis, and working-age adults (45-64 years) will account for almost one-third of the cases[70]. Osteoarthritis (OA) is the most common type of arthritis, clinically affecting an estimated 27 million US adults. The most common lower extremity joint affected by OA is the knee[119]. The estimated lifetime risk of developing symptomatic knee OA approaches 50% by age 85 years[116].

Arthritis of the knee often results in considerable loss of function, independence and quality of life. Total knee arthroplasty (TKA) has become the standard procedure for end stage knee arthritis. In 2005, over 555,000 TKA procedures were performed in the US, a 69% increase compared with 1997[112]. The high prevalence of knee arthritis in the population is reflected in the high cost of treatment, which has been estimated at $6.3 billion per year[112].

Total knee arthroplasty is a procedure in which articular surfaces of the medial and lateral compartments are replaced. The patellofemoral articular surface may or may not be replaced in TKA. The conventional method of achieving limb alignment in TKA includes use of anatomic landmarks and special jigs provided with the knee prosthesis. Conventional TKA (CONV-TKA) is the current standard for knee arthroplasty. Computer-navigated TKA (CN-TKA), a more expensive procedure, provides an alternative method of achieving correct limb alignment. More minimally invasive procedures that seek to treat only the diseased compartments of the knee have been recently developed and are now being advocated for younger more active patients. These procedures are referred to as partial knee arthroplasty and include the unicompartmental knee arthroplasty (UKA) or bicompartmental knee arthroplasty (BKA). UKA refers to surgical replacement of the articular surfaces of either the medial or lateral compartments of the knee. BKA refers to replacing the articular surfaces of the medial and patellofemoral compartments of the knee.

CONV-TKA for end stage knee arthritis is effective in improving short and long term outcomes and quality of life. However, questions remain about when the procedure is most appropriate and for whom, and whether certain types of procedures produce better results.

Key Questions

Key questions are developed by the Washington State Health Technology Assessment Program.

When used in adult patients:

1. What is the evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA? Outcomes to consider:
   a. Primary: Clinical outcomes, Revision rates
   b. Secondary: Radiographic, other reported outcomes

2. What is the evidence of efficacy and effectiveness of partial knee arthroplasty compared with conventional TKA? Include consideration of:
   a. Unicompartmental
   b. Bicompartmental
   c. Bi-unicompartmental

3. Whatis the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty? Including consideration of:
   a. Adverse events type and frequency (mortality, major morbidity, other)
   b. Deep venous thrombosis

4. What is the evidence that TKA or partial knee arthroplasty has differential efficacy or safety issues in sub populations? Including consideration of:
   a. Gender
   b. Age
   c. BMI
   d. Diagnosis, including osteoarthritis versus rheumatoid arthritis
   e. Psychological or psychosocial co-morbidities
   f. Other patient characteristics or evidence based patient selection criteria
   g. Provider type, setting or other provider characteristics
   h. Payor or beneficiary type, including worker's compensation, Medicaid, state employees
   i. Bilateral TKA (simultaneous or staged)

5. What is the evidence of cost implications and cost-effectiveness of computer-navigated TKA or partial knee arthroplasty compared with knee joint arthroplasty?

1.2. Outcomes Assessed

Efficacy and Effectiveness Outcomes are summarized in Table 1 and include:

Pain and Patient Satisfaction

- Pain was evaluated in a variety of ways, including the visual analogue scale (VAS) as well as patient descriptions of pain intensity.
- Patient, preference or opinion satisfaction was also reported in some studies.

Patient-Reported Outcomes

Two different disease-specific patient-reported functional outcome measures were used:

- The Western Ontario and McMaster Universities OA index (WOMAC)[16] reports scores based on pain, stiffness, and physical function.
- The Oxford Knee Score (OKS)[44] evaluates patient perceptions of pain and function.

Clinician-Reported Outcomes

Five different clinician-reported disease-specific outcome measures were used:

- The Knee Society Score (KS)/International Knee Society (IKS)[73] was used most frequently; the knee rating evaluates pain, stability, range of motion, and takes into consideration joint lag, contracture, alignment, and use of assistive devices, while the function rating assesses walking and stairs.
- Both the Bristol Knee Score (BKS)[102] and the Baily Knee Score[25]evaluate pain, function, movement, and deformity.
- The British Orthopaedic Association knee functional assessment chart (BOA)[8] evaluates patient perception of pain and function as well as knee motion, stability, and deformity.
- The Hospital for Special Surgery (HSS)[127] scale evaluates pain, function/walk/stairs, range of motion, muscle strength, deformity, and instability.
- The Bartlett Patellar Score[52] evaluates anterior knee pain, quadriceps strength, and the ability to rise from a chair and climb stairs.

Measures of quality of life

- The Short-form 36 (SF-36)[163] and Short-form 12 (SF-12)[162] questionnaires were used to evaluate both physical and mental health.
- The European Quality of Life (EQ-5D)[72] evaluates mobility, self-care, usual activity, pain, and anxiety/depression.

Revision Rate

- Revision, revision rate, time to revision, failure rate, and/or survival rate were reported by the majority of studies.

Other

- Other commonly reported outcomes include range of motion (ROM), measurements of extension, and return to work.

Radiographic Alignment

- Coronal plane axial alignment was assessed as a secondary outcome.

Table 1. Outcome measures

Outcome measure	Clinician or patient reported	Instrument type	Components	Score range	Interpretation
VAS pain (Visual Analogue Scale)	Patient	Generic	Pain	0–10 cm	No pain: 0 Worst pain imaginable: 10
OKS (Oxford knee score, or Oxford12-item knee questionnaire)	Patient	Disease specific	12 questions concerning the perception of pain and function (1–5 each)	12–60	Higher score = greater disability
WOMAC (Western Ontario and McMaster Universities OA index)	Patient	Disease specific	Pain (20) Stiffness (8) Physical function (68)	0–96	Higher score = greater disability
Baily knee score (adapted from HSS)	Clinician	Disease specific	Pain (15) Function (20) Movement (10) Deformity (5)	0–50	Good: 35–50 Fair: 30–34 Poor: < 30
Bartlett Patellar Score	Clinician	Disease specific	Anterior knee pain (30) Quadriceps strength (10) Ability to rise from chair (10) Ability to climb stairs (10)	0–60	Higher score = higher function
BOA (British Orthopaedic Association knee functional assessment chart)	Clinician	Disease specific	*2 subscales:* Perception of pain and function (7 items, 33 points) Knee motion, stability, and deformity (5 items, 22 points)	11–55	Higher score = higher function
BKS (Bristol knee score)	Clinician	Disease specific	Pain (15) Function (20) Movement (10) Deformity (5)	2–15	Excellent: 41–50 Good: 36–40 Fair: 30–35 Poor: <30
HSS (Hospital for Special Surgery knee scale)	Clinician	Disease specific	*6 subscales:* Pain (30) Function, walk/stairs (22) Range of motion (18) Muscle strength (10) Deformity (10) Instability (10)	0–100	Excellent: 85–100 Good: 70–84 Fair: 60–69 Poor: < 60
KSS or IKS* (International Knee Society or Knee Society Score; Insall)	Clinician	Disease specific	*Knee rating(4 subscales)* Pain (50) Stability (25) Range of motion (25) Deductions for joint lag, contracture, alignment, and assistive devices (-70) *Functional rating (3 subscales)* Walking (50) Stairs (50) Deductions for sticks (-20)	0–100 0–100	Lower the score, the greater the disability
EQ-5D (European Quality of Life)	Patient	Generic	Mobility (1–3) Self-care (1–3) Usual activity (1–3)	0–1*	Optimal health: 1 Death: 0

Outcome measure	Clinician or patient reported	Instrument type	Components	Score range	Interpretation
			Pain (1–3) Anxiety/depression (1–3)		
SF-12 (Short Form 12 health survey questionnaire)	Patient	Generic	2 subscales (# items) *Physical health* General health (1) Physical functioning (2) Physical role limitations (2) Bodily pain (1) *Mental health* Emotional role limitations (2) Social functioning (1) Vitality/mental health (3)	0–100 for each subscale	Lower score = greater disability
SF-36 (Short Form 36 health survey questionnaire)	Patient	Generic	8 subscales (# items) Physical functioning (10) Role limitations due to physical health problems (4) Bodily pain (2) General health (5) Vitality (4) Social functioning (2) Role limitations due to emotional problems (3) Mental health (5)	0–100 for each subscale (total score not used)	Lower score = greater disability

*IKS and KSS refer to the same outcome measure.

1.3. Washington State utilization and cost data

The following data were provided from the Washington State Health Care Authority and represent estimates for costs and utilization from the Uniform Medical Plan, Labor and Industry and Medicaid.

Demographics Table 1a: UMP/PEP Counts of TKA Surgeries by Age Group, Prosthetic Device Malfunctions and Use of Computer Guidance

TKA Counts by Age Group	2006	2007	2008	2009	4 Yr Total
66-125	308	293	353	427	**1381**
51-65	235	252	321	349	**1157**
36-50	14	17	24	29	**84**
19-35	1	0	0	1	**2**
0-18	0	1	0	2	**3**
All Ages	**558**	**563**	**698**	**808**	**2627**
Joint Device Malfunctions	**6**	**2**	**19**	**21**	**48**
Use of Computer Guidance	**33**	**52**	**106**	**110**	**301**

Demographics Table 1b: DLI TKA Counts of TKA Surgeries by Age Group, Prosthetic Device Malfunctions and Use of Computer Guidance 2005-2009

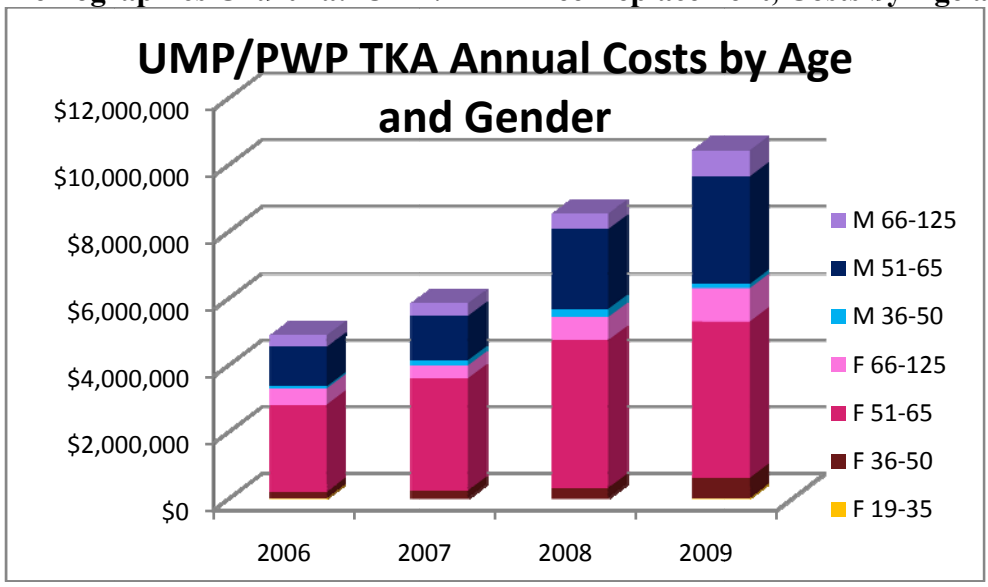
TKA Counts by Age Group	2005	2006	2007	2008	2009	5 Yr Total
66-125	14	26	16	23	20	94
51-65	135	138	171	204	235	838
36-50	80	68	84	95	95	398
19-35	1	3	0	1	4	8
0-18	1	1	0	0	0	2
All Ages	**231**	**236**	**271**	**323**	**354**	**1340**
Joint Device Malfunctions	**14**	**18**	**29**	**25**	**25**	**109**
Use of Computer Guidance	**0**	**0**	**0**	**37**	**33**	**69**

Demographics Table 1c: DSHS Counts of TKA Surgeries by Age Group, Prosthetic Device Malfunctions and Use of Computer Guidance, 2006-2009

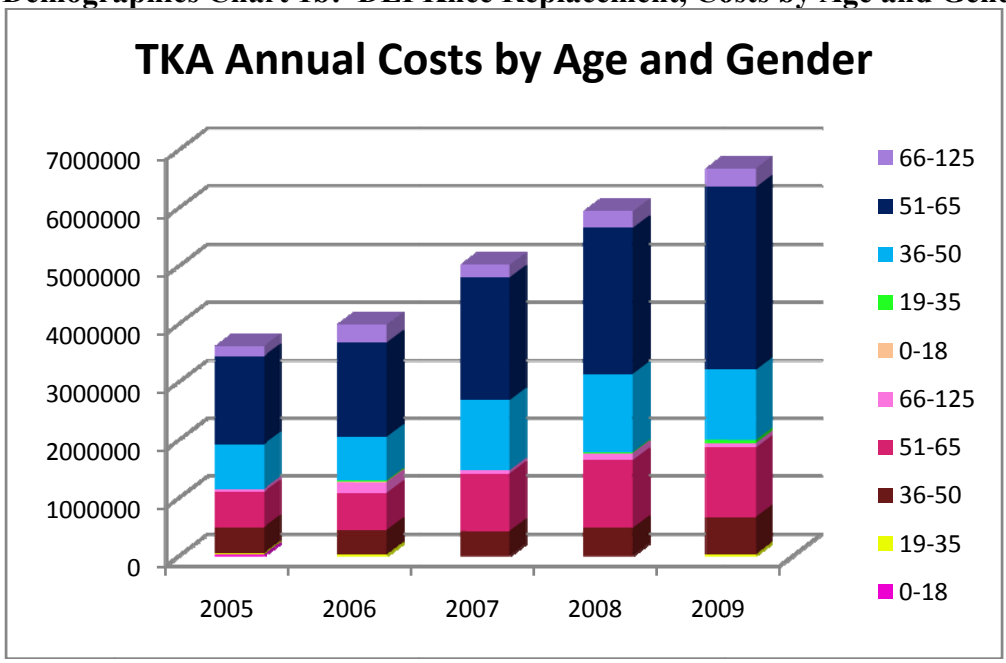
TKA Counts by Age Group	2006	2007	2008	2009	4 Yr Total
66-125	42	43	42	50	174
51-65	222	217	222	269	873
36-50	112	91	125	143	456
19-35	7	9	12	15	43
0-18	1	1	2	1	5
All Ages	**384**	**361**	**403**	**478**	**1551**
Joint Device Malfunctions*					
Use of Computer Guidance*					

**Under investigation*

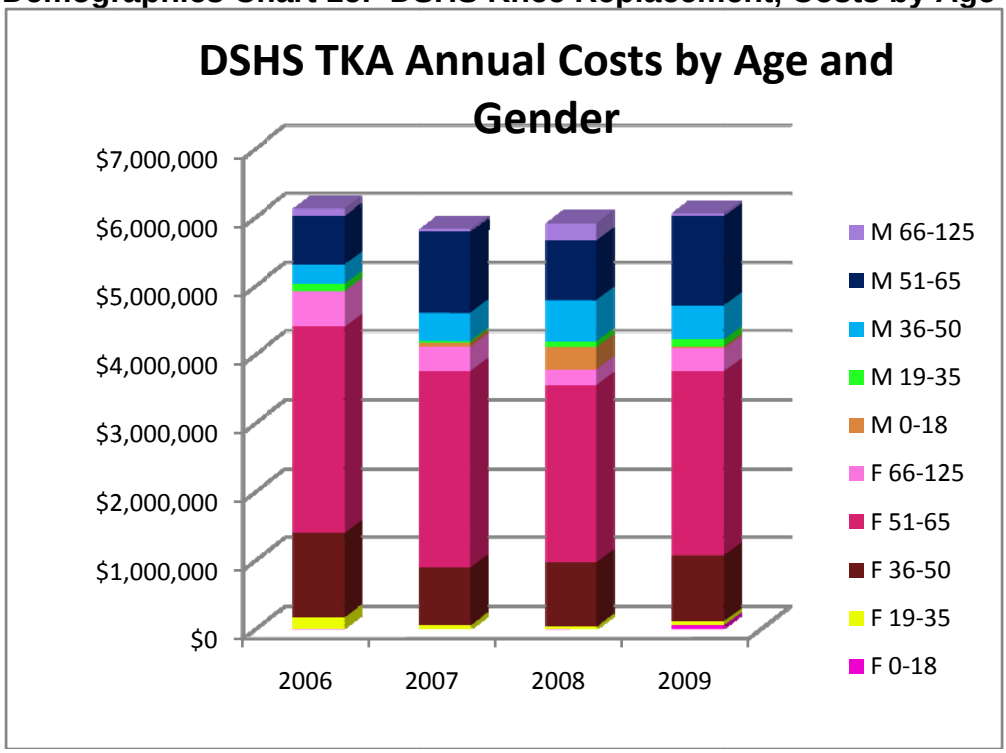
Demographics Chart 1a: UMP/PEP Knee Replacement, Costs by Age and Gender



Demographics Chart 1b: DLI Knee Replacement, Costs by Age and Gender



Demographics Chart 1c: DSHS Knee Replacement, Costs by Age and Gender



Cost Accumulation Comparison Table 2a: UMP/PEP All Knee Arthroplasty by Procedure Type, Costs and Averages 2005-2009

Costs by Type of Surgery	2006	2007	2008	2009	4 year cost
Complete Knee Replacement	$4,894,904	$5,852,095	$8,536,136	$10,438,594	$29,721,729
Knee Revision	$32,535	$45,482	$108,739	$33,313	$220,070
Partial Knee Replacement	$158,391	$475,736	$429,928	$231,709	$1,295,765
Total Costs by Year	$5,085,831	$6,373,313	$9,074,804	$10,703,617	$31,237,564
Counts by Type of Surgery	**2006**	**2007**	**2008**	**2009**	**4 year count**
Complete Knee Replacement	539	511	607	693	2350
Knee Revision	5	5	7	5	22
Partial Knee Replacement	43	40	36	29	148
Total Patient Count by Year	587	556	650	727	2520
Average Reimbursement per Patient by Type of Surgery	**2006**	**2007**	**2008**	**2009**	**4 year avg**
Complete Knee Replacement	$9,081	$11,452	$14,063	$15,063	$12,648
Knee Revision	$6,507	$9,096	$15,534	$6,663	$10,003
Partial Knee Replacement	$3,684	$11,893	$11,942	$7,990	$8,755
Overall Average Cost per Patient	$8,664	$11,463	$13,961	$14,723	$12,396

All costs are based on All Services, Day of Surgery figures
Patients may have had more than one procedure of the type specified but are counted only once per year.
Note that Patient count 4 year totals are not the sum of all patients, but a separate count of separate claims over four years.

Cost Accumulation Comparison Table 2b: DLI All Knee Arthroplasty by Procedure Type, Costs and Averages 2005-2009

Costs by Type of Surgery	2005	2006	2007	2008	2009	5 year cost
Complete Knee Replacement	$3,616,155	$3,991,918	$5,019,838	$5,940,883	$6,684,902	$25,253,697
Knee Revision	$892,556	$1,202,881	$1,342,060	$1,611,664	$2,057,996	$7,107,157
Partial Knee Replacement	$37,945	$45,812	$47,300	$23,411	$55,324	$209,792
Total Costs by Year	**$4,546,657**	**$5,240,611**	**$6,409,198**	**$7,575,958**	**$8,798,222**	**$32,570,645**
Counts by Type of Surgery	**2005**	**2006**	**2007**	**2008**	**2009**	**5 year count**
Complete Knee Replacement	231	236	271	323	354	1,340
Knee Revision	45	52	62	69	81	265
Partial Knee Replacement	5	5	3	2	3	17
Total Patient Count by Year	**281**	**293**	**336**	**394**	**438**	**1622**
Average Reimbursement per Patient by Type of Surgery	**2005**	**2006**	**2007**	**2008**	**2009**	**5 year avg**
Complete Knee Replacement	$15,654	$16,915	$18,523	$18,393	$18,884	$18,846
Knee Revision	$19,835	$23,132	$21,646	$23,357	$25,407	$26,819
Partial Knee Replacement	$7,589	$9,162	$15,767	$11,705	$18,441	$12,341
Overall Average Cost per Patient	**$16,180**	**$17,886**	**$19,075**	**$19,228**	**$20,087**	**$20,081**

All costs are based on All Services, Day of Surgery figures
Note that Patient count 5 year totals are not the sum of all patients, but a separate count of separate claims over five years.

Cost Accumulation Comparison Table 2c: DSHS All Knee Arthroplasty by Procedure Type, Costs and Averages 2006-2009

Costs by Type of Surgery	2006	2007	2008	2009	4 year cost
Complete Knee Replacement	$3,998,843	$3,904,592	$3,832,558	$4,048,579	$15,784,573
Knee Revision	$36,097	$56,888	$48,595	$75,988	$217,568
Partial Knee Replacement	$68,135	$205,470	$268,458	$286,258	$828,321
Total Costs by Year	**$4,103,075**	**$4,166,950**	**$4,149,611**	**$4,410,825**	**$16,830,461**
Counts by Type of Surgery	**2006**	**2007**	**2008**	**2009**	**4 year count**
Complete Knee Replacement	266	258	283	331	1049
Knee Revision	13	25	32	40	101
Partial Knee Replacement	3	5	3	5	16
Total Patient Count by Year	**282**	**288**	**318**	**376**	**1166**
Average Reimbursement per Patient by Type of Surgery	**2006**	**2007**	**2008**	**2009**	**4 year avg**
Complete Knee Replacement	$14,596	$14,943	$13,404	$11,981	$14,773
Knee Revision	$5,241	$8,091	$8,354	$7,111	$8,140
Partial Knee Replacement	$12,032	$11,376	$16,117	$15,191	$13,580
Overall Average Cost per Patient	**$14,137**	**$14,287**	**$12,921**	**$11,505**	**$14,182**

All costs are based on All Services, Day of Surgery figures
Note that Patient count 4 year totals are not the sum of all patients, but a count of distinct patients over four years.

Related Medical Codes		
Major CPT Codes		
Complete Knee Replacement	27446	Arthroplasty, knee, condyle and plateau; medial OR lateral compartments
	27447	Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing
Partial Knee Replacement	27437	Arthroplasty, patella; without prosthesis
	27438	Arthroplasty, patella; with prosthesis
	27440	Arthroplasty, knee, tibial plateau;
	27441	with debridement and partial synovectomy
	27442	Arthroplasty, femoral condyles or tibial plateau(s), knee;
	27443	with debridement and partial synovectomy
	27445	Arthroplasty, knee, hinge prosthesis
Knee Revision	27486	**Revision** total **knee arthroplasty,** one component
	27487	Revision of total knee arthroplasty, with or without allograft; femoral and entire tibial component
	27488	Removal of prosthesis, including total knee prosthesis, methylmethacrylate with or without insertion of spacer, knee
Additional Codes		
Computer/Imaging guidance CPT codes		
Valid 1/1/2008, possibly used in TKA procedures	20985	Computer-assisted surgical navigational procedure for musculoskeletal procedures; imageless. (List separately in addition to code for primary procedure.)
	20986	With image guidance based on intraoperatively obtained images (e.g. fluoroscopy, ultrasound). (List separately in addition to code for primary procedure.)
	20987	With image guidance based on preoperative images. (List separately in addition to code for primary procedure.)
Valid 1/1/2004 – 12/31/2007, possibly used in TKA procedures	0054T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image guidance based on fluoroscopic images. (List separately in addition to code for primary proc.)
	0055T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image guidance based on CT/MRI images. (List separately in addition to code for primary proc.)
	0056T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, imageless. (List separately in addition to code for primary proc.)
HCPCS	C1776	Joint Device Implantable
DRGs		

Associated with ICD-9 00.80 Revision of knee replacement, total (all components		
	461	Bilateral or Multiple Major Joint Procedures of Lower Extremity with MCC
	462	Bilateral or Multiple Major Joint Procedures of Lower Extremity without MCC
	466	Revision of Hip or Knee Replacement with MCC
	467	Revision of Hip or Knee Replacement with CC
	468	Revision of Hip or Knee Replacement without CC/MCC
Associated with ICD-9 00.81/2 Revision of knee replacement (00.81 tibial, 00.82 femoral)		
	466	Revision of Hip or Knee Replacement with MCC
	467	Revision of Hip or Knee Replacement with CC
	468	Revision of Hip or Knee Replacement without CC/MCC
Associated with ICD-9 00.83/4 Revision of knee replacement (00.83 patellar, 00.82 tibial insert/liner)		
	485	Knee Procedures with Principal Diagnosis of Infection with MCC
	486	Knee Procedures with Principal Diagnosis of Infection with CC
	487	Knee Procedures with Principal Diagnosis of Infection with CC/MCC
	488	Knee Procedures without Principal Diagnosis of Infection with CC/MCC
	489	Knee Procedures without Principal Diagnosis of Infection without CC/MCC
Associated with ICD-9 81.54 Total knee replacement		
	461	Bilateral or Multiple Major Joint Procedures of Lower Extremity with MCC
	462	Bilateral or Multiple Major Joint Procedures of Lower Extremity without MCC
	469	Major Joint Replacement or Reattachment of Lower Extremity with MCC
	470	Major Joint Replacement or Reattachment of Lower Extremity without MCC
Associated with ICD-9 81.55 Revision of knee replacement not otherwise specified		
	466	Revision of Hip or Knee Replacement with MCC
	467	Revision of Hip or Knee Replacement with CC
	468	Revision of Hip or Knee Replacement without CC/MCC
ICD-9 Procedure Codes	00.31	Computer assisted surgery with CT/CTA
	00.32	Computer assisted surgery with MR/MRA
	00.33	Computer assisted surgery with fluoroscopy
	00.34	Imageless computer assisted surgery with multiple datasets

	00.39	Other computer assisted surgery
	00.80	Revision of knee replacement, total (all components)
	00.81	Revision of knee replacement, tibial component
	00.82	Revision of knee replacement, femoral component
	00.83	Revision of knee replacement, patellar component
	00.84	Revision of total knee replacement, tibial insert, liner
	81.54	Total knee replacement
	81.55	Revision of knee replacement, not otherwise specified

2. Background

2.1. Total Knee Arthroplasty

Total knee arthroplasty (TKA) is the operative standard for treating end stage knee arthritis. The procedure involves replacing the distal ends of the femoral condyles and proximal tibia with metal or plastic components. Early TKA implants were first used in the late 1950s and poorly mimicked the natural motion of the knee. This resulted in high failure and complication rates. However, advances in TKA technology have enhanced the design and fit of knee implants, resulting in improved short- and long-term outcomes as confirmed by published Health Technology Assessments[3,81]. In addition, more minimally invasive procedures that seek to treat only the diseased compartments of the knee have been recently developed and are advocated for younger more active patients. These procedures are referred to as partial knee arthroplasty.

2.2. Knee Joint Compartments

The knee joint has three compartments:

1. Patellofemoral compartment: the patella articulating with the distal end of the femur
2. Medial compartment: the contact between the medial femoral condyle and the medial tibial plateau
3. Lateral compartment: the contact between the lateral femoral condyle and the lateral tibial plateau

2.3. Definitions

- TKA refers to the procedure in which the articular surfaces of the medial and lateral compartments are replaced. The patellofemoral articular surface may or may not be replaced in TKA.
- Primary TKA refers to the initial joint replacement as compared with revision TKA. The conventional method of achieving limb alignment in primary TKA includes use of anatomic landmarks and special jigs provided with the knee prosthesis.
- CN-TKA is an alternative method to CONV-TKA of achieving correct limb alignment. This is done by utilizing a real-time, patient-specific, 3-D image of the knee (created using comprehensive data pertaining to knee movement (kinematics) sent by minimally invasive tracking devices) which aids the surgeon in making bone cuts.
- UKA refers to surgical replacement of the articular surfaces of either the medial or lateral compartments of the knee.
- Bicompartmental knee arthroplasty refers to replacing the articular surfaces of the medial and patellofemoral compartments of the knee.
- Bi-unicompartmental knee arthroplasty refers to UKA performed in the medial and the lateral compartment.

2.4. Technologies Under Consideration

2.4.1. Computer Navigated TKA

The indications for CN-TKA and CONV-TKA are the same. The primary difference lies in the method of determining the size and location of the implants and associated alignment and ligament balance of the knee. CN-TKA allows for knee replacement to be performed without drilling a hole in the distal femur and pushing a metal rod into the femoral shaft to gauge alignment, as is the standard process in CONV-TKA. Instead, the patient's specific anatomical information is entered into a computer through a process called registration and a three-dimensional image of the patient's knee is simulated and displayed on a computer screen. The computer gives the surgeon real-time information, through a process called tracking (optical or electromagnetic trackers are attached to the regular surgical tools), which assists with bone cuts and accurate alignment of the parts, as well as helping the surgeon balance the soft tissues for better motion and stability.

CN-TKA may provide better function and fewer complications compared with CONV-TKA by providing better mechanical limb alignment. Several studies have shown that poor alignment leads to increased wear and loosening of parts, poor function, and ultimately failure of the TKA[36,40,41,68,77,123,128,130]. Several studies comparing the alignment between traditional knee replacement methods and CN-TKA techniques show that computer aid improves restoration of the leg axis and component orientation[10,13,14,19,30,32,43,45,63,143,147]. Whether this amount of improvement in alignment translates into better outcomes, however, is still not known.

Computer-navigated TKA can be divided into two types of systems: image-free or image-based. For the purpose of this report, our focus is on image-free systems. Image-free computer-navigated TKA systems gather all necessary information intra-operatively through a registration process by digitizing various anatomical landmarks with a navigated pointer.

Image-based systems require additional pre-operative imaging, such as computed tomography (CT) scans, magnetic resonance imaging (MRI), or the use of fluoroscopy machines. In CT or MRI-based computer-navigated TKA, registration of key anatomical points required to navigate the knee are matched to the patient's CT/MRI scan. This does not allow for intra-operative kinematic data to be obtained. Fluoroscopic systems consist of a specific frame that is attached to the fluoroscopy machine and allow automatic registration of the patient.

2.4.2. Partial Knee Arthroplasty

Approximately a third of patients with knee osteoarthritis have disease in one compartment. About 30% of these patients have medial joint arthritis, 3% have lateral joint arthritis and the rest have patello-femoral joint arthritis[90]. Due to the high prevalence of unicompartmental disease, attempts at treating a single compartment have been attempted for decades. Initially, the concept of placing a spacer in the diseased compartment was tried in the 1950s[111]. Today, UKA to treat medial or lateral compartment disease is common.

2.5. Indications and Contraindications for Knee Arthroplasty

2.5.1. Conventional and Computer Navigated TKA

Indications
According to the 2003 National Institutes of Health Consensus Statement[1], primary TKA is indicated in patients with:

- moderate to severe knee pain that has not adequately responded to a prolonged course of nonsurgical treatment,
- radiological evidence of joint damage**, and**
- lower quality of life due to clinically significant limitations in function.

Absolute contraindications[1]:

- active infection (local or systemic)
- significant comorbidities that increase the risk of serious complications or death

Relative contraindications[1]:

- severe peripheral vascular disease
- certain types of neurologic impairments
- significant comorbidities that increase the risk of serious complications or death

2.5.2. Unicompartmental Knee Arthroplasty:

The indications for unicompartmental knee arthroplasty are still evolving and likely vary by surgeon[96,115,158]. Traditionally, UKA was reserved for relatively inactive elderly patients. Today, UKA is being used with increasing frequency in younger, more active patients[96,115].

Indications

- Unicompartmental medical or lateral arthritis that has not adequately responded to a prolonged course of nonsurgical treatment
- Post-traumatic unicompartmental arthritis

- Osteonecrosis (CFL and PTL)
- Outcomes of varus osteotomy
- Outcomes of total and subtotal lateral meniscectomy
- Asymtpomaticfemoropatellar joint
- Axial deviation < 20°
- Wide and preserved ROM
- Complete extension, flexion at least 90°
- Weight < 85 kg
- Indications vary with respect to age:
  - Any age, or
  - Age preferably > 70 years

Contraindications

- Contraindications vary with respect to weight:
  - Weight over 85 kg
  - Obese patients or
  - Morbidly obese patients
- Significant loss of subchondral bone
- Ligament instability
- Inflammatory arthritis
- Crystalline arthropathy (gout)
- Grade IV chondromalacia in other compartments
- Compromised ACL unless functional instability is limited the femoral contact on the tibia is anterior (in extension), and tibiofemoral arthritis is anterior OR age over 70 years
- Moderate – severe patellofemoral arthritis
- Significant deformity
- Contractures
- Patellar maltracking
- High-impact activity
- Poor bone quality

2.5.3. High Tibial Osteotomy:

Indications[24]

- Isolated medial joint line pain
- Age between 40–60 years (age < 40 or 60—70 is possible, but not ideal)
- Misalignment < 15°
- Tibial bone varus angle > 5°
- Complete ROM
- Normal physiology of the lateral and patellofemoral components

- International Knee Documentation Committee osteoarthritis classification A, B, C, D/Ahlback I to IV
- No cupula
- Normal ligament balance

Contraindications[24]

- Bicompartmental OA
- Fixed flexion contracture > 25°
- Obese patients
- Patients who run or jump (other high-demand activities are well-suited for HTO)
- Meniscectomy in the compartment that will be loaded following the osteotomy
- Smokers

Possible contraindications[24]:

- Previous infection
- Flexion contracture > 15°
- Insufficiency of the ACL, PCL, or PLC
- Moderate patellofemoral arthritis
- Desire to engage in all sports

2.6. Potential Complications/Harms of Knee Arthroplasty

In addition to the risk of the general anesthetic, other potential complications of total knee arthroplasty include thromboembolism (deep vein thrombosis, pulmonary embolus), wound complications (deep and superficial infection, delayed healing), ischemic events (myocardial infarction and stroke, postoperative confusion), stiffness of the knee and arthrofibrosis. Thromboembolic prophylaxis methods include mechanical devices, such as compression stockings or foot pumps, and pharmaceutical agents, such as low-dose warfarin, low-molecular-weight heparin and aspirin. Infection may require treatment with antibiotics, debridement with prosthesis retention, resection arthroplasty, knee arthrodesis, one-stage or two-stage re-implantation. On rare occasion, amputation may be necessary[150].

2.7. Comparator

The comparator for the CN-TKA is the conventional, manual, jig-based TKA. The comparators for the partial knee arthroplasties include HTO for the UKA, and TKA (either CN-TKA or CONV-TKA) for UKA, bi-UKA or bicompartmental KA.

2.8. Common CN-TKA and Partial Knee Devices

2.8.1. CN-TKA

FDA approved devices

Surgical navigation systems require FDA clearance, but generally are subject only to 510(k) clearance since computer assisted surgery is considered analogous to a surgical information system in which the surgeon is only acting on the information that is provided by the navigation system. They are considered by the FDA to be substantially equivalent to other legally marked Class II stereotaxic instruments that are tracked through infrared tracking markers imposed onto computer images. For all devices, approved indications for use can be summarized by the following statements:

- To support the surgeon during specific orthopedic surgical procedure by providing information on bone resection, instrument and implant positioning during joint replacement
- To provide computer assistance to the surgeon based on anatomical landmarks and other specific data obtained intra-operatively that are used to place surgical instruments

Several imageless navigation systems have received FDA clearance and are listed in Appendix A.

2.8.2. UKA, Bicompartmental Knee Arthroplasty

FDA approved devices
To be granted clearance by the FDA, a new prosthesis must be found substantially equivalent (ie, same/similar indication for use, principles of operation, materials, sizes, type of interface, fixation, packaging, and sterility) to the predicate devices previously cleared for market. Several prostheses for use in UKA and bicomparmental knee arthroplasty have received FDA clearance and are listed in Appendix A.

2.9. Clinical Guidelines

2.9.1. National Guideline Clearinghouse

No specific guidelines were found that addressed unicompartmental, bicompartmental, bi-unicompartmental, total knee arthroplasty, or computer-assisted knee arthroplasty for the treatment of end-stage knee arthritis. Key word searches performed were: "*osteoarthritis*," "*knee replacement*," "*knee arthroplasty*," and "*knee surgery*." Any guidelines that addressed knee replacement were specific for non-surgical management, or prevention of venous thromboembolism post-surgery.

One guideline was found from the Work Loss Data Institute that mentioned total knee arthroplasty: (*Work Loss Data Institute. Knee & leg (acute & chronic). Corpus Christi (TX): Work Loss Data Institute; 2008. p.289)*

> **"Arthritis**: …Total knee arthroplasties are well accepted as reliable and suitable surgical procedures to return patients to function."

2.9.2. National Institute for Health and Clinical Excellence

No specific guidelines were found that addressed unicompartmental, bicompartmental, bi-unicompartmental, total knee arthroplasty, or computer-assisted knee arthroplasty for the treatment of end-stage knee arthritis from the National Institute for Health and Clinical Excellence (NICE), which provides guidance on health technologies and clinical practice for the National Health Service in England and Wales. Key word searches performed were: "*osteoarthritis*," "*knee replacement*," "*knee arthroplasty*," and "*knee surgery*."

2.9.3. NIH Consensus Statement on Total Knee Replacement.

NIH Consens State Sci Statements. 2003 Dec 8–10; 20(1) 1–32.

Relevant statements:

"Technical factors in performing surgery may influence both the short- and long-term success rates. Proper alignment of the prosthesis appears to be critical in minimizing long-term wear, risk of osteolysis, and loosening of the prosthesis. Computer navigation may eventually reduce the risk of substantial malalignment and improve soft tissue balance and patellar tracking. However, the technology is expensive, increasing operating room time, and the benefits remain unclear."

"There is clear evidence of racial/ethnic and gender disparities in the provision of TKR in the United States. The limited role of economic and other access factors in these racial or ethnic disparities can be demonstrated by significant differences in the rate of procedures in the VA system, where cost and access are assumed equivalent across race or ethnic groups."

2.9.4. Ontario Health Technology Advisory Committee (OHTAC)

In a published guideline from 2004, it was concluded that computer-assisted arthroplasty using navigation systems is considered to be in the investigational stage. Current studies have only assessed short-term outcomes, and long-term effectiveness (need for revision, implant longevity, pain, functional performance) has not been demonstrated.

2.9.5. Osteoarthritis Research Society International (OARSI)

OARSI published 23 treatment guidelines for the management of hip and knee osteoarthritis identified from a literature search, including six opinion-based, five evidence-based and 12 based on both expert opinion and research evidence[174]. Relevant guidelines for this report are:

> "22. Unicompartmental knee replacement is effective in patients with knee osteoarthritis restricted to a single compartment. Strength of Recommendation: 76% (95% CI = 64–88)"
>
> "23. …For the young and physically active patient with significant symptoms from unicompartmental knee osteoarthritis, high tibial osteotomy may offer an alternative intervention that delays the need for joint replacement some 10 years. Strength of Recommendation: 75% (95% CI = 64–86)."

2.9.6. AmericanAcademy of Orthopedic Surgeons (AAOS)

No specific clinical guidelines for knee arthroplasty were found, however, recommendations are due to be published in September, 2010.

2.10. Previous Systematic Reviews/Technology Assessments

Previous technology assessments and systematic reviews have mixed results about whether computer-assisted navigation for knee arthroplasty (CN-TKA) is significantly better than conventional methods for overall health outcomes of patients. Some data suggests CN-TKA is effective in reducing malalignment, especially in complicated surgical cases. However, no strong conclusions have been made about long-term functional outcomes.

Two other extensive reports evaluating TKA and UKA concluded UKA is similar to TKA with respect to function and pain, and that TKA overall is associated with improved knee function.

One extensive AHRQ report (2003) focused on the efficacy of conventional TKA (CONV-TKA), in contrast to the focus of this report which is on the comparison of CN-TKA with CONV-TKA, and partial KA with TKA. The relevant results are highlighted in the table.

All reviews noted more multi-center, randomized-controlled trials are necessary. Table 2 summarizes the previous assessments:

Table 2. Overview of previous systematic reviews/technology assessments of knee arthroplasty for the treatment of end-stage knee joint arthritis.

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
Brin YS, Nikolaou VS, Joseph L et al. (2010) *International Orthopaedics(SICOT) Imageless computer assisted versus conventional total knee replacement. A Bayesian meta-analysis of 23 comparative studies.*	through 10/2008	Computer Navigated TKA Aesculap; Stryker; BrainLAB; Navitrack; PiGalileo; Medtronic	• 10 RCTs (%f/u NR); N = 1,629; compared CN-TKA with CONV-TKA. • 13 observational studies (%f/u NR); N = 2,434.	yes	• Main outcome evaluated was the reduction of outliers in the limb mechanical axis and coronal position of the implants. • Analysis was performed on prospective RCTs separate from observational studies, in addition to analysis of all studies combined, with similar results.	**Efficacy:** The use of CN-TKA significantly reduces the number of outliers in the mechanical axis and coronal position of the implants by a rate of approximately 80%. CN-TKA seems to improve accurate component positioning, however, the long-term clinical significance of this remains unknown. **Safety:** N/A **Economic:** N/A
Medical Services Advisory Committee (MSAC) (2009) *Computer-navigated total knee arthroplasty*	through 2008	Computer Navigated TKA Stryker surgical instruments; BrainLAB/DePuy; ORTHOSoft; Orthopilot; Medtronic	• 15 RCTs (%f/u NR); N = 1,395; compared CN-TKA with CONV-TKA • 7 pseudo-RCTs (%f/u NR); N = 957. • 21 comparative studies (%f/u NR); N = NR.	yes	• Directly evaluated efficacy, safety, and cost-analysis of CN-TKA vs. CONV-TKA.	**Efficacy:**Evidence of postoperative mechanical alignment of TKA with long-term clinical effectiveness was poor and did not unequivocally prove a link between malalignment and revision surgery. Thus, at the present time, it is not possible to prove that the radiological alignment improvements conferred by computer-navigation lead to an improved clinical outcome for the patient. **Safety:** Among the 31 comparative and 10 case series studies included for safetyit appears that computer-navigated total knee arthroplasty is as safe as conventional total knee arthroplasty. **Economic:** CN-TKA is potentially a cost-effective treatment for TKA in the long-term provided the corresponding improvement in the 10-year revision rate of

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
						TKA improves by 2 per cent or more.
BCBS Tec Assessment Program (2008) *Computer-assisted navigation for total knee arthroplasty*	01/1980 through0 8/2007	Computer Navigated TKA *Several devices cleared by the FDA:* PiGalileo; Computer-Assisted Orthopedic Surgery System, PLUS Orthopedics; OrthoPilot Navigation System; Braun; Navitrack Navigation System; ORTHOSoft.	• 9 RCTs (%f/u 83% –100%); N = 692; compared CN-TKA with CONV-TKA	yes	• Adequate randomization and allocation of treatment • Specific to tricompartmental knee replacement (i.e., total knee) for patients with end-stage degenerative arthritis • Only outcome that could be measured across studies was alignment. RCTs did not have enough power to compare long term health outcomes (e.g., pain, function, or need for revision surgery)	**Efficacy:** Consistent demonstration across studies thatCN-TKA was more effective than conventional therapyforthe reduction in alignment outliers. Pooled data suggest malalignment of greater than 3 degrees will be avoided in approximately 15.5% of patients (95% CI: 9.4–21.7%) when CN-TKA is used. However, no meaningful conclusion could be made about improvement in overall health outcomes. **Safety:**CN-TKA-related complications could not be evaluated from the included studies. **Economic:**N/A
Bauwens K, Matthes G, Wich M, et al. (2007) *J Bone Joint Surg Am* 89(2):261-9. *Navigated total knee replacement. A meta-analysis.*	01/1986 through 01/2006	Computer Navigated TKA	• 33 studies – *combined analysis of RCTs, quasi-RCTs, non-randomized cohorts,* (% f/u NR); N = 3423; compared CN-TKA with CONV-TKA	yes	• End-point analysis was based primarily on radiographic evidence of limb axis alignment. • Secondary assessment was duration of surgery, rates of infection and thromboembolic events, and functional outcomes.	**Efficacy:** No conclusive inference could be drawn on functional outcomes or complication rates. Navigated knee replacement provides few advantages over conventional surgery on the basis of radiographic end points. **Safety**: There was no evidence of a difference in infection rates (RR, 0.97; 95% CI, 0.33 to 2.85) or the onset of thromboemolic events RR, 0.64; 95% CI, 0.31 to1.34) between study arms. **Economic**: Cited a recent Markov analysis suggesting that, with extra charges of $430 per case, computer-assisted knee replacement proves

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
						cost-effective in the long run. Discounted costs of conventional and navigated knee replacement were predicted at $14,300 and $13,200 after 10 years, mainly caused by a cumulative 1.6% reduction in complex revision rates.
Mason JB, Fehring TK, Estok R, et al. (2007) *J Arthroplasty* 22(8):1097-106 *Meta-analysis of alignment outcomes in computer-assisted total knee arthroplasty surgery.*	01/1990 through 01/2007	N/A	• 29 studies – *combined analysis of RCTs, quasi-RCTs, non-randomized cohorts, and historical cohorts* (% f/u NR); N = 3437; compared CN-TKA with CONV-TKA.	yes	• Funding received for this research from corporate sources. • Report uses many of the same studies included in the Bauwens report, and have attributed the difference in conclusions to analytic error.	**Efficacy:** Alignment outcomes for CN-TKA vs. CONV-TKA indicates significant improvement in component orientation and mechanical axis when CN-TKA is used. **Safety**: N/A **Economic**: N/A
Ontario Health Technology Assessment Series (2004) *Computer-assisted hip and knee arthroplasty. Navigation and Active Robotic Systems*	01/1996 through 11/2003	OrthoPilot; Stryker; Navitrak; Vectorvision; Achieve system.	• 1 RCT (%f/u NR); N = 240; compared CN-TKA with CONV-TKA • 1 prospective cohort (%f/u NR); N = 120; compared CN-TKA with CONV-TKA • 2 case control studies; (%f/u NR); N = 260	yes	• Graded evidence as level 1 (good RCT); level 2 (small RCT); or 3 (observational study).	**Efficacy:** Evidence from one RCT found a statistically significant difference in alignment and angular deviation between CN-TKA and CONV-TKA in favor of CN-TKA. However, long-term effects are unknown. **Safety**: N/A **Economic**: N/A
Madekwe UI, Zywiel MG, Bonutti PM et al. (2010) *Expert Rev Med Devices* 7(2); 219-239. *Scientific evidence for the use of modern unicompartmental knee arthroplasty*	N/A	N/A	• 1 RCT (%f/u NR); N = 40; compared UKA vs. TKA • 5 observational studies (%f/u NR); N = 562; compared UKA vs TKA	yes	• Although studies were critically evaluated, search methods and inclusion/exclusion criteria were not defined.	**Efficacy:** Based on the outcomes analyzed (knee society score, revision rate, and range of motion), UKA may result in less morbidity, and comparable clinical results to patients also considering CONV-TKA or CN-TKA. Main conclusion was UKA remains a viable alternative for the treatment of monocompartmental knee osteoarthritis. **Safety:** N/A

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
						Economic: N/A
Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP/S) (2005) *Unicompartmental Knee Arthroplasty for Unicompartmental Osteoarthritis: A systematic review.*	through 04/2004	UKA: *St Georg Sled; Tricon M, P; Unicondylar, Oxford Knee, Wessinghagesled, Miller-Galante* TKA: *Kinematic/Kinematic Plus; Tricon M, P; Total condylor knee; Press-fit condylar; PFC Sigma, NexGen*	• 1 RCT (89%f/u); N = 94 (102 knees); compared UKAto TKA • 6 non-randomised comparative (%f/u NR or >95%); N = 405 (419 knees); compared UKA to TKA. • 2 retrospective comparative (95% f/u, or NR); N = 815 (1,011 knees)	yes	• Evidence base for this review was rated as average, meaning most of the evidence is from high quality quasi-RCTs, or from non-randomized comparative studies without significant flaws.	**Efficacy:** Suggests UKA was similar to TKA for knee function and pain, although it was difficult to compare across studies due to the variability in knee and pain scores used. Range of motion was significantly better in UKA than TKA. Overall conclusion was UKA was at least as efficacious as TKA in terms of function. **Safety**: No significant differences in overall rates of complications between UKA and TKA, although deep vein thrombosis appeared to be reported more often after TKA than UKA. Other complications included delayed healing and infections. Rate of revision was reported in less than half of the studies. **Economic**: N/A
Ontario Health Technology Assessment Series (2005) *Total knee replacement*	through 2005	N/A	• 19 observational studies (%f/u NR); N = 12,574; measured the percent change between preoperative and postoperative standardized scores.	yes	• Objective of the study was to assess the effectiveness, in terms of pain reduction and functional improvement, of TKA for people with osteoarthritis for whom less invasive treatments have failed.	**Efficacy:** Patients who undergo TKA for osteoarthritis have substantial improvements in terms of reduction of pain and improvement of function. UKA seems to be as effective as TKA for people who have osteoarthritis limited to one knee compartment. **Safety**: Risks and complications associated with knee replacement are deep venous thrombosis (DVT), infection, stiffness, loosening, and osteolysis (the softening and loss of bone). Specific complication

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
						percentages from cited studies were not given. **Economic**: Cited only device costs and hospital costs (no analysis)
Kane RL, SalehKJ, Wilt TJ, et al.(2003) AHRQ Publication No. 04-E006-2. Rockville, MD: Agency for Healthcare Research and Quality. *Total Knee Replacement. Evidence Report/Technology Assessment No. 86*	1995 through 04/2003	N/A	• Primary TKA indicators: 62 studies (study type not defined, %f/u NR); N = 21,360.	yes	• Report addressed three areas: 1) primary indicators for TKA; 2) TKA revisions; and 3) access to care.	**Efficacy**: TKA is associated with improved function. The strongest evidence exists over a follow-up of two years, but even 5 and 10 year follow-up show positive results. There is no evidence that age, gender, or obesity is a strong predictor of functional outcomes. **Safety**: Complications occurred in 5.4% of patients and 7.6% of knees. The vast majority were "knee related" or deep venous thrombosis. There were only 8 cardiovascular or pulmonary complications reported among nearly 6,000 patients suggesting these adverse effects were not fully addressed in the literature. **Economic**: N/A
Virolainen P, and Aro HT (2003) *Arch Orthop Trauma Surg* 124:258-261. *High tibial osteotomy for the treatment of osteoarthritis of the knee: a review of the literature and a meta-analysis of follow-up studies.*	1970-1988	N/A	• 19 studies (did not report study type); (%f/u NR); N = 412.	N/A	• Main question analyzed was the final outcome of high tibial osteotomy.	**Efficacy**: Meta-analysis showed that high tibial osteotomy has an averaged probability of a good result in 60.3% of patients even after 100 months. The overall failure rate, including re-osteotomies, **arthroplasties**, meniscectomies, ligament reconstructions, infections, and non-unions, was 24.6% at 10 years. **Safety**: N/A

Assessment (year)	Lit search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
						Economic: N/A

NR: Not Reported
N/A: Not Available
*Percent follow-ups were not given for all RCTs or case series
†N reflects numbers before loss to follow-up
‡Critical appraisal refers to formal evaluation of individual study quality using criteria such as the Jadad or GRADE methods of scoring and the determination of overall strength of evidence.

2.11. Medicare and Representative Private Insurer Coverage Policies

There are no coverage policies for total knee arthroplasty (TKA) published from the Centers for Medicare and Medicaid Services.Coverage policies are consistent for TKA for other selected bell-weather payers. The payers will provide coverage for TKA, as long as implantation of the device is used as a last resort (after all other treatment modalities have failed), and certain patient conditions are met. Table 3 provides an overview of policy decisions.

- Medicare
  The Centers for Medicare and Medicaid Services have no published National (NCD) or Local coverage determinations (LCD) for knee arthroplasty or for any of the comparators (TKA, unicompartmental, or computer navigated).

  There is one relevant excerpt from LCD 24364: "…In addition, there is currently no convincing literature to support the use of any other clinically available devices for use in performing joint replacement surgery, either knee or hip. Though it does appear that the technology allows arguably more precise positioning of the joint replacement hardware, there is no long-term data supporting the assertion that this improves patient outcomes or long-term viability of the repair as compared to traditional methods of performing these procedures. Therefore, CPT codes 20985, 0054T, and 0055T will be denied as not proven effective."

- Regence
  Computer assisted navigation for orthopedic procedures involving the pelvis and appendicular skeleton is considered investigational, based on recent RCTs with short to mid-term follow-up that have not shown improved health outcomes with CN-TKA.

- CIGNA
  CIGNA considers total knee replacement as medically necessary when there is radiographic evidence of advanced joint disease and BOTH of the following conditions are met:
    - Persistent pain despite an appropriate course of nonsurgical management (e.g., nonsteroidal anti-inflammatory agents [NSAIDS], analegesics, light exercise, assistive device, bracing, viscoelastic supplementation);
    - Functional limitation resulting in impaired, age-appropriate activities of daily living.

  CIGNA considers a unicompartmental knee replacement as medically necessary, as an alternative to total knee replacement, when ALL of the following conditions are met:
    - Severe osteoarthritis is limited to a single compartment
    - Knee examinations demonstrate good alignment and ligamentous stability
    - Persistent knee pain despite an appropriate course of nonsurgical management (e.g., nonsteroidal anti-inflammatory agents [NSAIDS], analegesics, light exercise, assistive device, bracing, viscoelastic supplementation)

- Functional limitation resulting in impaired, age-appropriate activities of daily living, secondary to the knee

CIGNA does not cover ANY of the following because each is considered experimental, investigational, or unproven:

- Bicompartmental knee replacement, including bi-unicompartmental
- Computer assisted guidance during knee arthroplasty
- Minimally invasive approaches to knee arthroplasty
- Unicondylarinterpositional spacer
- Customized knee replacement prosthesis

AETNA

- Aetna considers unicompartmental knee arthroplasty using FDA-approved devices medically necessary for members with osteoarthritis of the knee affecting only one compartment, who have pain and/or limited range of motion, and have had an inadequate response to conservative measures
- Aetna considers the UniSpacerinterpositional spacer for the treatment of osteoarthritis affecting the medial compartment of the knee experimental and investigational
- Aetna considers bicompartmental and bi-unicompartmental knee arthroplasty experimental and investigational for osteoarthritis of the knee and all other indications because their effectiveness has not been established

Table 3. Overview of payer technology assessments and policies for knee arthroplasty for the treatment of end-stage knee-joint arthritis.

Payer (year)	Lit search dates	Evidence base available*	Policy	Rationale/comments
Centers for Medicare and Medicaid Services (CMS)	N/A	N/A	• No NCDs or LCDs. However, the policy for CN-TKA is consistent with other payers that the procedure is investigational and there is no long-term data to support improved clinical outcomes.	N/A
Regence (2009) *Computer assisted navigation for orthopedic procedures of the pelvis and appendicular skeleton.*	through 2009	• 2007 BCBS Tec Assessment • 1prospective multicenter study • 1 meta-analysis	• Computer assisted navigation for orthopedic procedures involving the pelvis and appendicular skeleton is considered investigational	• Recent RCTs with short to mid-term follow-up have not shown improved health outcomes with CAN.
CIGNA (2010) *Knee Arthroplasty/ Replacement*	through 2010	• 1 Meta-analysis • 2 SR • 7 Retrospective case series • 2 Prospective case series	CIGNA covers total knee replacement as medically necessary when there is radiographic evidence of advanced joint disease and BOTH of the following conditions are met: • Persistent pain despite an appropriate course of nonsurgical management (e.g., nonsteroidal anti-inflammatory agents [NSAIDS], analegesics, light exercise, assistive device, bracing, viscoelastic supplementation); • Functional limitation resulting in impaired, age-appropriate activities of daily living. CIGNA covers a unicompartmental knee replacement as medically necessary, as an alternative to total knee replacement, when ALL of the following conditions are met: • Severe osteoarthritis is limited to a single compartment; • Knee examinations demonstrate good alignment and ligamentous stability; • Persistent knee pain despite an appropriate course of nonsurgical management (e.g., nonsteroidal anti-inflammatory agents [NSAIDS], analegesics, light exercise, assistive device, bracing, viscoelastic supplementation); • Functional limitation resulting in impaired, age-appropriate activities of daily living,	• Total knee replacement (TKR) and unicompartmental knee replacement (UKR), for medial, lateral, or patellofemoral compartment joint disease, is supported with sufficient clinical evidence as safe and effective in relieving pain and improving joint function and mobility. There is insufficient evidence to support safety, efficacy, and improved long-term outcomes for bicompartmental or bi-unicompartmental knee replacement (BKR). • CPT codes if selection criteria is met: 27438, 27445, 27446, 27447.

Payer (year)	Lit search dates	Evidence base available*	Policy	Rationale/comments
			secondary to the knee. CIGNA does not cover ANY of the following because each is considered experimental, investigational, or unproven: • Bicompartmental knee replacement, including bi-unicompartmental; • Computer assisted guidance during knee arthroplasty; • Minimally invasive approaches to knee arthroplasty; • Unicondylarinterpositional spacer • Customized knee replacement prosthesis.	
Aetna (2009) *Clinical Policy Bulletin: Unicompartmental, Bicompartmental, and Bi-unicompartmental knee arthroplasties*	through 2009	• Primary studies, systematic reviews, previous HTAs, and guidelines all cited (39 references).	• Aetna considers unicompartmental knee arthroplasty using FDA-approved devices medically necessary for members with osteoarthritis of the knee affecting only one compartment, who have pain and/or limited range of motion, and have had an inadequate response to conservative measures; • Aetna considers the UniSpacerinterpositional spacer for the treatment of osteoarthritis affecting the medial compartment of the knee experimental and investigational. • Aetna considers bicompartmental and bi-unicompartmental knee arthroplasty experimental and investigational for osteoarthritis of the knee and all other indications because their effectiveness has not been established.	• No rationale for policy given • CPT codes if selection criteria is met: 27438, 27445, 27446, 27447.

N/A: Not Available
*Medicare does not report the current evidence available.

3. The Evidence

3.1. Methods of the Systematic Literature Review

3.1.1. Inclusion/exclusion

Inclusion and exclusion criteria are summarized in Table 4.

- *Population.* Studies of adults who underwent primary knee replacement for arthritis (non-inflammatory or inflammatory) were included.
- *Intervention.* Included studies evaluated CN-TKA or partial knee arthroplasty. Studies reporting results on revision CN-TKA or revision partial knee arthroplasty were excluded, as were studies reporting on patellofemoral arthroplasty only.
- *Comparator.* Conventional TKA when comparing CN-TKA; CONV-TKA and high tibial osteotomy when comparingpartial knee arthroplasty. Studies reporting results on revision TKA were excluded.
- *Outcomes.* Eligible studies reported on at least one of the following outcomes: revision, clinician reported or patient reported functional outcomes (e.g. WOMAC, Knee Society Score, Oxford Knee Score), perioperative and postoperative complications (e.g. infection/fracture, venous thromboembolism). Radiographic alignment for computer navigation
- *Study design.* Eligible studies compared total CN-TKA with CONV-TKA utilizing a randomized or cohort study design. In order to provide additional context regarding key long term revision rates and differential efficacy (key questions 1, 2, and 4) registry studies were included. Formal economic analyses published in peer-reviewed journals were eligible for inclusion to help answer key question 5 as were cost data reported in other technology assessments.

Table 4. Summary of inclusion and exclusion criteria

Study Component	Inclusion	Exclusion
Participants	Adults with knee: ◆ Non-inflammatory arthritis (osteoarthritis, traumatic arthritis, osteonecrosis) ◆ Inflammatory arthritis (rheumatoid arthritis)	◆ Age ≤18 years
Intervention	◆ Computer navigation knee arthroplasty ◆ Partial knee arthroplasty	◆ Revision of total knee arthroplasty ◆ Patellofemoral arthroplasty only
Comparators	◆ Standard total knee arthroplasty	
Outcomes	*Efficacy/Effectiveness* ◆ Revision Rate ◆ Time to revision ◆ Clinician reported and patient reported outcomes ◆ Radiographic alignment for computer navigation only (secondary outcome) *Safety* ◆ Complications and adverse effects ◆ Infection ◆ Fracture ◆ Blood loss ◆ Thromboembolic effect	◆ Non clinical outcomes
Study Design	◆ Meta-analyses ◆ RCTs ◆ Comparative observational studies ◆ Registry studies to assess long term revision rates and special populations	◆ Case reports ◆ Non-clinical studies ◆ Case series except for long term revision rates
Publication	◆ Studies published in English in peer reviewed journals, published HTAs or publically available FDA reports ◆ Full formal economic analyses (e.g. cost-utility studies) published in English in a HTA or in a peer-reviewed journal published after those represented in previous HTAs	◆ Abstracts, editorials, letters ◆ Duplicate publications of the same study which do not report on different outcomes ◆ Single reports from multicenter trials ◆ Studies reporting on the technical aspects total knee arthroplasty ◆ White papers ◆ Narrative reviews ◆ Articles identified as preliminary reports when results are published in later versions ◆ Incomplete economic evaluations such as costing studies ◆ Studies using administrative databases

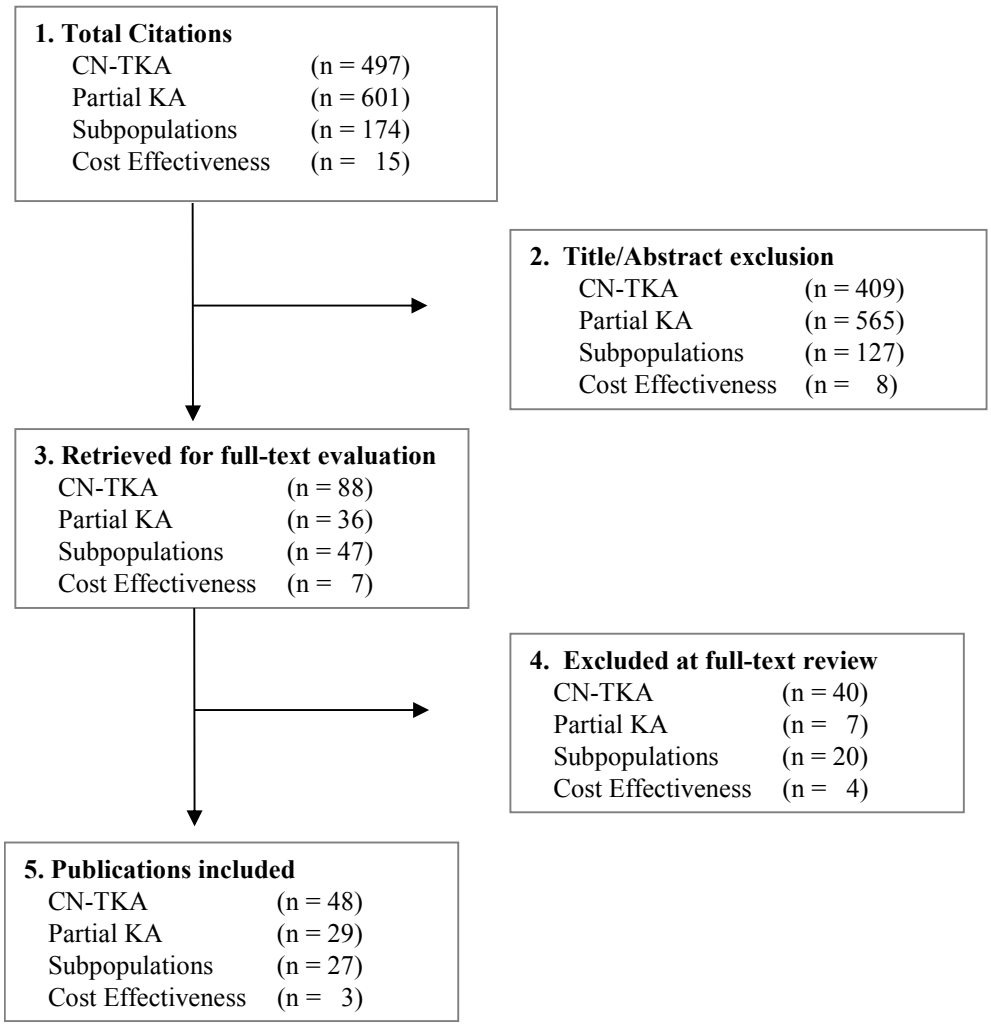
3.1.2. Data Sources and Search Strategy

The clinical studies included in this report were identified using the algorithm shown in Appendix B. The search took place in four stages. The first stage of the study selection process consisted of a comprehensive literature search using electronic means and hand

searching. We then screened all possible relevant articles using titles and abstracts in stage two. This was done by two individuals independently. Those articles that met a set of *a priori* retrieval criteria based on the criteria above were included. Any disagreement between screeners that were unresolved resulted in the article being included for the next stage. Stage three involved retrieval of the full text articles remaining. The final stage of the study selection algorithm consisted of the selection of those studies using a set of a priori inclusion criteria, again, by two independent investigators. Those articles selected form the evidence base for this report.

Electronic databases searched included PubMed, EMBASE, CINAHL, ClinicalTrials.gov, CRISP, HSTAT, *The Cochrane Library*, EconLIT, PsychINFO, AHRQ, and INAHTA for eligible studies, including health technology assessments (HTAs), systematic reviews, primary studies and FDA reports. Reference lists of all eligible studies were also searched. The search terms and strategies usedare shown in Appendix C. **Figure 1** shows a flow chart of the results of all searches for included primary studies. Articles excluded at full-text review are listed in Appendix D.

Figure 1. Flow chart showing results of literature search



3.1.3. Data Extraction

Reviewers extracted the following data from the included clinical studies: study population characteristics, study type, study period, patient demographics and preoperative diagnoses, study interventions, follow-up time, study outcomes (revision, functional and clinical scores, motion, radiographic alignment), complications/adverse events (infection, fracture, blood loss, venous thromboembolism, death). An attempt was made to reconcile conflicting information among multiple reports presenting the same data. For economic studies, data related to sources used, economic parameters and perspectives, results, and sensitivity analyses were abstracted.

3.1.4. Study Quality Assessment: Level of Evidence (LoE) Evaluation

The method used by Spectrum Research, Inc. (SRI) for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of the rating

scheme developed by the Oxford Centre for Evidence-based Medicine[125], precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group[11], and recommendations made by the Agency for Healthcare Research and Quality (AHRQ)[168].

Details of the Level of Evidence (LoE) methodology are found in Appendix E. Each clinical/human study chosen for inclusion was given a LoE rating based on the quality criteria listed in Appendix E. Standardized abstraction guidelines were used to determine the LoE for each study included in this assessment.

3.2. Quality of Literature Available

3.2.1. Quality of Studies Retained

We initially found 1287 citations using the search strategy in Appendix C and searching select bibliographies. We summarize the results of 107 articles for this review.

For the comparison of CN-TKA with CONV-TKA, we identified and included 48 studies (51 articles): 26 randomized controlled trials (RCTs) and 20 cohort studies that reported data on clinical, functional or safety outcomes, and 2 systematic reviews summarizing radiographic alignment. One RCT[33] received a level of evidence (LoE) grading of I; all other RCTs were graded as LoE II. Three cohort studies were graded LoE II; all other cohorts were graded as LoE III (Appendix F).

For the comparison of partial knee arthroplasty, we included 29 studies (31 articles): one RCT (LoE II) and 21 cohort studies (LoE III) that reported data on clinical, functional or safety outcomes comparing UKA with TKA. Four additional studies compared UKA with high tibial osteotomy (HTO): two RCTs (LoE II) and two cohort studies (LoE III). Bicompartmental or bi-unicompartmental knee arthroplasty versus TKA, were addressed by three cohort studies,all LoE III.

To determine if there was differential efficacy, effectiveness or safety in subpopulations for the technologies of interest, we included 27 studies: 19 cohort studies (1 LoE I, 2 LoE II, 16 LoE III), six total joint registry studies (5 LoE II and 1 LoE IV) and two systematic reviews (LoE II).

3.2.2. Critical Appraisal

Randomized Controlled Trials(APPENDIX F)

CN-TKA versus CONV-TKA

Of the 26 RCTs, only one study received a level of evidence (LoE) grading of I[33]; all the other RCTs were graded as LoE II.

Sample Size

Across the 26 RCTs, sample sizes ranged from 24 patients (24 knees) to 320 patients (420 knees). Thirteen studies had a total of 100 or more patients but only three of these study had more than 100 patients in each group[84,106,147]. Not all studies differentiated well between unilateral and bilateral arthroplasty – there were frequent discrepancies between the number of patients and the number of knees treated for whichthey were not always explicitly accounted.

Randomization and ConcealedAllocation

Only 14/26 RCTs reported adequate methods of allocation including sealed envelopes, computerized permutation algorithms, and computer generated number tables[30,33,35,45,67,79,84,85,97,99,106,109,140,157].

Blinding

Only 14/26 RCTs reported independent or blind assessment of the outcomes[33-35,45,49,51,85,106,120,124,140,148,157,167]. Blinding of patients or assessors of outcomes was not discussed in the remaining 12 studies. Though blinding of patients and outcomes assessors may not be possible, there is no indication that an independent evaluator was used to collect outcomes data.

Statistical Analysis

All 26 RCTs clearly delineated the descriptive and inferential statistics employed and all but three[15,147,157] prospectively determined an alpha level for statistical significance at ≤ .05. Analysis by intention-to-treat was attempted by only two trials[33,99] and one other study specifically stated that the short follow-up period prevented intention-to-treat analysis[84]. All but five RCTs[15,79,85,124,147] stated that they controlled for possible confounding factors via various statistical methods, including linear regression and multivariate analysis.

Follow Up Time and Percent of Patients Followed

Follow-up periods ranged from postoperative to 2 years across the RCTs. The shortest follow-up period in which functional outcomes were reported was 3 months. For six studies which reported on safety data only, such as blood loss or venous thromboembolism (VTE), follow-up periods were assumed to be extremely short, i.e. postoperative, given the nature of the outcome. Of the 26 RCTs, nine reported a complete follow-up of 85%–100% of patients[33,45,85,97,100,106,109,148,157]and 12 studies, which reported only immediate postoperative outcome or safety-related outcomes[15,34,35,38,67,78,79,84,120,124,147,167] were inferred to have 100% follow-up given the extremely short observation time. The remaining five did not report loss to follow-up[17,49,51,105,137].

UKA versus TKA

We found only one study (two publications) that performed a randomized controlled trial comparing UKA with TKA.

NEWMAN (1998 & 2009)
Newman et al. reported the results of a randomized controlled trial (RCT) in which 94 patients with 102 knees were randomized to undergo either total knee arthroplasty with a posterior cruciate-conserving Kinematic Modular (Howmedica, Rutherford, New Jersey) component fixed with Palacos G cement or unicompartmental knee arthroplasty with a St. Georg Sled (Waldemar, Link, Hamburg, Germany) component fixed with Palacos G cement. Preoperative diagnosis was unicompartmentaltibiofemoral osteoarthritis (OA) with "normal" other compartments, intact cruciate ligaments, flexion deformity $\leq 15°$, and varus/valgus deformity $\leq 15°$. Mean patient age was 70 (range 47–89), and 41.5% of the patients were male. Randomization was performed using random number tables; however, there was neither mention of concealment nor a description of the random allocation process to determine the likelihood of concealment. Evaluators assessing knee motion and the clinical outcomes (e.g. Bristol) were not blinded to intervention. There was no indication of patients receiving other than the randomized treatment and no mention of intention-to-treat analyses. The objectives of the study were to evaluate whether there were differences between the groups in the Bristol Knee Score outcomes as well as range of motion and radiographic outcomes. A follow up rate at 5 years of 88.5% and at 15 years of 51% was reported. Benefits were received but were directed solely to a research fund, foundation, educational, institutional, or other non-profit organization with which one or more of the authors were associated. This study received a level of evidence (LoE) grade of II.

UKA versus HTO

Two randomized controlled trials evaluated UKA versus HTO, both graded a level of evidence II.

STUKENBORG-COLSMAN (2001)
Stukenborg-Colsman published the results of a randomized control trial (RCT) in which 60 patients (62 knees) were randomized to undergo either a high tibial osteotomy (HTO) or unicompartmental arthroplasty (UKA). A unicondylar knee sliding prosthesis was used for the UKA patients; for HTO patients, a lateral-based wedge of bone was resected, attempting to overcorrect to at least 8° valgus. Patients were included if they had medial unicompartmental osteoarthritis, varusmalalignment< 10°, flexion contraction < 15°, ligament instability < 2nd degree, and age over 60 years. The mean age was 67 years, which ranged from 60 to 80 years, and 41.7% of the patients were male. The HTO group contained more than twice the percentage of males than the UKA group (59% vs. 21%), but this was not discussed by the authors and it is unclear whether sex was controlled for in the Cox regression. Patients were "computer-randomized" to a treatment. There was neither mention of concealment nor a description of the random allocation process to determine the likelihood of concealment. Blinding of patients or assessors of outcomes was not discussed,and though blinding of patients and outcomes assessors is probably not possible, there is no indication that an independent evaluator was used to collect outcomes data.There was no indication of patients receiving other than the randomized treatment and no mention of intention-to-treat analyses. The objectives of this study were to evaluate whether there were differences between the two treatment groups in long-term functional outcomes and safety. A complete follow-up rate of 68.3% was reported at final follow-up; the mean final follow-up was 7.5 years (6.6–10 years). Results at a mean follow-up of 2.5 years and 4.5 years were also reported; however, the percent followed was not reported. Funding of the study was not discussed. This study received a level of evidence (LoE) grade of II(downgraded from a score of I due to inadequate sample size, inadequate percent follow-up, and failure to indicate concealment or intention-to-treat analysis).

WEIDENHIELM (1993)/BORJESSON (2005)
Weidenhielm and Borjesson published in two reports the results of a randomized control trial (RCT) in which 100 patients (number of knees not stated) were randomized to undergo either a high tibial osteotomy (HTO) or unicompartmental arthroplasty (UKA). A Brigham prosthesis was used for the UKA patients; for HTO patients, a Coventry closing wedge osteotomy was performed, attempting to overcorrect to 4° valgus. Patients were included in the original RCT (n = 50 in each group) if they had medial unicompartmental osteoarthritis (Ahlbäck's I – III) and were 55–70 years of age. Only 59 patients "with strictly unilateral osteoarthritis" were included in the results reported at 1 year follow-up and 40 patients at 5 year follow-up. The mean age was 64 years, which ranged from 59 to 69 years, and 47.5% of the patients were male (demographics were reported for the 59 patients included in the analyses). Patients were randomly assigned to a treatment by drawing lots. Blinding of patients or using independent outcomes

assessors was not discussed. There was no indication of patients receiving other than the randomized treatment and no mention of intention-to-treat analyses. The objective of these studies was to evaluate any differences between the two treatments regarding functional performance. The low follow-up rate for this study seriously jeopardizes its internal validity.Funding of either study was not indicated. This study received a level of evidence (LoE) grade of II.

Comparative Cohort Studies (APPENDIX F)

CN-TKA versus CONV-TKA

Of the 20 cohort studies, only three studies received a LoE II[83,121,175] grading; all other cohorts were graded LoE III.

SAMPLE SIZE

For the 20 nonrandomized studies, sample sizes ranged from 50 patients (50 knees) to 565 patients (565 knees). Seven studies had a total of 100 or more patients[20,28,39,50,80,83,136] and four studies had more than 100 patients in each group[39,80,83,136]. Not all studies differentiated well between unilateral and bilateral arthroplasty – there were frequent discrepancies between the number of patients and the number of knees treated that were not always explicitly accounted for.

INDEPENDENT OR BLIND ASSESSMENT

Only 7/20 cohort studies reported the use of independent or blind assessment[27,29,50,83,121,154,175].

STATISTICAL ANALYSIS

All 20 cohort studies delineated the descriptive and inferential statistics employed and all but three prospectively determined an alpha level for statistical significance at ≤ .05[20,39,154]. All but two of the cohort studies[27,141] stated that they controlled for possible confounding factors via various statistical methods.

FOLLOW-UP TIME AND PERCENT OF PATIENTS FOLLOWED

Follow-up periods ranged from postoperative to 5 years across allcohort studies, with the majority of studies reporting mid-term follow-up of 2–3 years. For studies which reported on safety data only, such as blood loss or operative time, follow-up periods were assumed to be extremely short, i.e. postoperative, given the nature of the outcome. Of the 20cohorts, six studies[20,83,108,114,138,154,175] reported complete follow-up of 91% to 100% of patients while three other cohorts (1 prospective, 2 retrospective)[39,65,80] reported follow-ups of only 80%, 64%, and 27%. For five cohort studies[28,31,121,136,141]which reported only safety-related outcomes, follow-up was assumed to be 100% given the extremely short follow-up time. No patient follow-up data were available for the remaining six studies.

UKA versus TKA
All 22 cohort studies (14 prospective and eight retrospective) were graded LoE III.

SAMPLE SIZE
For the 22 nonrandomized studies, sample sizes ranged from 34 patientsto 50,493 patients. The number of knees was not reported for all studies and is given when possible. All but six studies[26,42,54,74,89,169]had a total of 100 or more patients but only eight studies had more than 100 patients in each group[6,57,59,86,94,132,161,170], three of which had over 1500 patients in each group[57,86,132].

INDEPENDENT OR BLIND ASSESSMENT
Only 2/20 cohort studies (one prospective and one retrospective) reported the use of independent or blind assessment[9,169].

CONTROLLING FOR CONFOUNDING
Only 11/22 cohort studies, seven prospective and three retrospective,[9,26,42,54,57,86,89,94,132,135,170,172]stated that they controlled for possible confounding factors via various statistical and other methods.

FOLLOW-UP TIME AND PERCENT OF PATIENTS FOLLOWED
Follow-up periods ranged from 6 weeks[110] to 15 years[86] in both the UKA and TKA groups across allcohort studies, excluding five studies for which follow-up periods could not be determined[53,59,132,169]. Of these studies, two prospective cohorts reported follow-up between 6 and 7 years[6,89] and two (one prospective, one retrospective) between 10 and 15 years[57,86]. The percent of patients followed ranged from 76% to 100% in the UKA groups and from 67% to 100% in the TKA groups in 12 studies (eight prospective and three retrospective)[6,9,26,42,64,71,74,86,89,135,161,164]. One retrospective cohort reported patient follow-up for the entire population only, which was low at 67%[170]. No patient follow-up data was available for the remaining nine studies (four prospective and five retrospective)[53,54,57,59,94,110, Robertsson, 2000 #109,132,169,172].

4. Results

For key question 1, we identified a total of 16 RCTs and 12 cohort studies that reported data on clinical or functional outcomes. The primary indication for CN-TKA or CONV-TKA was primary osteoarthritis (OA). Secondary OA, rheumatoid arthritis (RA), and occasionally, avascular necrosis, were also included diagnoses in some studies. An overwhelming majority of patients were female and ages ranged from 41 to 88 years across the RCTs. The majority of patients appear to have undergone unilateral TKA; however, in some studies, bilateral TKA was performed. Two RCTs reported on patients undergoing bilateral, sequential primary TKA acting as their own control, with one knee undergoing TKA with computer navigation and the other conventional TKA[85,167]. Appendix G lists the study characteristics of the included RCTs.

4.1. Key question 1

What is the evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA?

4.1.1. CN-TKA Efficacy

Knee pain, CN-TKA Efficacy (Table 5)

Four RCTs reported on pain outcomes following CN-TKA compared with CONV-TKA. One study reported that 58% and 61% of patients, respectively, were considered pain-free at 6 months follow-up[49]. This same study reported VAS pain scores postoperatively only, and they were not statistically different between groups (both < 2 cm out of 10 cm). Another study reported that 78% and 70% of patients in the CN-TKA and CONV-TKA groups, respectively, had no pain (any) at 2 years; 21% and 30% had mild pain, respectively; and 1% in the CN-TKA group was experiencing moderate pain[85]. Anterior knee pain was reported in 8% of patients in each group in one RCT[106] and in 44% and 47% of patients following CN-TKA and CONV-TKA, respectively, in another; however, only 16% and 7%, respectively, complained of moderate to severe pain in the latter trial[148]. There was no statistically significant difference between the two groups in incidence of anterior knee pain in either RCT[148].

Table 5. Pain outcomes in RCTs comparing CN-TKA with CONV-TKA.

Pain measure	CN-TKA	CONV-TKA	*P*-value	Follow-up
VAS pain				
*Dutton 2008**	< 2 cm	< 2 cm	ns	postop
% pain free (n/N)				
Dutton 2008	58% (30/52 pts)	61% (34/56 pts)	ns	6 months
% of patients experiencing pain(n/N)				
Kim 2007†				2 years
None	78% (78/100 knees)	70% (70/100 knees)	NR	
Mild	21% (21/100 knees)	30% (30/100 knees)	NR	
Moderate	1% (1/100 knees)	----	NR	
% of patients experiencing anterior knee pain (n/N)				
Martin 2007	8% (8/100 pts)	8% (8/100 pts)	ns	3 months
Spencer 2007‡				2 years
Any	44% (14/32 pts)	47% (14/30 pts)	ns	
Moderate to severe	16% (5/32 pts)	7% (2/30 pts)	ns	

*Out of 10 cm.
†In Kim 2007, 100 patients underwent sequential bilateral TKA.
‡A total of 62 patients completed the postal survey of anterior knee pain, 32 CN-TKA and 30 CONV-TKA (whereas only 60 patients, 30 in each group, were available for further clinical and radiological follow-up).

Knee Function, Patient Reported and Clinician Based, CN-TKA Efficacy(Table 6)

Oxford Knee Score, *CN-TKA Efficacy*
No significant differences were identified in Oxford Knee Scores between CN-TKA and CONV-TKA groups at 6 months as reported by one RCT[49] or at 2 years as reported by two RCTs[51,148]. Across the three studies, follow-up Oxford Knee Scores in the computer-navigated group ranged from 20.0 to 26.7 and from 18.8 to 22.0 in the conventional group. None of the studies reported a significant difference in the preoperative scores between groups.

WOMAC, *CN-TKA Efficacy*
Four RCTs compared WOMAC scores between CN-TKA and CONV-TKA[45,46,97,140,148]. No significant differences between treatment groups were reported in any study. Overall, total WOMAC scores ranged from 7 to 31 and from 7 to 32, respectively, across three RCTs[97,140,148] with follow-up times ranging from 6 weeks to 2 years. Pain scores ranged from 0.9 to 6.1 and 1.2 to 6.3, respectively, across three studies[46,97,140] with follow-up times ranging from 6 weeks to 2 years. Stiffness scores ranged from 1 to 2.3 to 1 to 2.8, respectively, and physical function scores from 1.6 to 5 and 1.9 to 6, respectively, across two studies [46,97] with follow-up times of 6 weeks and 1 year.

Knee Society Score, *CN-TKA Efficacy*
No significant differences were reported in KSS Knee or Function scores in six RCTs[33,49,85,97,99,157] comparing CN-TKA with CONV-TKA. Follow-up times ranged from 6 weeks to 2 years after surgery. KSS Knee scores ranged from 65 to 93 and 66 to 94, respectively, and KSS Function scores ranged from 66 to 86 and 68 to 84, respectively. Four studies[105,106,109,148] reported only a total KSS, assumed to be a sum of the Knee and Function scores, which also did not differ statistically between groups in any study at any of the follow-up periods (postoperative to 2 years). A KSS Pain score was also reported by one study[85] at 2 years, also revealing no significant intergroup difference. None of the studies reported a significant difference in the preoperative scores or demographic data between groups.

Hospital for Special Surgery Knee Scale, *CN-TKA Efficacy*
Three RCTs compared HSS scores between CN-TKA and CONV-TKA[17,85,140]. No statistically significant differences between groups were reported in total, pain, or function scores by any study with follow-up periods ranging from 7 months to 2 years. Total HSS scores ranged from 82 to 92 in the CN-TKA group and from 83 to 91 in the CONV-TKA group in three RCTs[17,85,140]. In two RCTs[85,140]HSS pain scores were 28.7 and 25 and 29.2 and 25, respectively. One study[85] reported HSS function scores of 15 and 17, for the CN-TKA and the CONV-TKA groups, respectively. None of the studies reported a significant difference in the preoperative scores between groups.

Bartlett Patellar Score, *CN-TKA Efficacy*
Only one study[149] reported the Bartlett Patellar Score and found no difference between the CN-TKA and the CONV-TKA groups at 2 years (23.0 vs. 23.8, respectively).

Table 6. Results of Randomized Controlled Trials Comparing CN-TKA with CONV-TKA

Outcome	CN-TKA	CONV-TKA	*P*-value*	Follow-up
PATIENT REPORTED KNEE SCORES				
Oxford Knee Score				
Total Score (mean ± sd)				
Dutton 2008	20	22	ns	6 months
Ensini 2007	20.0 ± 7.2	18.8 ± 6.6	ns	2 years
Spencer 2007	26.7 ± 21.8	20.1 ± 15	ns	2 years
Western Ontario McMasters OA Index				
Total Score (mean ± sd or range)				
Seon 2009	31.3 (24–59)	32.2 (24–59)	ns	2 years
Luring 2008†	8 ± 7	11 ± 10	ns	6 weeks
	7 ± 9	7 ± 6	ns	3 months
Spencer 2007	24.0 ± 19.7	24.4 ± 16.8	ns	6 months
	23.4 ± 21.5	13.6 ± 13.0	ns	2 years
Pain Score (mean ± sd or range)				
Seon 2009	6.1 (4–9)	6.3 (4–13)	ns	2 years
Luring 2008†	2 ± 2	2 ± 3	ns	6 weeks
	1 ± 2	2 ± 1	ns	3 months
Decking 2005, 2007	1.9 ± 2.0	1.9 ± 1.7	ns	3 months
	0.9 ± 0.9	1.2 ± 1.0	ns	1 year
Stiffness Score(mean ± sd or range)				
Luring 2008†	2 ± 1	2 ± 1	ns	6 weeks
	1 ± 1	1 ± 1	ns	3 months
Decking 2005, 2007	2.3 ± 1.8	2.8 ± 1.9	ns	3 months
	2.0 ± 2.1	2.0 ± 1.8	ns	1 year
Physical Function Score (mean ± sd or range)				
Luring 2008†	4 ± 5	6 ± 6	ns	6 weeks
	5 ± 6	4 ± 5	ns	3 months
Decking 2005, 2007	2.0 ± 1.6	2.3 ± 1.5	ns	3 months
	1.6 ± 1.5	1.9 ± 1.8	ns	1 year

Table 6. Results of Randomized Controlled Trials Comparing CN-TKA with CONV-TKA

Outcome	CN-TKA	CONV-TKA	*P*-value*	Follow-up
CLINICIAN BASED KNEE SCORES				
Knee Society Score				
Total Score (mean, sd or range)‡				
Martin 2009	166 (122–200)	162 (101–200)	ns	post-op
	173 ± 19	169 ± 20	ns	3 months
Martin 2007	160 ± 24	160 ± 22	ns	3 months
Matziolis 2007	149 ± 34	144 ± 29	ns	6 months
Spencer 2007§	153.5 ± 26.9	152.2 ± 36.0	ns	1 year
	156.4 ± 33.1	158.9 ± 29.0	ns	2 years
Knee Score (mean, sd or range)				
Lützner 2010 (median)	89 (49–95)	89 (48–95)	ns	2 years
Choong 2009**††‡‡	90.0	89.0	ns	3 months
	93.0	94.0	ns	1 year
van Strien 2009	65 (± 13.8)	66 (± 17.6)	ns	1 year
Dutton 2008	84	85	ns	6 months
Luring 2008†	86 ± 8	83 ± 9	ns	6 weeks
	87 ± 9	86 ± 9	ns	3 months
Kim 2007	93 (89–100)	94 (91–100)	ns	2 years
Function Score (mean, sd or range)				
Lützner 2010 (median)	67.5	70.0	ns	3 months
Choong 2009**††‡‡	67.5	70.0	ns	3 months
	80.0	80.0	ns	1 year
van Strien 2009	66 (± 33.5)	80 (± 16.9)	ns	1 year
Dutton 2008	67	68	ns	6 months
Luring 2008†	83 ± 9	80 ± 10	ns	6 weeks
	86 ± 10	83 ± 11	ns	3 months
Kim 2007	85 (78–100)	84 (79–100)	ns	2 years
Pain Score (mean, range)				
Kim 2007	44 (35–50)	46 (35–80)	ns	2 years
Hospital for Special Surgery Knee Scale				
Total Score (mean, range)				
Seon 2009	92 (83–100)	91 (81–100)	ns	2 years
Kim 2007	90 (75–100)	89 (76–100)	ns	2 years
Böhling 2005	82 (39–94)	83 (62–97)	ns	7 months
Pain Score (mean, range)				
Seon 2009	28.7 (25–50)	29.2 (25–45)	ns	2 years
Kim 2007	25 (20–30)	25 (21–30)	ns	2 years
Function Score (mean, range)				
Kim 2007	15 (11–22)	17 (13–22)	ns	2 years
Bartlett Patellar Score(mean ± sd)				
Spencer 2007	23.0 ± 5.8	23.8 ± 4.7	ns	2 years

CN-TKA: computer-navigated total knee arthroplasty; CONV-TKA: conventional total knee arthroplasty; ns: not statistically significant.
*Studies with statistically significant findings controlled for baseline data and possible confounding factors.
†Scores at 1 week follow-up are also available, see Appendix H.
‡Total KSS reported only for studies which do not report separate Knee and Function scores. Total scores are assumed to be a sum of the Knee and Function scores.
§Scores at 3 and 6 months of follow-up are also available, see Appendix H.
**Authors used International Knee Society (IKS) scores which is the same assessment as the KSS.

††Scores are reported in a subset of patients with a mechanical axis within 3º of neutral.
‡‡Scores at 6 weeks and 6 months of follow-up are also available, see Appendix H.

Quality of Life, CN-TKA Efficacy (Table 7)

Two RCTs reported general health status and quality of life using the SF-36[49,148], one using the SF-12[33], and one using the EQ-5D[99]. The only significant difference between the CN-TKA and the CONV-TKA groups was reported in the Role Emotional subscale of the SF-36 at 6 months in one study[148], 66.7 versus 83.3, respectively, $P = .024$; however, at 2 years follow-up this difference was no longer statistically significant. None of the studies reported a significant difference in the preoperative scores between groups.

Table 7. Quality of life in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*	Follow-up
QUALITY OF LIFE MEASURE				
Short Form 36				
Physical (mean)				
Dutton 2008	46	43	ns	6 months
Mental (mean)				
Dutton 2008	57	58	ns	6 months
Physical Functioning (median)				
Spencer 2007	55.0	55.0	ns	6 months
	56.0	60.0	ns	2 years
Role Physical (median)				
Spencer 2007	56.3	56.3	ns	6 months
	50.0	65.7	ns	2 years
Bodily Pain (median)				
Spencer 2007	42.0	52.0	ns	6 months
	62.0	61.5	ns	2 years
General Health (median)				
Spencer 2007	65.0	67.0	ns	6 months
	67.0	64.5	ns	2 years
Vitality (median)				
Spencer 2007	50.0	50.0	ns	6 months
	56.3	50.0	ns	2 years
Social Functioning (median)				
Spencer 2007	75.0	75.0	ns	6 months
	75.0	87.5	ns	2 years
Role Emotional (median)				
Spencer 2007	66.7	83.3	.024	6 months
	87.5	83.3	ns	2 years
Mental Health (median)				
Spencer 2007	70.0	82.5	ns	6 months
	75.0	80.0	ns	2 years
Short Form 12 (mean)				
Physical				
Choong 2009†‡	42.5	37.5	ns	3 months
	46.6	44.9	ns	1 year
Mental				
Choong 2009†‡	58.4	60.0	ns	3 months
	57.6	57.3	ns	1 year
EuroQoL Questionnaire (median)				
Lützner 2010	70 (35–100)	65 (30–100)	ns	2 years

CONV-TKA:conventional total knee arthroplasty; CN-TKA: computer-navigated total knee arthroplasty; EuroQol: European Quality of Life questionnaire; NS: not statistically significant; SF-36: Short-form 36; SF-12: Short-form 12.
*Studies with statistically significant findings controlled for baseline data and possible confounding factors.
†The "n" for each group reflects a subset of patients with a mechanical axis within 3º of neutral.
‡Scores at 6 weeks and 6 months of follow-up are also available, see Appendix H.

Patient satisfaction, CN-TKA Efficacy(Table 8)

Two RCTs reported on patient satisfaction at 2 years follow-up. One study reported an average satisfaction score of 3.6 in both groups indicating that the majority of patients were either satisfied or very satisfied with the surgical outcome, regardless of the treatment type[51]. Likewise, in the second RCT, 86.7% and 83.3% of patients in the CN-TKA and the CONV-TKA groups, respectively, indicated they were very satisfied or somewhat satisfied with their TKA[148].

Table 8. Patient satisfaction in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value	Follow-up
PATIENT SATISFACTION				
*Ensini 2007** (mean ± sd)	3.6 ± 0.8	3.6 ± 0.6	ns	2 years
Spencer 2007† % (n/N)	86.7% (26/30 pts)	83.3% (25/30 pts)	ns	2 years

*Satisfaction was scored as: 1, dissatisfied; 2, barely satisfied; 3, satisfied; or 4, very satisfied.
†Percentage of patients who reported that they were very satisfied/somewhat satisfied with the result of their TKA.

Revision, CN-TKA Efficacy(Table 9)

Three studies reported the incidences of revision surgery following CN-TKA and CONV-TKA, however, none reported whether any differences between groups were significant. In one study, 3.7% and 8.0% of patients underwent revision surgery within 6 weeks following CN-TKA compared with CONV-TKA, respectively[46]. Another study compared postoperative outcomes between the treatment groups and reported revision rates of 1.4% and 0%, respectively[15]. In the third study, no patient in either group underwent a revision over a period of 2 years[148].

Table 9. Revision in RCTs comparing computer-navigated TKA with conventional TKA.

	CN-TKA	CONV-TKA	*P*-value	Follow-up
REVISION				
Bejek 2007(n/N)	1.4% (1/69 knees)	0% (0/69 knees)	NR	postop
*Decking 2007** (n/N)	3.7% (1/27 knees)	8.0% (2/25 knees)	NR	6 weeks
Spencer 2007(n/N)	0% (0/30 pts)	0% (0/30 pts)	NR	2 years

CN-TKA: computer-navigated total knee arthroplasty; CONV-TKA:conventional total knee arthroplasty.
*Decking 2005 also reported revision within 3 months of TKA; no further revisionsbetween the 6 weeks and 3 month follow-up.

ROM, CN-TKA Efficacy (Table 10)

Range of motion was reported by six RCTs[85,105,106,109,140,157]. No significant differences in total motion were found between groups across the five studies, either postoperatively

or at 2 years, with ROM ranging from 102º to 129º in the CN-TKA group and from 100º to 129º in the CONV-TKA group. At 1 year follow-up, one study reported significantly greater flexion followingCN-TKA (131.9º vs. 125.4º, respectively, $P = .001$)[138], while another found no difference between treatment groups[157]. No differences in both extension and extension lag, as reported by two separate RCTs[138,157], were seen at 1 year.

Table 10. Motion in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*	Follow-up
ROM				
Total Motion (mean, range)				
Martin 2009	113º (80º–150º)	109º (80º–130º)	ns	post-op
Martin 2007				3 months
MBK	102º (80º–130º)	100º (70º–140º)	ns	
LPS Flex Mobile	109º (70º–140º)	108º (75º–135º)	ns	
Seon 2009	129º (90º–145º)	129.º (100º–145º)	ns	post-op
Kim 2007	127º (0º–127º)	126º (-1º to 127º)	ns	2 years
Matziolis 2007	108º (70º–140º)	109º (100º–120º	ns	6 months
Flexion(mean, sd or range)				
van Strien 2009	116º (± 11.4º)	117º (± 12.6º)	ns	1 year
Seon 2005	132º (110º–140º)	125º (110º–140º)	.001	1 year
Extension(mean, sd)				
van Strien 2009	-1º (± 7.5º)	-3.4º (± 6.5º)	ns	1 year
Extension lag(mean, range)				
Seon 2005	1.2º (0º–10º)	2.0º (0º–15º)	ns	1 year

CONV-TKA: conventional total knee arthroplasty; CN-TKA: computer-navigated total knee arthroplasty; LPS: Legacy Posterior Stabilized Flex Mobile Prosthesis (NexGen); MBK: Mobile Bearing Knee Prosthesis (NexGen); NS: not statistically significant.
* Studies with statistically significant findings controlled for baseline data and possible confounding factors.

Radiographic Alignment, CN-TKA Efficacy

We identified six meta-analyses/systematic reviews[2-4,14,23,107] that evaluated radiographical outcomes following CN-TKA versus CONV-TKA. We report below in more detail the result of Bauwens et al. and the Medical Services Advisory Committee reports as two meta-analyses that include the most clinical trials.

Characteristics of Included Meta-analyses

BAUWENS (2007) META-ANALYSIS

Bauwens et al (2007)[14] assessed radiographic alignment and the risk of obtaining misalignment from the mechanical axis, which was defined by critical thresholds of >3° or > 2°. All studies published between January 1986 and January 2006 that compared computer-navigated imageless or CT-based TKA with CONV-TKA were included, regardless of patient diagnosis. A total of 33 studies (N = 3423), including 10 RCTs, eight quasi-RCTs (qRCTs), three prospective and seven retrospective cohorts, as well as five matched-pair studies, met these criteria and were selected for inclusion. Actual publication dates ranged from 2001 to 2006. All relevant studies evaluated primary TKA only. The mean (plus or minus standard deviation) patient age was 67.3 ± 4.1 years, and

62.6% of patients were female. The underlying condition was primary osteoarthritis in 83.7% of patients; one trial included only patients with rheumatoid arthritis. The mean deviance from the mechanical limb axis was 2.3° ± 5.1° at baseline. Demographics were similar between the CN-TKA (n =1707) and CONV-TKA (n = 1716) groups, with mean preoperative deviances from the axis of 2.4° ± 5.1 and 2.2° ± 5.3, respectively (P = .423). The authors concluded that although there was no publication bias, there was significant statistical heterogeneity across studies (P< .1) and random-effects modeling was therefore used. Imageless navigation was used in all but four studies, which employed CT-based imaging. Systems for navigation and implants used varied; most studies used the same implant for both groups, although three studies used different implants for computer-navigated versus CONV-TKA, and implant type was not specified in two studies. Although the authors stated that their primary goal was to assess outcomes from RCTs and that their secondary goal was to compare results from the RCTs with those from other studies (quasi-RCTs, cohort studies, and studies with a historical cohort), separation of results by study type was not done in the main text but was included in the supplemental material.

AUSTRALIAN HTA[4]

The Australian HTA evaluated mechanical axis alignment, deviation from the axis, and the odds of achieving satisfactory alignment. Imageless CN-TKA was compared with CONV-TKA. Comparative studies published in or after 1997 were included, and no limitations were placed on type of underlying condition. In sum, 43 comparative studies were included, consisting of 15 RCTs, 7 qRCTs, and 21 nonrandomized cohort studies.

Limb axis alignment, mean differences

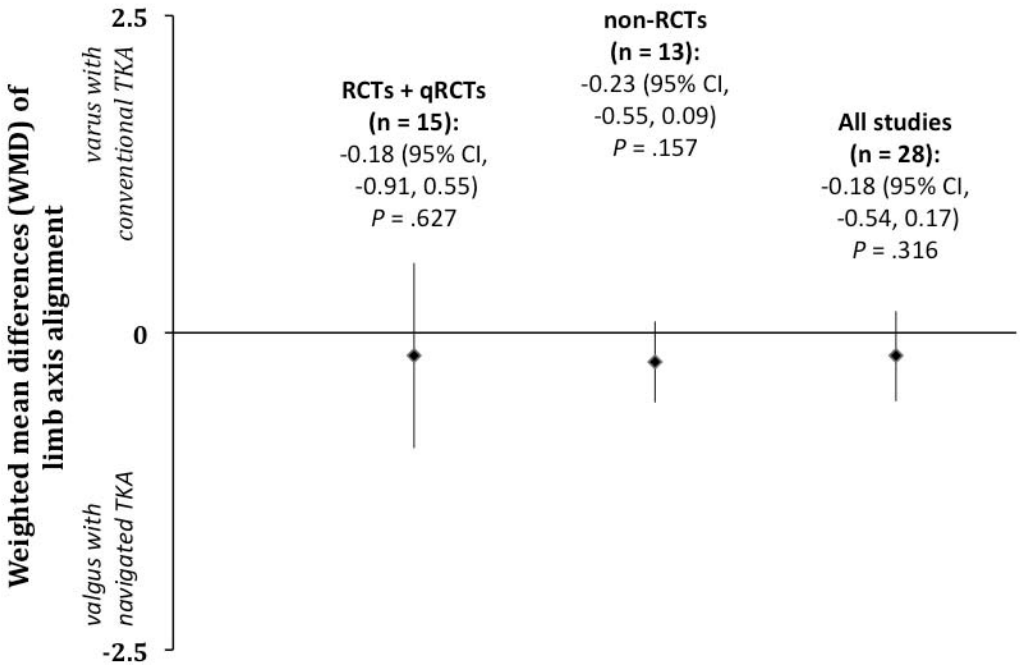
BAUWENS (2007)

Twenty-eight studies (eight RCTs, seven quasi-RCTs, three prospective and five retrospective cohorts, and 5 matched-pair studies) evaluated radiographic alignment of the mechanical limb axis following primary CN-TKA versus primary CONV-TKA. Alignment was measured on full-length radiographs with the patient in standing position.

Random-effects modeling of all 28 studies suggested that there was not a significant difference in the mean alignment achieved by CN-TKA (179.7°; 95% CI, 179.2°, 180.3°) compared with CONV-TKA (179.9°; 95% CI, 179.2°, 180.6°) with a weighted mean difference of -0.18° (95% CI, -0.54°, 0.17°; P = .316), Figure 2. There was significant heterogeneity between studies (P< .001), and the percentage of variance due to heterogeneity as opposed to chance (I^2) was 76.4%. Eight studies had significantly better alignment following navigated versus CONV-TKA, and three studies reported significantly better results following CONV-TKA.

Similar results were found when assessing data from 1) the RCTs plus the quasi-RCTs, and 2) non-RCT studies.

Figure 2. Limb axis alignment following CN-TKA or CONV-TKA: data from one meta-analysis (Bauwens, 2007).



AUSTRALIAN HTA

The mean of mean postoperative deformities was calculated using data from 16 studies (four RCTs, three quasi-RCTs, and nine cohort studies). Of these, five studies were also reported in the Bauwens study (2 RCTs and 3 cohort studies). The authors reported the mean of mean postoperative deformities and the pooled standard deviation. Statistical significance was not calculated. The mean of mean postoperative deformities from all 16 studies was slightly better following CN-TKA (n = 928) compared with CONV-TKA (n = 924) (0.79º ± 2.21º versus 0.90º ± 2.95º, respectively).

Data from the RCTs and quasiRCTs similarly suggested that CN-TKA (n = 314) yields slightly better postoperative deformities than CONV-TKA (n = 316) (1.10 ± 1.97 versus 1.33 ± 2.61, respectively). The authors did not report data from the non-random studies separately.

The mean deviation from the mechanical axiswas evaluated by fixed-effects modeling using data from eight studies (1 RCT, 1 qRCT, and 6 cohort studies). The mean difference in deviation was reduced by a mean of -0.74º (95% CI, -0.89º, -0.59º; $P<$ .0001) in patients treated with CN-TKA versus CONV-TKA. The studies were relatively homogenous (I^2 = 16%). CN-TKA yielded significantly lower mean deviations than CONV-TKA across all studies.

Limb axis alignment, satisfactory alignment (Figure 3)

BAUWENS (2007)

The risk of unsatisfactory alignment by more than 3º was evaluated using data from 22 studies (4 RCTs, 7 quasi-RCTs, 1 prospective and 6 retrospective cohorts, and 4 matched-pair studies). Patients who underwent primary CN-TKA had a significantly lower risk of misalignment by more than 3º than those who were treated with primary CONV-TKA, with a risk ratio of 0.78 (95% CI, 0.71, 0.87) (*P*< .001) and a risk difference of 19.2% (95% CI, 12.7%, 25.6%) (Figure 3a).Again, there was significant heterogeneity between studies (*P*< .001), and the percentage of variance across studies due to heterogeneity versus chance (I^2) was 92.1%. Of the 22 studies, 13 found significantly lower risk of misalignment with CN-TKA versus CONV-TKA, and the remaining 8 favored navigated TKA over CONV-TKA although the results were not statistically significant.

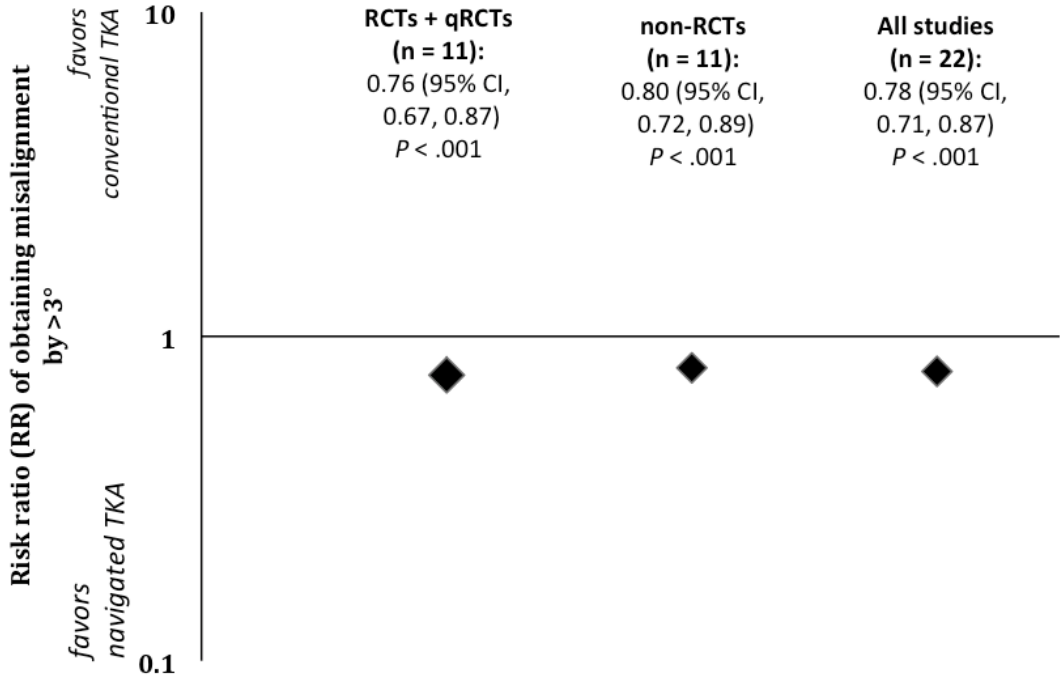
The risk of unsatisfactory alignment by more than 2º(Figure 3b) was calculated from 21 studies, 16 of which were similarly used to calculate the risk of deviance by more than 3º (above). The 21 studies included five RCTs, six quasi-RCTs, two prospective and five retrospective cohorts, as well as three matched-pair studies. Again, there was significantly lower risk of misalignment by more than 2º in patients treated with primary CN-TKA versus those who received primary CONV-TKA, with a risk ratio of 0.76 (95% CI, 0.71, 0.82) (*P*< .001) and a risk difference of 19.8% (95% CI, 15.2%, 24.4%). Significant heterogeneity between studies (*P* = .026) again prompted random-effects modeling, and there was an estimated 41.2% variance across studies due to heterogeneity rather than chance (I^2). Twelve of the studies reported significantly lower risk of more than 2º deviance from the straight axis in patients treated with CN-TKA rather than CONV-TKA; results from the remaining nine studies all favored CN-TKA over CONV-TKA although statistical significance was not achieved.

As the threshold of deviance from the straight axis increases (from 2º up to 6º), the benefits of CN-TKA over CONV-TKA decreases. The risk ratio (RR) in favor of CN-TKA versus CONV-TKA decreases with increasing thresholds of misalignment: 4º: RR = 0.87 (95% CI, 0.83 0.92); 5º: RR = 0.94 (95% CI, 0.91, 0.98); 6º: RR = 0.98 (95% CI, 0.96, 1.00).

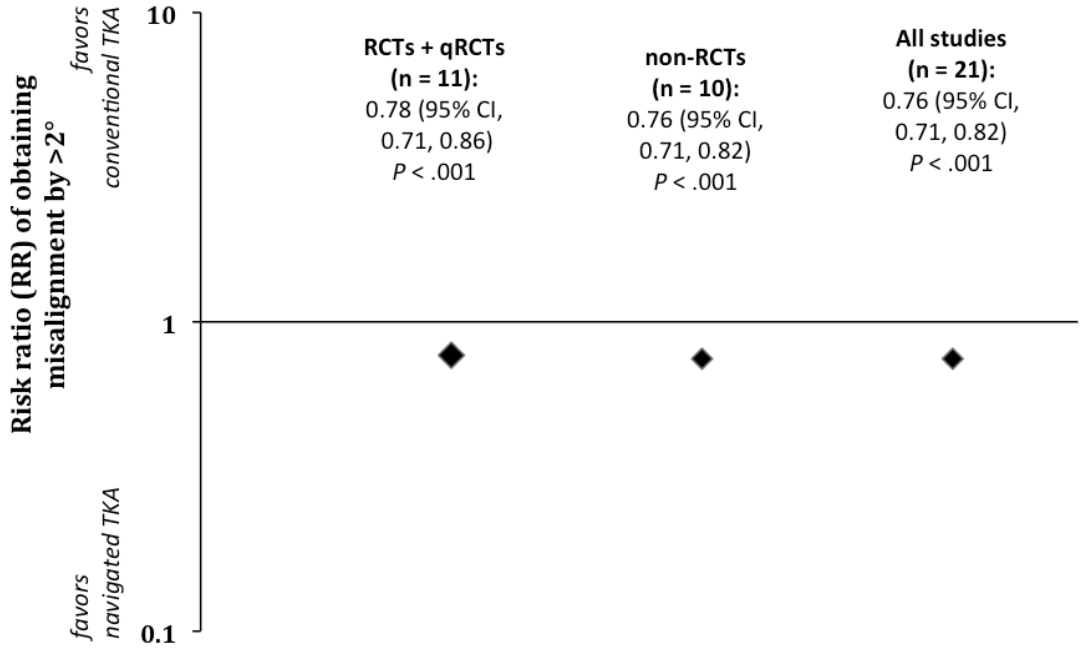
Similar results were found when assessing data from 1) RCTs and quasi-RCTs, and 2) non-RCT studies.

Figure 3. Risk of misalignment from the mechanical axis following CN-TKA or CONV-TKA: data from one meta-analysis (Bauwens, 2007).

a. Risk of misalignment by > 3°



b. Risk of misalignment by > 2°



AUSTRALIAN HTA

Overall results: Theodds of achieving satisfactory alignment (defined as ≤ 3º from the mechanical axis) was calculated using data from 25 studies (5 RCTs, 6 quasi-RCTs, and 14 cohort studies). Of these, 10 studies were also reported in the Bauwens study (1 RCT, 1 qRCT, and 8 cohort studies).

Random-effects modeling of all 25 studies suggested that patients treated with CN-TKA had 4.14 times higher odds of achieving satisfactory alignment risk than those treated with CONV-TKA (odds ratio (OR): 4.14 (95% CI, 3.03, 5.66); *P*< .00001). There was a moderate amount of heterogeneity between studies (I^2 = 58%). The significance of this result was reported in all 25 studies.

Similar results were found using random-effects modeling of only the RCTs and quasiRCTs (OR: 4.04 (95% CI, 2.37, 6.88); *P*< .00001); (I^2 = 57%).

Radiographic Alignment and Function, CN-TKA

The relationship between radiographic implant alignment and patient function following TKA is not entirely clear, though it is thought to be important[95]. In particular, some argue that a failure to correct lower limb coronal alignment to within 3º of the normal mechanical axis can lead to an increased rate of aseptic loosening[77,128,156]. We found one RCT that evaluated the clinical relevance of improved radiographic alignment in patients receiving CN-TKA or CONV-TKA.

Choong (2009) RCT

Choong et al (2009)[33] assessed whether improvements in the alignment of the mechanical axis in the coronal plane correlated with improvements in function and quality of life outcomes at one year following TKA. Cemented TKA was performed in 115 patients; patients were randomized to receive either CN-TKA (n = 60) or CONV-TKA (n = 55). The preoperative diagnosis of the 111 patients (97%) available for follow-up was osteoarthritis (93%) or rheumatoid arthritis (7%). The median age was 70 years (range, 45 to 89) and 60% of patients were female. Females comprised 70% of patients in the CN-TKA group but only 50% of those in the CONV-TKA group (*P* = .05); patient ages were similar in both groups. The median premechanical axis was -5.0 (range, -20.0 to 20.0) and the median BMI was 29.5 kg/m^2 (range, 17.4 to 47.7); there were no significant differences between groups in either of these baseline characteristics.

RADIOGRAPHIC ALIGNMENT

The authors reported significant improvements in the alignment of the mechanical axis in the coronal plane following CN-TKA compared with CONV-TKA: 88% (50/57) of patients in the CN-TKA group had an alignment within 3º of neutral, while only 61% (33/54) of those in the CONV-TKA group achieved the same outcome (*P* = .003). Similar results were found in a subpopulation of obese patients (BMI ≥ 30) (93% versus 56%, respectively; *P* = .003).

FUNCTIONAL AND QUALITY OF LIFE OUTCOMES: IKS, SF-12

Significant functional and quality of life improvements were found in patients who achieved radiographic alignment in the coronal plane within 3º of neutral, n = 83 (CN-TKA, n = 50; CONV-TKA, n=33) compared with those who did not achieve this outcome, n = 28 (CN-TKA, n = 7; CONV-TKA, n = 21), Table 11. Of the patients who achieved alignment within 3º of the axis, there were no differences in IKS or SF-12 scores between those who underwent CN-TKA versus CONV-TKA. These results suggest that alignment ≤3º of neutralfollowing TKA may correlate with improvements in patient function and quality of life compared with alignment >3º of neutral. However, the authors did not report whether there were any differences in the preoperative SF-12 and IKS scores between patients with postoperative alignment within versus more than 3º of the neutral axis; preoperative differences could potentially account for the results, since those with worse postoperative alignment may have had more severe disease preoperatively and could be expected to have worse postoperative outcomes.

Table 11. Summary of functional and quality of life outcomes by post operative alignment.

	Alignment		
	≤3º	>3º	*P*-value
FUNCTION AND QUALITY OF LIFE			
Knee Society Score (Knee)*			
3 month	89.0	75.0	<.001
6 months	92.0	79.0	<.001

12 months	93.5	78.0	<.001
Knee Society Score (Function)*			
3 month	70.0	50.0	.004
6 months	77.5	55.0	.030
12 months	80.0	60.0	.008
SF-12 physical			
3 month	40.25	33.43	.013
6 months	43.36	36.23	.003
12 months	45.94	35.59	.046
SF-12 mental			
3 month	58.27	55.71	.284
6 months	55.61	55.49	.718
12 months	57.62	46.96	.034

*Higher score equals better function

4.1.2. CN-TKA Effectiveness

Knee pain, CN-TKA Effectiveness (Table 12)

The percentage of patients still experiencing pain at 2 years was compared between those who received CN-TKA and CONV-TKA in one retrospective cohort[39]. No statistically significant difference was found between the two treatment groups: 12% versus 20%, respectively. Another retrospective cohort reported short term pain results (VAS) following CN-TKA and CONV-TKA. VAS pain scores were not significantly different between groups at postoperative day 1 or 2 (5.6 vs. 5.8 and 4.0 vs. 4.6, respectively)[27].

Table 12. Pain outcomes in nonrandomized studies comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value	Follow-up
PAIN MEASURE				
% experiencing pain				
Czurda 2010 (n/N)	12% (15/125)	20% (42/210)	ns	2 years
Visual analog scale				
Chaiyakit 2009 (mean ± sd)	5.6 (± 2.4)	5.8 (± 2.8)	ns	1 day
	4.0 (± 1.9)	4.6 (± 2.0)	ns	2 days

Knee Function, Patient Reported and Clinician Based, CN-TKA Effectiveness(Table 13)

Oxford Knee Score

One prospective[29] and one retrospective[80] cohort reported Oxford Knee Scores and found no statistically significant differences between the CN-TKA group and the CONV-TKA group at 6 months, 1, 3, and 5 years follow-up. Neither of the studies reported a significant difference in the preoperative scores between groups.

WOMAC

Two cohorts reported WOMAC total, pain, stiffness, and physical function scores. One prospective study reported a significant difference between the CN-TKA and the CONV-TKA groups, respectively, in total (36 vs. 43, $P < .001$), pain (6.8 vs. 8.6, $P < .001$), and function scores (25 vs. 31, $P = .004$) at 1 year[138]. Conversely, the second, retrospective cohort found no statistically significant differences in any WOMAC score between the CN-TKA and the CONV-TKA groupsat 2 years follow-up[98]. None of the studies reported a significant difference in the preoperative scores between groups.

Knee Society Score

Ten studies reported KSS Knee and Function scores including three prospective[20,31,83] and seven retrospective cohorts [27,50,80,98,108,114,153], with follow-up times ranging from 1 to 5 years. No statistically significant differences in either KSS score between CN-TKA and CONV-TKA groups were reported in any of the studies except for Ek et al. In that study, the CN-TKA group had a higher mean KSS score after 2 years; however, no baseline KSS scores were reported and there was no mention of accounting for any baseline differences.

Hospital for Special Surgery Knee Scale

One prospective study reported significant differences in total HSS scores between the CN-TKA and the CONV-TKA groups at 1 year (92.5 vs. 89.4, respectively; $P< .036$)[138].

Table 13. Functional outcomes in nonrandomized trials comparing CN-TKA with CONV-TKA.

Outcome	CN-TKA	CONV-TKA	*P*-value	Follow-up
PATIENT REPORTED KNEE SCORES				
Oxford Knee Score (mean, ± sd or range)				
Chang 2006	20.9 ± 1.1	22.1 ± 2.8	ns	6 months
*Kamat 2009**	24.4 (12–54)	25.8 (12–59)	ns	1 year
	25.7 (12–52)	24.5 (12–49)	ns	3 years
	26.9 (12–45)	25.2 (12–48)	ns	5 years
Western Ontario and McMasters OA index (median, range)				
Total Score				
Luring 2009†	16 (0–63)	16 (1–63)	ns	2 years
Seon 2005	36.1 (24–59)	42.8 (26–64)	.001	1 year
Pain Score				
Luring 2009†	4 (0–12)	2 (0–12)	ns	2 years
Seon 2005	6.8 (5–12)	8.6 (5–14)	.001	1 year
Stiffness Score				
Luring 2009†	2 (0–7)	2 (0–6)	ns	2 years
Seon 2005	3.5 (2–6)	4.0 (2–6)	ns	1 year
Physical Function Score				
Luring 2009†	10 (0–43)	12 (1–44)	ns	2 years
Seon 2005	25.0 (17–43)	30.9 (13–45)	.004	1 year
CLINICIAN BASED KNEE SCORES				
Knee Society Score (mean, ±sd or range)				
Knee Score				
Chaiyakit 2009	86 ± 13	89 ± 10	ns	1 year
Cheung 2009	91 (65–100)	89 (69–97)	ns	post-op
Kamat 2009	86.5	85.8	ns	3 years
Kim 2009†	92 (91–100)	93 (89–100)	ns	3 years
Luring 2009 (median)‡	90 (70–100)	90 (45–95)	ns	2 years
Bonutti 2008	91 (40–100)	93 (64–100)	ns	3 years
Ek 2008§	84 ± 15	77 ± 19	.05	2 years
Molfetta 2008	84 (73–91)	85 (70–91)	ns	5 years
Matsumoto 2006	85 (53–100)	90 (73–97)	ns	2 years
*Stulberg 2006***	83 ± 19	85 ± 18	ns	6 months
Function Score				
Chaiyakit 2009	72 ± 19	72 ± 20	ns	1 year
Cheung 2009	67 (45–100)	65 (15–100)	ns	post-op
Kamat 2009	72 ± 19	72 ± 20	ns	1 year
Kim 2009†	83 (69–100)	81 (69–100)	ns	3 years
Luring 2009 (median)‡	93 (60–100)	85 (NR)	ns	2 years
Ek 2008§	66 ± 27	58 ± 15	ns	2 years
Molfetta 2008	90 (78–92)	87 (78–90)	ns	5 years
Matsumoto 2006	94 (80–100)	96 (80–100)	ns	2 years
*Stulberg 2006***	64 ± 19	62 ± 16	ns	6 months
Pain Score				
Kim 2009†	42 (41–50)	43 (39–50)	ns	3 years
*Stulberg 2006***	37 ± 16	40 ± 11	ns	6 months
Deformity Score				
Kim 2009†	0.4 (0–2)	0.5 (0–5)	ns	3 years
Hospital for Special Surgery Knee Scale				

Total Score (mean, range)				
Seon 2005	92.5 (80–100)	89.4 (77–98)	.036	1 year

CONV-TKA = conventional total knee arthroplasty; CN-TKA = computer-navigated total knee arthroplasty; HSS = Hospital for Special Services; IKS = International Knee Society; KSS = Knee Society Score; NR = not reported; NS = not statistically significant; OKS = Oxford Knee Score; WOMAC = Western Ontario and McMaster Universities Index of Osteoarthritis.
*Follow-up data for 2 and 4 years are also available; see Appendix H.
†Patients underwent primary bilateral sequential TKAs and each patient had a TKA with use of computer-assisted surgical navigation in one knee and conventional technique in the other.
‡Scores estimated from box plot figures provided in original article.
§Reported in article as the International Knee Score (IKS).
**Follow-up data for 1 month is also available, see Appendix H.

Quality of Life, CN-TKA Effectiveness (Table 14)

SF-12, CN-TKA Effectiveness

One study reported general health and quality of life at 2 years follow-up using the SF-12[50]. A significant difference was reported between the CN- TKA group and the CONV-TKA group in the physical component score (41 vs. 37, respectively, *P* = .04) but not the mental component score (50 vs. 49, respectively).

Table 14. Quality of life in nonrandomized studies comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*	Follow-up
QUALITY OF LIFE				
Ek 2008				
SF-12, Physical	41 ± 9	37 ± 8	.04	2 years
SF-12, Mental	50 ± 11	49 ± 12	ns	2 years

CONV-TKA = CN-TKA = computer-navigated total knee arthroplasty; conventional total knee arthroplasty; NS = not statistically significant.
*Studies with statistically significant findings controlled for baseline data and possible confounding factors.

Revision, CN-TKA Effectiveness (Table 15)

Two studies reported similar, low rates of revision after both types of treatment at 3 years follow-up[20,80]. A prospective cohort reported incidences of revision surgery of 1.2% in both the CN-TKA and CONV-TKA groups. One retrospective cohort reported rates of 0.4% and 0.3%, respectively, both involving only resurfacing of a previously unsurfaced patella.

Table 15. Revision rates in nonrandomized studies comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value	Follow-up
REVISION				
Kamat 2009	0.4% (1/263 knees)	0.3% (1/302 knees)	ns	3 years
Bonutti 2008	1.2% (1/81 knees)	1.2% (1/81 knees)	ns	3 years

ROM, CN-TKA Effectiveness(Table 16)

Total motion was reported by three prospective cohorts and three retrospective cohorts. A significant difference between the CN-TKA and the CONV-TKA groups was reported by one prospective study postoperatively[31]and one retrospective study at 2 years[108]: 100º versus 94º and 113º versus 106º, respectively[108](*P* = .04 and .01, respectively). However, no significant differences were seen in the other four studies that reported total ROM over follow-up periods ranging from 6 months to 5 years. Flexion was reported by one prospective[138]and two retrospective cohorts[27,98]. Significant differences between CN-TKA and CONV-TKA were reported by one retrospective cohort at both 3 months (102.3º vs. 111.2º, respectively; *P*< .05) and 1 year (103.8º vs.107.7º, respectively; *P*< .05), with restricted flexion in the CN-TKA group compared with the CONV-TKA group[27]. Conversely, significantly greater flexion at 1 year was reported following CN-TKA versus CONV-TKA in one prospective study (131.9º vs. 125.4º, respectively, *P* = .001)[138]. No differences in extension lag, as reported by on prospective study, were seen at 1 year[138].

Table 16. ROM in nonrandomized studies comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*	Follow-up
ROM				
Total motion (mean, range)				
Cheung 2009	100º (55º–130º)	94º (70º–125º)	.04	post-op
Kim 2009†	123º (115º–145º)	126º (100º–145º)	ns	3 years
Bonutti 2008	114º (90º–120º)	117º (95º–120º)	ns	3 years
Molfetta 2008	97º (85º–110º)	96º (88º–105º)	ns	5 years
Matsumoto 2006	113º (85º–130º)	106º (50º–125º)	.01	2 years
Stulberg 2006‡	117º (105º–135º)	116º (100º–135º)	ns	6 months
Flexion (mean, ± sd or range)				
Chaiyakit 2009§	102.3º ± 13.1º	111.2º ± 11.3º	< .05	3 months
	103.8º ± 12.9º	107.7º ± 8.1º	< .05	1 year
Luring 2009	113º ± 12.91º	108º ± 13.73º	ns	2 years
Seon 2005	132º (110º–140º)	125º (110º–140º)	.001	1 year
Extension lag (mean , range)				
Seon 2005	1.2º (0º–10º)	2.0º (0º–15º)	ns	1 year

CN-TKA = computer-navigated total knee arthroplasty;CONV-TKA = conventional total knee arthroplasty; NS = not statistically significant; ROM = range of motion.
*Cheung 2009 controlled for baseline data and possible confounding factors; Chaiyakit did not.
†Patients underwent primary bilateral sequential TKAs and each patient had a TKA with use of computer-assisted surgical navigation in one knee and conventional technique in the other.
‡Follow-up data for 1 month is also available; see Appendix H.
§Follow-up data for 1 and 6 months are also available; see Appendix H.

4.2. Key Question 2

What is the evidence of efficacy and effectiveness of partial knee arthroplasty compared with conventional TKA?

For key question 2, we identified only one RCT[117] and 19 cohort studies[6,9,26,42,54,56,59,64,71,74,86,89,94,110,134,135,161,164,170] that reported data on clinical or functional outcomes following UKA compared with TKA. For the comparison between UKA and HTO, two RCTs (3 publications)[21,153,166] and two cohort studies (3 publications)[25,75,165] were found that reported on clinical results. No RCTs were found for either the bi-UKA versus TKA or the bicompartmental TKA versus tricompartmental TKA comparisons; one retrospective, matched-pairs cohort study was identified which compared clinical outcomes in patients undergoing bi-UKA versus TKA[37] and two registry studies were found which reported outcomes following bicompartmental compared with tricompartmental TKA[56,91]

4.2.1. UKA versus TKA, Efficacy

Knee Function, UKA versus TKA Efficacy (Table 17)

Bristol knee scores, UKA Efficacy
In the one RCT[117] comparing UKA with TKA, the mean Bristol Knee Score was similar between the UKA and TKA groups 5 and 15 years following surgery: 91.1 (range, 32 to 100) and 92 (range 32 to 100) compared with 86.7 (range 48 to 98) and 88 (range 48 to 98). A larger percentage of the UKA group reported excellent Bristol scores at 5 and 15 year follow up (76% and 71% respectively) than in the TKA group (57% and 53%, respectively), though this did not reach statistical significance.

Revision or Failure, UKA versus TKA (Table 17)

Revision rate, UKA Efficacy
At the 15 year follow up, there were no statistically significant differences in revision. Thirteen percent of the UKA group and 16% of the TKA group had experienced revision.

Survival rate, UKA Efficacy
There was no statistically significant differences in survival rate at 15 year follow up: 89.8% (95% CI, 74.3-100) for the UKA group and 78.7% (95% CI, 56.2-100) for the TKA group ($P > .05$).

Failure rate, UKA Efficacy
Statistically significant differences in failure rate defined as revision or a Bristol Knee Score <60 were not reported; however, at 15 year follow up, 17% of the UKA group and 24% of the TKA group had experienced failure.

Range of motion, UKA Efficacy (Table 17)

At five year follow up, a significantly greater percentage of the UKA group achieved ≥ 120° flexion than the TKA group (69% versus 17%, respectively, *P*< .01.)

Table 17. Outcomes in one randomized controlled trial comparing UKA with TKA (Newman 1998, 2009).

	UKA	TKA	*P*-value	Follow-up
OUTCOME				
Knee scores				
Bristol Knee Score (mean)	91.1 (32–100)	86.7 (48–98)	ns	5 years
	92 (32–100)	88 (48–98)	ns	15 years
BKS Excellent results, % (n/N)	76 (34/45)	57 (26/46)	ns	5 years
	71 (15/21)	53 (10/19)	ns	15 years
BKS pain score, Excellent results, % (n/N)	89 (40/45)	83 (38/46)	ns	5 years
Range of Motion				
≥ 120 flexion, % (n/N)	69 (31/45)	17 (8/46)	< .01	5 years
Revision/Survival				
Revision, % (n/N)	13% (3/23)	16% (4/25)	ns	15 years
Survival (end point: failure*), % (n/N)	89.8%	78.7%	ns	15 years
Failure rate*				
Failure rate, % (n/N)	17% (4/24)	26% (6/23)	ns	15 years

*revision or Bristol Knee Score <60.

4.2.2. UKA versus TKA, Effectiveness

Pain, UKA vs. TKA Effectiveness (Table 18)
A slightly lower proportion of patients receiving UKA reported >20 out of 40 pain points on the Bristol knee score compared with TKA in one study after 6 years of follow-up (91% in the UKA group, 96% in the TKA group, *P*< .05)[6]. In one study patients received a UKA in one knee and TKA in the contralateral knee on the same hospital admission[89]. After nearly 7 years, a higher proportion of patients reported no or slight pain in the UKA group (96%) compared with the TKA group (83%), though this did not reach statistical significance. One other study reported a non statistical difference in pain measured on a 10 point scale at a mean follow up of nearly 7 years[135].

Knee Function, UKA vs. TKA Effectiveness (Table 18)
Several studies assessed function using a patient reported or clinician based outcomes measure. In general, scores between the UKA and TKA groups were similar after 6 months[74], 1 year[26,69,110,170], 2 to 4 years[42,94,164] and 5 to 6 years[6,9,135] following surgery. One study reported a statistical difference between total patient reported Oxford Knee Scores after more than a year follow up in favor of the UKA, 22.2 versus 24.5, *P* = .04[161]. However, differences in baseline scores were not obtained and these scores are not adjusted.

Patient satisfaction, UKA vs. TKA Effectiveness (Table 18)

Patients were slightly more satisfied with their surgery following UKA in one study after a mean of two years (88%, UKA; 80%, TKA), however this did not reach statistical significance[69]. In one study of bilateral knee replacement where one knee is UKA and the other TKA, Laurencin[89] reports that a higher proportion of patients preferred the UKA knee to the TKA knee (44% versus 12%) after a mean of 7 years.

Revision and Prosthesis Survival, UKA vs. TKA Effectiveness (Table 18)
Rates of revision were slightly higher in the UKA group in eight[6,9,26,56,89,94,132,164] of nine[135] studies reporting a mean follow up between 2 and 10 years, though only two were statistically significant. The range of revision in the UKA group was from 4% to 15%, while the range in the TKA group was 0% to 11%. Long term survival rates with revision surgery as the endpoint favored the TKA over the UKA group in 2 large studies. Gioe et al report 10 year survival for UKA of 88.6% versus TKA of 94.8%[59], and a 14 year survival of 67.7% for UKA versus 84.5% for TKA, $P = .002$[60]. Koskinen et al report a similar survival relationship at 10 years (73% for UKA compared with 90% for TKA) and 15 years (60% for UKA compared with 80% for TKA), $P < .01$[86].

Range of motion, UKA vs. TKA Effectiveness
Of the cohort studies that found significant differences in the range of motion between the UKA group and the TKA group, all found that the UKA group had a higher, statistically significant, range of motion. In the study by Ackroyd et al., the UKA group had a range of motion measured in mean degrees of 109.3 ± 14 while the TKA group had a mean range of motion of 99.9 ± 18 ($P< .01$) at last follow up. The same study also found a greater percentage of the UKA group versus the TKA group achieving ≥ 90 degrees ROM at last follow up, 94% versus 84% respectively ($P< .05$). Dalury et al found a significantly higher flexion (measured in mean degrees) in the UKA group versus the TKA group, 123 ± 9 versus 119.8 ± 7, respectively ($P< .05$), at last follow up. Lombardi et al also found a significantly higher range of motion (measured in mean degrees) in the UKA group versus the TKA group, 120 ± 7.8 (85-135) versus 115 ± 11.4 (70–140), respectively ($P< .01$), at last follow up. McAllister et al found significantly greater level of flexion, measured in mean degrees, in the UKA group versus the TKA group at several follow up time points. At 6 weeks follow up, flexion was 118 versus 107 in UKA versus TKA, respectively ($P< .05$); at 12 weeks follow up, flexion was 125 versus 117 in UKA versus TKA, respectively ($P< .05$); at 24 weeks follow up, flexion was 127 versus 122 in UKA versus TKA, respectively ($P< .05$); and at 52 weeks follow up, flexion was 128 versus 122 in UKA versus TKA, respectively ($P< .05$). Rougraff et al also found a significantly higher ROM in the UKA group versus TKA group: 113 (75–142) versus 98 (65–135), respectively ($P< .01$), at last follow up. Finally, Yang et al found a significantly shorter time to achieve 90 degree flexion in days, in the UKA group versus the TKA group (3.6 ± 1.1 (2–7) versus 6.9 ± 2.5 (3–18), respectively, $P< .01$). The same study also found a significantly higher level of flexion in the UKA group (122 ± 14 (107–148)) versus the TKA group (108 ± 17 (92–139)), $P< .01$.

Employment, UKA vs. TKA Effectiveness (Table 18)

Foote et al[54] examined outcomes surrounding employment and found similar proportions of patients in each group returning to work (82% in each group) and at similar times following surgery (median of 11 months for the UKA group and 12 months for the TKA group).

Table 18. Outcomes in cohort studies comparing UKA with TKA.

	UKA	TKA	*P*-value	Follow-up
PAIN				
Total pain score > 20 points on the Bristol pain score (out of 40)-				
Ackroyd 2002	91%	96%	< .05*	5.7 ± 3.6 years
No pain or slight pain (n/N)			ns	
Laurencin 1991	96%	83%	ns	6.8 years
Pain 10 score (mean, range)				
Rougraff 1991	0.8 (0-10)	1.9 (0-10)	ns	6 years (0.2–15)
PATIENT REPORTED KNEE SCORES				
Oxford Knee Score				
Total Score (mean±sd)				
Hopper 2008	17.9	21.6	ns	1 year
Isaac 2007	38.2 ± 2.63	35.5 ± 3.15	ns	.5 year
Lombardi 2009	5.4 ± 5.6	4.3 ± 5.8	ns	2.5 years (0.14.3)
Walton 2006	22.17 ± 9.03	24.5 ±9.68	< .05*	≥1 year
Weale 2001	36.5 ± 10.0	36.5 ±11.0	ns	2.3 ± 1 years
Kneeling Ability Improved				
Hassaballa 2007	55%	41%	NR	1 year
Stairs Easily or with Little Difficulty (%)				
Hassaballa 2007	86%	73%	NR	1 year
Western Ontario McMasters OA Index				
Pain Score (mean, ±sd)				
Wylde 2008	81.6 ± 19.3	81.5 ± 20.8	NR	NR
Pain Score (mean, ±sd)				
Wylde 2008	79.1 ± 20.5	76.3 ± 21.4	NR	NR
CLINICIAN BASED KNEE SCORES				
Knee Society Score				
Knee Score (mean, range)				
Amin 2006	82	84	ns	5 years (0.6–6)
Dalury 2009	89.7 (87–99)	90.3 (87–98)	ns	3.7 years (0.5-12)
Lombardi 2009	92 (48–100)	90 (40–100)	ns	2.5 years (0.1-4.3)
McAllister 2008	99.5	96.25	NR	1 year
Rougraff 1991	90 (76–100)	85 (47–100)	<.01*	6 years (0.2–15)
Function score (mean, range)				
Amin 2006	85	84		5 years (0.6–6)
Dalury 2009	87 (68.6–100)	87.8 (80–100)	ns	3.7 years (0.5-12)
Lombardi 2009	80 (20–100)	76 (20–100)	ns	2.5 years (0.1-4.3)
McAllister 2008	100	96	ns	1 year
Hospital for Special Surgery Knee Scale				
Excellent or Good Results (n/N)				
Cameron 1988	55% (12/20)	35% (7/20)	ns	0.25 year
	80% (16/20)	90% (18/20)	ns	1 year
Bristol Knee Score				
Excellent or Good Results (n/N)				
Ackroyd 2002	78% (318/408)	75% (398/531)	NR	5.7 ± 3.6 years
PATIENT SATISFACTION				
Satisfied or very satisfied (%)				
Hopper 2008	88.2%	80.3%	ns	1.8 years (1–3.5)
Better of the two knees† *(%)*				
Laurencin 1991	44%	12%	ns	6.8 years
Patient satisfaction (%)				

Table 18. Outcomes in cohort studies comparing UKA with TKA.

	UKA	TKA	*P*-value	Follow-up
Rougraff 1991	93%	93%	ns	6 years (0.2–15)
REVISION/SURVIVAL RATE				
Revision rate (%, n/N)				
Ackroyd 2002	6.1% (25/408)	3.8% (20/531)	NR	5.7 ± 3.6 years
Amin 2006	14.6% (6/54)	0% (0/54)	NR	5 years (1–6)
Cameron 1988	15% (3/21)	0% (0/21)	NR	3 years (2–7)
Furnes 2002	8.9% (82/2288)	6.3% (52/3032)	< .01	10 years
Laurencin 1991	4% (1/24)	0% (0/24)	NR	6.8 years
Lombardi 2009	6% (7/115)	3% (3/115)	NR	2.5 years (0.14.3)
Robertsson 1999	7% (752/10,624)	3.7% (568/15,437)	< .01	NR
Rougraff 1991	4.2% (5/120)	11.1% (9/81)	ns	6 years (0.2–15)
Weale 2001	9% (2/31)	1% (1/130)	NR	2.3 ± 1 years
Cumulative revision rate (%)				
Robertsson 1999‡	15.8%	11.5%	< .01	10 years
	19.2%	17.2%	ns	15 years
Survival rate (%, 95% CI) (end point: revision)				
Ackroyd 2002	87.5 (82.5–92.6)	89.6 (71.8–86.9)	ns	5.7 ± 3.6 years
Amin 2006	88 (79–97)	100 (100)	< .05	5 years (0.6-6)
Gioe 2003	92.6 (90.0–95.2)	97.9 (97.4–98.4)	NR	5 years
	88.6 (85.0–92.2)	94.8 (93.5–96.0)	NR	10 years
Gioe 2007	67.7 (49.3–86.1)	84.5 (75.3–93.7)	.002	14 years
Koskinen 2008	73 (70–76)	90 (89–90)	< .01	10 years
	60 (54–66)	80 (79–81)	< .01	15 years
Survival rate (%, 95% CI) (end point: revision& pain)				
Ackroyd 2002	79.4 (73.2–85.6)	79.4 (71.8–86.9)	ns	5.7 ± 3.6 years
Amin 2006	92 (75–95)	100 (100)	< .05	5 years (0.6–6)
Survival rate (%, 95% CI)(end point: worst case)				
Ackroyd 2002	74.2 (67.8–80.7)	74.7 (67.0–82.5)	ns	5.7 ± 3.6 years
Amin 2006	85 (75–95)	98 (94–100)	< .05	5 years (0.6–6)
Survival rate (%, 95% CI) (end point: asceptic loosening)				
Rougraff 1991	99.1 ± 4	97.4 ± 0.03	NR	5 years
	99.6 ± 4	65.3 ± 12	NR	10 years
Survival rate (%, 95% CI) (end point: unspecified)				
Furnes 2002	80.1 (76.0–84.2)	92.0 (90.4–93.6)	ns	10 years
EMPLOYMENT				
Employed following surgery (%)				
Foote 2010	61.3%	56.1%	ns	3 years (1.1–5)
Median time to return to work (months)				
Foote 2010	11 (0–24)	12 (4–52)	ns	3 years (1.1–5)
Return to work (mean weeks)				
Lombardi 2009	8.2 ± 6.2 (1-32)	8.0 ± 5.6 (0-32)	ns	2.5 years (0.14.3)

*This score was not adjusted for pre-operative values, which were not provided.
†All patients received UKA on one knee and a TKA on the contralateral knee.
‡10 year follow-up on patients operated on during 1986-1995; 15 year follow-up on patients operated during 1980-1995.

4.2.3. UKA versus HTO, Efficacy

Knee pain, UKA vs. HTO Efficacy (Table 19)
One RCT (Weidenhielm /Borjesson) reported pain using the Borg scale (0–10 scale, 10 indicates worst pain imaginable) following 4 minutes of walking at a comfortable free walking speed. There was no significant difference in pain scores between the HTO (mean 1.0, median 0) and UKA groups (mean 0.5, median 0) at 1- and 5-year follow-up, respectively.

Knee function, UKA vs. HTO Efficacy (Table 19)
Two clinician based outcomes measures were used to assess knee function, the Knee Society Score (KSS) and the British Orthopaedic Association (BOA) Knee Score. No significant differences were identified in KSS or BOA scores between HTO and UKA treatment groups at any follow-up period (2–5 year, 4–7 year or 7–10 year follow-up, KSS; one and five year follow-up, BOA) as reported in two RCTs.

- Using the KSS, Stukenborg-Colsman[153] reported in one RCT that the mean knee and function scores were 76 and 71 for the HTO group and 74 and 59 for the UKA group, respectively, after 7–10 years. The Knee Society scoring system (the lower the score, the greater the disability) has separate knee and function scores. In the same study, 71% and 67% of the patients in the HTO group reported excellent or good knee and knee function scores, respectively, compared with 65% and 50% of the UKA patients, but this difference was not tested statistically.

- In another RCT[166], the knee scores were not statistically different for the HTO group (mean 38, median 37) compared with the UKA group (mean 37, median 37) after 1- and 5-year follow-up, respectively. This study used the British Orthopaedic Association kneefunctional assessment (the lower the score, the greater the disability), which includes functional and pain scores.

Failure and revision, UKA vs. HTO Efficacy (Table 19)
Two RCTs reported revisions after HTO and UKA. One RCT[153] reported 31.3% revisions after HTO and 20% revisions after UKA,RR 0.64; 95% CI 0.27,1.54[61]. The same study also reported Kaplan-Meier knee survival with revision as the predictive event. Knee survival at 5- and 10-year follow-up, respectively, was not statistically different between the UKA (82%, 77%) and HTO (78%, 60%). The other RCT[21,166] reported one case of revision in the UKA group and none in the HTO group.

Range of motion, UKA vs. HTO Efficacy
Two RCTs reported postoperative range of motion (ROM) for HTO and UKA. In one study[153], total mean ROM after –10 years follow-up was 117° for the HTO group and 103° for the UKA group, but this difference was not tested statistically. In another RCT[166], there was no significant difference in flexion contracture/flexion arc between the HTO group (mean 1°/121°, median -2°/121°) and UKA group (mean 4°/119°, median 2°/121°) at one and five-year follow-up, respectively.

Table 19. Efficacy outcomes comparing UKA with HTO.

Outcome	UKA	HTO	*P*-value	Follow-up
PAIN				
Pain During Walking(Borg Scale)				
Weidenhielm 1993(mean, sd)	0.5±0.9	1.0±1.4	ns	1 year
Borjesson 2005 (median, range)	0 (0–2)	0 (0–2)	ns	5 years
CLINICIAN BASED KNEE SCORES				
Knee Society Score				
Stukenborg-Colsman 2001				
Knee Score (mean, range)	74 (31–94)	76 (29–100)	ns	7.5 years
Function Score (mean)	59 (0-100)	71 (0-100)	ns	7.5 years
Excellent or Good Results,Knee (%, n/N)	65% (13/20)	71% (15/21)	NR	7.5 years
Excellent or Good Results, Function (%)	50% (10/20)	67% (14/21)	NR	7.5 years
British Orthopaedic Association Knee Score				
Weidenhielm 1993(mean)	37±2	38±2	ns	1 year
Borjesson 2005 (median, range)	37 (31–39)	37 (36–39)	ns	5 years
REVISION/SURVIVAL				
Revision (%, n/N)*				
Stukenborg-Colsman 2001	20% (6/30)	31.3% (10/32)	NR	
Weidenhielm 1993	2.8% (1/36)	0% (0/23)	NR	0.5 years
Survival (end point: revision)				
Stukenborg-Colsman 2001	82%	78%	ns	5 years
	77%	60%	ns	10 years

*denominator = number of knees.
NR: Not Reported; ns: not significant.

Summary, Efficacy UKA vs. HTO

In the two RCTs providing data on the efficacy of HTO compared with UKA, there were no significant differences in knee pain, knee function, failure or revision, or ROM between the groups.

4.2.4. UKA versus HTO, Effectiveness

Knee pain, UKA vs. HTO Effectiveness (Table 20)

One cohort study (2 publications) reported a significant difference in postoperative pain between the two treatment groups. In this study[25,165], a higher percentage of the UKA group (66.7%) reported no pain at the 5–10 year follow-up compared with the HTO group (25.6%, *P*< .001) using the Baily (Bristol) Knee pain score (a subset of the Baily knee score; 0–15 scale, lower score indicates more pain). The same study found that 40%

of the UKA group reported no pain at the 12–17 year follow-up compared with 4.8% of the HTO group, but this difference was not tested statistically.

Knee function, UKA vs. HTO Effectiveness (Table 20)

One cohort study (2 publications) reported on knee function using the Baily (Bristol) Knee Score[25,165]. After 5–10 year and 12–17 year follow-up, respectively, mean knee scores were 35 and 31 for HTO patients and 42 and 34 for UKA, but these differences were not significant at the first follow-up and were not tested statistically at the second follow-up.The UKA group had a significantly higher percentage of patients reporting excellent or good results (76.2%) compared with the HTO group (42.9%, *P*< .01).

Failure and revision UKA vs. HTO Effectiveness (Table 20)

One cohort study (2 publications)[25,165] reported revisions after HTO and UKA, but the differences between the treatment groups were not tested statistically. The HTO group had 14.3% and 24.3% revisions at a 5–10 year and 12–17 year follow-up, respectively, compared with the UKA group (5.8%, 9.6% revisions). This study also reported a mean time to revision of 4.4 years for the HTO compared with 2.6 years for the UKA group, but this difference was not tested statistically.

Range of motion UKA vs. HTO Effectiveness

No significant differences were found in ROM in one non-randomized study[76]. At a six-month follow-up, the HTO group had a greater ROM (121°) compared with the UKA group (112°).

Table 20. Effectiveness outcomes comparing UKAwith HTO.

Outcome	UKA	HTO	*P*-value	Follow-up
Knee scores				
Weale 1994				
Baily Knee Score (mean)	42	35	ns	5–10 years
	34	31	NR	12–17 years
Baily excellent orgood (%)	76.2% (32/42)	42.9% (21/49)	< .01	5–10 years
Ivarsson 1991				
Lysholm Score (mean)	47±14	61±18	NR	pre-op
	91±11	NR	NR	6 months
	NR	78±19	NR	1 year
Lysholmexcellent or good (%)	80% (8/10 pts)	NR	NR	6 months
	NR	40% (4/10 pts)	NR	1 year
Pain during walking				
Broughton 1986				
Baily no pain	66.7% (26/39)	25.6% (10/39)	< .001	5–10 years
	40% (6/15)	4.8% (1/21)	NR	12–17 years
Ivarsson 1991				
100-mm analogous scale (mean)	38±23	33±28	ns	pre-op
	4.1±2.9	NR	ns	6 months
	NR	6.3±2.1	ns	1 year
Revision/Survival				

Weale 1994				
Revision	5.8% (3/52)	14.3% (10/70)	NR	5–10 years
	9.6% (5/52)	24.3% (17/70)	NR	12–17 years
Average time to revision	2.6 years (0.25–4.5)	4.4 years (0.5–6)	NR	

NR: Not Reported; ns: not significant

4.2.5. Bi-UKA versus TKA, Effectiveness

There were no RCTs comparing Bi-UKA with TKA. One retrospective, matched-pairs cohort study made the comparison and is summarized here[37].

Population characteristics
In the study comparing bi-UKA with TKA, the primary reason for surgery was medial and lateral compartment knee arthritis. The study population was comprised of a total of 44 patients (22 in each group), mean age 60 years (range, 48–68), and 36% male, with a minimum follow-up of 4 years.

Revision and Survival
No revisions were reported in either the bi-UKA or TKA groups after 4 years of follow-up.

Functional knee scores
Preoperative scores between the two groups were similar.

Western Ontario and McMaster Universities Osteoarthritis Index
No significant difference between the bi-UKA and TKA groups was reported for the pain score. However, significantly better scores were reported in the bi-UKA group compared with the TKA group for stiffness (1.5 vs. 2.3, respectively, $P = .009$) and function (7.8 vs. 9.2, respectively, $P = .045$).

Knee Society Score
No significant differences between groups were reported in the KSS Knee or Function scores at latest follow-up.

Italian Orthopaedic UKR Users Group (GIUM) score
No significant differences between groups were reported in GIUM score and no poor or abnormal results were seen in either group.

Radiographic and motion outcomes
There were no statistically significant differences in preoperative hip-knee-ankle (HKA) angle and flexion between the two groups. However, at final follow-up, the mean HTA angle was lower in the bi-UKA than the TKA group, 176.8º versus 179.4º, respectively, $P < .00008$ and range of motion greater than 120º was reported on all patients following bi-UKA compared to only 15 (68%) following TKA, $P = .009$.

Operative data
No differences in surgical times between the bi-UKA and TKA groups were reported, however hospital stay was longer following bi-UKA compared with TKA, 6.3 versus 7.9 days, *P*< .007. In both groups, 36% of patients required blood transfusions postoperatively.

4.2.6. Bicompartmentalversus tricompartment TKA, Effectiveness

There were no RCTs comparing bicompartmental TKAwithtricompartmental TKA. Two registry studies made the comparison and are summarized here.

Population characteristics
For the two studies comparing bi- versus tri-compartmental TKA, one study had a total of 7137 (bi: n = 4653; tri: n = 2484) patients, mean age 70 years, 26% male; and the other reported a total of 16,067 (bi: n = 10,928; tri: n = 5139) patients with no further demographic data given. Follow-up ranged from 1–6 years.

Revision and Survival, Bicompartmental vs. TKA, Effectiveness (Table 21)
The two registry studies reported low revision rates in both the bi- and tri-compartmental groups: 1.5% and 1.6% at 2 years follow-up and 3.2% and 2.8%, respectively, at 2 to 4 years follow-up. No significant differences in overall revision rates between the two treatment groups were reported by either study. Furthermore, one registry study looked at the 5-year survival between bi- and tri-compartmental TKA using cemented, hybrid, or uncemented methods of fixation, and found no statistically significant difference between any of the comparisons[56]. However, when this same study considered the reason for revision, pain accounted for a 5.7 times higher risk (RR = 5.7, 95% CI, 2.7–12; *P*< .001) of revision following bi- versus tri-compartmental TKA. Conversely, the risk of revision because of infection was lower in the bi- versus tri-compartmental group (RR = 0.41, 95% CI, 0.18–0.93; *P* = .03).

Table 21. Revision and survival comparing bicomparmental with tricompartmental TKA.

	Bicompartmental TKA	TricompartmentalTKA	*P*-value	Follow-up
REVISION (%, n/N)				
Furnes 2002	3.2% (145/4585 knees)	2.8% (68/2439 knees)	ns	2–4 years
Lindstand 2001	1.5% (168/10,928 knees)	1.6% (82/5139 knees	ns	2 years
SURVIVAL (95% CI)				
Furnes 2002				
Cemented	93.8% (92.6%–95.1%); RR = 1.3 (0.90–1.7)	95.9% (94.7%–97.0%); Referent	ns	2–4 years
Hybrid	94.0% (90.7%–97.3%); RR = 1.2 (0.70–2.2)	98.5% (96.8%–100%); RR = 0.47 (0.15–1.5)	ns	2–4 years
Uncemented	96.7% (93.1%–100%); RR = 0.93 (0.28–3.0)	88.3% (80.1%–96.4%); RR = 2.2 (0.91–5.3)	ns	2–4 years

4.3. Key Question 3

What is the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty?

A total of 25 RCTs and 14 nonrandomized studies (seven prospective and seven retrospective) were identified that reported safety outcomes in patients following CN-TKA compared with CONV-TKA.

4.3.1. CN-TKA versus CONV-TKA, Safety

Thromboembolism, CN-TKA vs. TKA (Tables 22, 23, 24)

Deep vein thrombosis (DVT)
Six RCTs[15,30,33,35,100,147] and two prospective cohorts[20,29]reported the incidence of DVT following CN-TKA and CONV-TKA. No statistically significant differences were reported in any of the studies with events ranging from 0% to 8% of patients in the CN-TKA groups compared with 0% to 10% of patients in the CONV-TKA groups. Of these eight studies, one RCT[35] and one prospective cohort[29] reported no occurrences of DVT in either group.

Pulmonary embolism (PE)
Four RCTs[30,33,35,167] and two cohort studies, one prospective[29] and oneretrospective[27], reported the incidence of PE following CN-TKA and CONV-TKA. No statistically significant differences were reported in any of the studies with events ranging from 0% to 2% of patients in the CN-TKA groups compared with 0% to 3% of patients in the CONV-TKA groups. Of these six studies, two RCTs[35,167] and the two cohort studies[27,29] reported no instances of PE in either treatment group.

Venous thromboembolism (VTE)
One RCT was conducted specifically to investigate whether CN-TKA resulted in a lower rate of VTE compared withCONV-TKA, due to the elimination of intramedullary rodding[120]. A significant difference was found in the Mayo Clinic score between the two treatment types, with a lower (better) score in the CN-TKA group as compared to the twoCONV-TKA groups which consisted of patients who received TKA with an intramedullary femur guide and an extramedullary tibia guide, and those with intramedullary guides for both the tibia and the femur(4.2 vs. 5.1 and 5.4, respectively, P = .02, .04).

Number of detectable emboli
Two RCTs reported the mean number of detectable emboli between treatment groups[35,78]and both found a significantly lower number in the CN-TKA group as

compared with the CONV-TKA group, 4.89 versus 6.15 and 0.64 versus 10.7, *P* = .004 and .0003, respectively. One of these studies also reported the percentage of patients with greater than two detectable emboli, reporting an incidence of 0% in the CN-TKA group compared to 43% in the CONV-TKA group, *P* = .0003[78].

Ischemic events, CN-TKA vs. CONV-TKA (Tables 22, 23, 24)
In one RCT, AMI was reported in 2% of patients in both the CN-TKA and the CONV-TKA groups[33]. Transient ischemia was noted in 0% and 3% of patients, respectively, in another RCT[30].Acute post-operative confusion, attributed to transient hypoxia, was reported by these same RCTs, one of which found a much lower rate in the CN-TKA group compared with the CONV-TKA: 3% and 28%, respectively (*P* = .007)[30], and 0% and 4%, respectively[33].

Wound Complications, CN-TKA vs. CONV-TKA (Tables 22, 23, 24)
Nine RCTs[30,33,35,45,49,100,124,147,167] and seven cohort studies, five prospective[20,29,31,82,175]and two retrospective[27,80],reported on infection rates following CN-TKA versus CONV-TKA. No significant differences were reported between the two treatment groups in any of the studies. Deep infections were noted in six studies ranging from 0% to 4% and from 0% to 2%, respectively[27,33,49,80,100,147]. Superficial wound infections were reported in three studies[30,45,80] affecting 0% to 7% of patients following CN-TKA and 0% to8% of patients following CONV-TKA. One retrospective cohort reported incidences of 0% and 0.3%, respectively, for superficial infection with delayed wound healing[80]. Eight studies reported no incidences of any infection (either superficial or deep infection) in either treatment group in their populations[20,29,31,35,82,124,167,175]. Delayed wound healing ranged from 0% to 3% and 0% to 1%, respectively, as reported by three RCTs[15,100,147]. Persistent wound drainage of less than 10 days was reported in 4% of knees in both treatment groups in one retrospective cohort[27]. Another retrospective cohort reported necessary re-exploration for hematoma with delayed wound healing in 0.4% and 0% of patients following CN-TKA and CONV-TKA, respectively[80]. No incidences of other wound complications were reported by two prospective cohorts[28,175]and one retrospective cohort[19].

Other Complications, CN-TKA vs. CONV-TKA (Table 22, 23, 24)
No statistically significant differences between treatment groups in frequency of other complications were reported by eight RCTs[15,30,33,85,100,124,147,167] and seven cohort studies, four prospective[20,29,31,82] and three retrospective[19,27,80]. Pneumonia was reported in 2% of patients following CN-TKA and none of the patients following CONV-TKA in one RCT[33]. In another RCT, hemiarthrosis was reported in 2% of patients in both the CN-TKA and the CONV-TKAgroupsand 2% and 0% of patients, respectively, had a hematoma[33]. Somewhat higher incidences of anterior femoral notching in the CN-TKA

group were reported by one RCT[85], 6% versus 1%, and two prospective cohorts[29,83], 4% versus 0% and 24% versus 14%, respectively. Minor leg swelling was reported in 11% and 8% of knees following CN-TKA versus CONV-TKA, respectively, in one retrospective cohort[27]. No incidences of soft-tissue injury were reported by another retrospective cohort[19]. Two RCTs looked at the incidence of stiff knees requiring manipulation under anesthesia and reported rates of 3% and 1% in the CN-TKA group and 0% and 4% in the CONV-TKA group[30,147]. Fractures were reported in 4% and 0% of knees, respectively, in one prospective cohort[29]. Conversely, no perioperative fractures were reported in two RCTs[124,167] and three cohort studies[19,29,108]. Furthermore, no pin-site problems or fractures at the pin site were reported in one prospective[29] and one retrospective study[27]. Knee crepitus was reported in 3% and 7% of patients following CN-TKA and CONV-TKA, respectively, in one retrospective cohort[108] but had no impact on pain or function. No incidences of patellofemoral syndrome were noted in either group in the same cohort. Two prospective cohorts reported reoperation following CN-TKA compared with CONV-TKA for stiffness (5% and 6% of knees, respectively) and fracture through the pin site (3% and 0% of knees, respectively) in one[20], and for patellar ligament rupture (3% and 0%, respectively) in the other[175].

Operative Time, Tourniquet Time and Blood Loss, CN-TKA vs. CONV-TKA

Operative time

Eight of 14 RCTs[30,33,35,45,49,85,100,106]and six of ten cohort studies, four prospective[20,28,83,175] and two retrospective[50,136],reported significantly longer mean operative times for CN-TKA as compared with CONV-TKA. In these 14 studies, the mean differences in operative time ranged from 13 to 24 minutes ($P \leq .001$) across the RCTs and from 10 to 63 minutes ($P \leq .001$ to = .002) across the cohort studies. Four RCTs[105,109,139,157] and two cohort studies[27,65]did not find any significant differences in operative times between treatment groups, and threeRCTs[17,120,124] and two cohorts[108,141] did not report *P*-values. However, the operative times in the latter five studies were longer in the CN-TKA groups than in the CONV-TKA groups (ranges: 81–124 vs. 62–105, respectively). Across all 24 trials, mean operative times ranged from 65 to 162 minutes in the computer-navigated TKA groups and from 57 to 160 minutes in the conventional TKA groups.

Tourniquet time

Seven of nine RCTs[38,45,67,78,79,85,167] and five of seven cohort studies, three prospective[31,83,121]and two retrospective[19,136]reported significantly longer tourniquet times for CN-TKA as compared with CONV-TKA. In these 12 studies, mean differences in tourniquet times ranged from 13 to 22 minutes ($P< .001$ to = .002) across the RCTs and from 10 to 26 minutes ($P< .001$ to = .003) across the cohort studies. One RCT[34]and one

retrospective cohort[27]did not report a significant difference between the two groups, and one RCT[120] and one retrospective cohort[154] did not report *P*-values. However, the tourniquet times in the two latter studies were longer for the CN-TKA group than for the CONV-TKA group (92 vs. 73 minutes and 100 vs. 73 minutes, respectively). Across all 16 trials, mean tourniquet times ranged from 59 to 134 minutes in the computer-navigated TKA groups and from 44 to 116 minutes in the conventional groups.

Blood loss, CN-TKAvs. CONV-TKA

Five of ten RCTs reported significantly less mean blood loss following CN-TKA as compared with CONV-TKA (*P*-values ranged from .001 to .028)[30,38,67,79,167]. In these five studies, mean differences in blood loss between the two treatments ranged from 117 mL to 396 mL. Two other RCTs also reported less mean blood loss in the computer navigated group (338 mL vs. 361 mL and 469 mL vs. 520 mL)[34,109], but the differences were not statistically significant. Of eight cohort studies, five prospective[20,28,83,121,141] and three retrospective[27,50,136],that reported mean blood loss, only one retrospective cohort reported significantly less blood loss in the CN-TKA group (1242 mL vs. 1375 mL, *P* = .036)[136]; all other studies reported no significant difference between the two treatments. Conversely, slightly more blood loss following CN-TKA as compared with CONV-TKA was reported in three RCTs[45,85,121] and one prospective cohort[141], however the differences were not statistically significant. Across all 18 studies, mean blood loss ranged from 66 mL to 1677 mL in the CN-TKA group and from 55 mL to 1974 mL in the CONV-TKA groups.

Other blood parameters, CN-TKAvs. CONV-TKA

One prospective cohort specifically investigated the levels of C-reactive protein (CRP), considered a marker for surgical trauma, in patients who had CN-TKA versus CONV-TKA[141]. CRP levels peaked at day 2 in both groups and were significantly lower in the computer-navigated group, 60 mg/L versus 115 mg/L, *P*< .001.

Summary: Safety, CN-TKA versus CONV-TKA

Evidence from 39 studies (25 RCTs, 14 cohorts) suggests that CN-TKA is just as safe as CONV-TKA. CN-TKA resulted in significantly longer operative and tourniquet times when compared with conventional TKA; however, it significantly reduced the mean peri-operative blood loss. It is thought that computer-navigation, which does not use intramedullary alignment rods, will lead to fewer embolic events. In these studies, the rates of DVTs and PEs were similar for both treatment groups across all the studies; however, three RCTs reported significantly better Mayo Clinic scores for VTE, as well as fewer detectable emboli in the CN-TKA groups compared with the CONV-TKA groups. No significant differences in infection, either deep or superficial, between treatment

groups were reported in any study. Incidences of all other complications, such as AMI, pneumonia, hemiarthrosis, hematomas, transient ischemia, perioperative fractures, anterior femoral notching, and reoperations were also similar between treatment groups

Table 22. Safety outcomes in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*
Randomized Controlled Trials			
Thromboembolic events (%, n/N)			
DVT			
Choong 2009	2% (1/57 pts)	2% (1/54 pts)	ns
Lützner 2008	8% (3/40pts)	10% (4/40pts)	ns
Bejek 2007	1% (1/69 knees)	0% (0/69 knees)	ns
Church 2007	0% (0/14pts)	0% (0/12pts)	ns
Chauhan 2004	3% (1/35pts)	6% (2/36pts)	ns
Sparmann 2003	1% (1/120 pts)	1% (1/120 pts)	NR
PE			
Choong 2009	2% (1/57 pts)	0% (0/54 pts)	ns
Weng 2009	0% (0/60 knees)	0% (0/60 knees)	ns
Church 2007	0% (0/14pts)	0% (0/12pts)	ns
Chauhan 2004	0% (0/35pts)	3% (1/36pts)	ns
VTE (mean Mayo score)			
Ooi 2008	4.2†	5.1†‡ and 5.4†‡	.02–.04
Mean detectable emboli			
Church 2007	4.89 (3–7); no emboli > 0.5cm	6.15 (4–8); no emboli > 0.5 cm	.004
Kalairajah 2006	0.64 (± 0.74)	10.7 (± 13.5)	.0003
> 2 detectable emboli per patient			
Kalairajah 2006	0% (0/10pts)	43% (6/14pts)	.0003
Ischemic events (%, n/N)			
AMI			
Choong 2009	2% (1/57 pts)	2% (1/54 pts)	ns
Transient ischemia			
Chauhan 2004	0% (0/35pts)	3% (1/36pts)	ns
Confusion			
Choong 2009	0% (0/57 pts)	4% (2/54 pts)	ns
Chauhan 2004	3% (1/35pts)	28% (10/36pts)	.007
Wound complications (%, n/N)			
Deep infection			
Choong 2009	4% (2/57 pts)	2% (1/54 pts)	ns
Dutton 2008	0% (0/52 pts)	2% (1/56 pts)	ns
Lützner 2008	0% (0/40pts)	0% (0/40pts)	ns
Sparmann 2003	1% (1/120 pts)	0% (0/120 pts)	NR
Superficial wound infection			
Decking 2005	7% (2/27pts)	8% (2/25pts)	ns
Chauhan 2004	3% (1/35pts)	6% (2/36pts)	ns
Superficial/deep infection			
Weng 2009	0% (0/60 knees)	0% (0/60 knees)	ns
Church 2007	0% (0/14pts)	0% (0/12pts)	ns
Perlick 2004	0% (0/50 pts)	0% (0/50 pts)	NR
Delayed wound healing			
Lützner 2008	0% (0/40pts)	0% (0/40pts)	ns
Bejek 2007	1% (1/69 knees)	1% (1/69 knees)	ns
Sparmann 2003	3% (3/120 pts)	1% (1/120 pts)	NR
Other Complications (%, n/N)			
Pneumonia			
Choong 2009	2% (1/57 pts)	0% (0/54 pts)	ns
Hemiarthrosis			

Table 22. Safety outcomes in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*
Randomized Controlled Trials			
Choong 2009	2% (1/57 pts)	2% (1/54 pts)	ns
Hematoma			
Choong 2009	2% (1/57 pts)	0% (0/54 pts)	ns
Perioperative fractures			
Weng 2009	0% (0/60 knees)	0% (0/60 knees)	ns
Perlick 2004	0% (0/50 pts)	0% (0/50 pts)	NR
Anterior femoral notching			
Kim 2007	6% (6/100 knees)	1% (1/100 knees)	ns
Excessive resection of tibia requiring a tibial insert of 14 mm			
Kim 2007	1% (1/100 knees)	0% (0/100 knees)	ns
Stiff knee requiring manipulation under anesthesia			
Chauhan 2004	3% (1/35pts)	0% (0/36pts)	ns
Sparmann 2003	1% (1/120 pts)	4% (4/120 pts)	NR
Operative time, tourniquet time, and blood loss			
Operative time, minutes (mean ± sd or range)			
Choong 2009	105(60–145)	90(50–140)	.001
Martin 2009	108 (70–162)	98(49–225)	ns
van Strien 2009	148 ± 25.0	137 ± 43.3	ns
Dutton 2008	107	83	< .001
Lützner 2008	median 89(73–125)	median 80(57–115)	< .001
Ooi 2008	123	105	NR
Church 2007	74 (60–89)	57 (49–63)	.0003
Kim 2007	97 (50-119)	82(65-94)	< .001
Martin 2007	88 ± 16	68 ± 18	< .001
Matziolis 2007	101 ± 17	94 ± 18	ns
Bohling 2005	93(55–145)	80(40–135)	NR
Decking 2005	92 ± 9	79 ± 8	< .001
Chauhan 2004	80 (60–120)	67 (55–90)	.001
Perlick 2004	81 (66–115)	62 (44–90)	NR
Tourniquet time, minutes (mean± sd or range)			
Conteduca 2009	90 (80–110)	75 (60–85)	< .001
Hinarejos 2009 (ischemia/tourniquet)	89.4 ± 17.7	75.8 ± 19.8	.002
Weng 2009	94 ± 23	72 ± 21	< .0001
Chontanaphuti 2008	105	100	ns
Ooi 2008	92.4	73.4	NR
Kim 2007	59 (53–81)	44 (32–56)	< .001
Kalairajah 2006	86.8 (72–105)	73.4 (62–95)	< .001
Decking 2005	88 ± 12	71 ± 12	< .001
Kalairajah 2005	89 (55–125)	74 (40–132)	.002
Blood loss, mL (mean ± sd or range)			
Conteduca 2009	1677 (500–2634)	1974 (450–3930)	.028
Hinarejos 2009	447 ± 235	613 ± 268	.007
Weng 2009	619 ± 268	736 ± 358	.025
Chontanaphuti 2008	338 ± 121	361 ± 48	ns
Kim 2007	277 (80–700)	265 (40–850)	ns
Martin 2007	434 ± 272	394 ± 350	ns
Matziolis 2007	469 (50–1120)	520(50–1015)	ns
Decking 2005	1088	985	ns

Table 22. Safety outcomes in RCTs comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*
Randomized Controlled Trials			
Kalairajah 2005	1351 (175–2890)	1747 (1100–3030)	.001
Chauhan 2004	252 (25–6200)	446 (100–1100)	.001

AMI: acute myocardial infarction; CN-TKA: computer-navigated total knee arthroplasty; CONV-TKA: conventional total knee arthroplasty; DVT: deep vein thrombosis; NA: not applicable (intraoperative or immediately postop); NR: not reported; NS: not statistically significant; PE: pulmonary embolism; VTE: venous thromboembolism.

*All studies expect for Kalairajah 2005 and Kim 2007 controlled for baseline data and possible confounding factors.

†The Modified Mayo Clinic grading system for echogenic emboli looks at 3 different variables: the amount of right atrium filled by echogenic particles (1 = < 50%; 2 = 50%–70%; 3 = > 75%), the duration of echogenesis during one minute video segments looking at time to peak intensity (1 = < 25 seconds; 2 = 25–35 seconds; 3 = > 35 seconds), and the size (diameter in centimeters) of the largest echogenic particle (1 = < 0.5; 2 = 0.5–1.0; 3 = > 1.0).

‡The CONV-TKA group (n = 20) was comprised of two groups of 10 patients each: Group A = TKA with an intramedullary femur guide and an extramedullary tibia guide; and Group B = TKA with intramedullary guides for both the tibia and the femur. Mean Mayo scores are reflected for Groups A and B, respectively.

Table 23. Safety results in prospective cohorts comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*
Prospective cohorts			
Thromboembolic events (%, n/N)			
DVT			
Bonutti 2008	2% (1/55pts)	2% (1/55pts)	ns
Chang 2006	0% (0/50 knees)	0% (0/29 knees)	ns
PE			
Chang 2006	0% (0/50 knees)	0% (0/29 knees)	ns
Wound complications (%, n/N)			
Infection			
Cheung 2009	0% (0/47pts)	0% (0/47tps)	ns
Kim 2009	0.6% (1/160 knees)	0% (0/160 knees)	ns
Bonutti 2008	2% (1/55pts)	0% (0/55pts)	ns
Chang 2006	0% (0/50 knees)	0% (0/29 knees)	ns
Zumstein 2006	0% (1/30 knees)	0% (0/30 knees)	ns
Other wound complications			
Chang 2010	0% (0/50pts)	0% (0/50pts)	ns
Zumstein 2006	0% (0/30 knees)	0% (0/30 knees)	ns
Other Complications (%, n/N)			
Reoperation			
For stiffness			
Bonutti 2008	5% (4/81 knees)	6% (5/81 knees)	ns
For fracture through pin site			
Bonutti 2008	3% (2/81 knees)	0% (0/81 knees)	ns
For patella ligament rupture			
Zumstein 2006	3% (1/30 knees)	0% (0/30 knees)	NR
Fractures			
At pin site			
Cheung 2009	0% (0/47pts)	0% (0/47pts)	ns
Any			
Chang 2006	4% (2/50 knees)	0% (0/29 knees)	ns
Bleeding requiring aspiration			
Bonutti 2008	7% (4/55 pts)	0% (0/55 pts)	ns
Peroneal nerve palsy			
Bonutti 2008	2% (1/55 pts)	0% (0/55 pts)	ns
Anterior femoral notching			
Kim 2009	4% (6/160 knees)	0% (0/160 knees)	ns
Chang 2006	24% (12/50 knees)	14% (4/29 knees)	ns
Stiff knee requiring manipulation under anesthesia			
Zumstein 2006	3% (1/30 knees)	0% (0/30 knees)	NR
Operative time, tourniquet time, and blood loss			
Operative time, minutes (mean ± sd or range)			
Chang 2010	119.2 (87–155)	90.9 (60–141)	< .001
Haytmanek 2010	Unilateral (n = 41) 65 (43–95); Bilateral (n = 6) 128 (112–144)	Unilateral(n = 38) 71 (31–125) Bilateral: (n = 10) 135 (94–172)	ns ns
Kim 2009	97 (65–110)	79 (55–91)	< .001
Shen 2009	95	74	NR
Bonutti 2008	121 (59–202)	58 (37–137)	.001
Chang 2006	101 (65–145)	93 (66–134)	.027

Table 23. Safety results in prospective cohorts comparing CN-TKA with CONV-TKA.

	CN-TKA	CONV-TKA	*P*-value*
Zumstein 2006†	114 ± 22	91 ± 51	.01
Tourniquet time, minutes (mean± sd or range)			
Cheung 2009	111 (59–143)	98 (45–143)	.003
Kim 2009	75 (59–90)	49 (56–85)	< .001
Pang 2009	134 (93–168)	116 (80–150)	< .001
Blood loss, mL (mean ± sd or range)			
Chang 2010	471(103–1097)	483(37–988)	ns
Kim 2009	231(65–550)	246(110–620)	ns
Pang 2009	266(100–600)	284(100–500)	ns
Shen 2009	481	453	NR
Bonutti 2008	66(0–300)	55(0–300)	ns
Other blood parameters			
Peak C-reactive protein (CRP) levels, mg/L (mean, range)			
Shen 2009	60 (50–80)‡	115 (98–130)‡	< .001

CN-TKA: computer navigated total knee arthroplasty; CONV-TKA: conventional total knee arthroplasty; DVT: deep vein thrombosis; NR: not reported; NS: not statistically significant.

*All prospective cohorts, except for Shen 2009, controlled for baseline data and possible confounding factors.

†Operative time was only analyzed for 24 patients in the image-free navigation group and 22 patients in the conventional group.

‡Estimated from box plots provided in original article.

Table 24. Safety outcomes in retrospective cohorts comparing CN-TKA with CONV-TKA.

Safety	CN-TKA	CONV-TKA	*P*-value*
Retrospective cohorts			
Thromboembolic events (%, n/N)			
Fatal PE			
Chaiyakit 2009	0% (0/46 knees)	0% (0/24 knees)	ns
Wound complications (%, n/N)			
Deep wound infection			
Chaiyakit 2009	0% (0/46 knees)	0% (0/24 knees)	ns
Kamat 2009	0% (0/263pts)	0.3% (1/302pts)	ns
Superficial infection			
Kamat 2009	0.4% (1/263pts)	0% (0/302pts)	ns
Superficial infection with delayed wound healing			
Kamat 2009	0% (0/263pts)	0.3% (1/302pts)	ns
Persistent wound drainage < 10 days			
Chaiyakit 2009	4% (2/46 knees)	4% (1/24 knees)	ns
Re-exploration for hematoma with delayed wound healing			
Kamat 2009	0.4% (1/263pts)	0% (0/302pts)	ns
Other			
Bolognesi 2005	0% (0/50 knees)	0% (0/50 knees)	ns
Other complications (%, n/N)			
Soft tissue injury			
Bolognesi 2005	0% (0/50 knees)	0% (0/50 knees)	ns
Pin-site problems			
Chaiyakit 2009	0% (0/46 knees)	0% (0/24 knees)	ns
Fractures			
Matsumoto 2006	0% (0/30 pts)	0% (0/30 pts)	ns
Bolognesi 2005	0% (0/50 knees)	0% (0/50 knees)	ns
Minor leg swelling			
Chaiyakit 2009	11% (5/46 knees)	8% (2/24 knees)	ns
Nerve palsy			
Kamat 2009	0.4% (1/263pts)	0.3% (1/302pts)	ns
Knee crepitus			
Matsumoto 2006	3% (1/30 pts)	7% (2/30 pts)	NR
Patellofemoral symptoms			
Matsumoto 2006	0% (0/30 pts)	0% (0/30 pts)	ns
Operative time, tourniquet time, and blood loss			
Operative time, minutes (mean ± sd or range)			
Schnurr 2010	126 (65–185)	116 (60–175)	< .001
Chaiyakit 2009	162 ± 25.1	160 ± 31	ns
Ek 2008	122	108	.002
Matsumoto 2006	124	104	NR
Tourniquet time, minutes (mean± sd or range)			
Schnurr 2010	108 (55–160)	98 (55–150)	< .001
Chaiyakit 2009	101 ±18	105 ± 24	ns
Stulberg 2006	100 ± 16.3	73 ± 13.7	NR
Bolognesi 2005	68(67–145)	57(62–126)	.004
Blood loss, mL (mean ± sd or range)			
Schnurr 2010	1242 (28–3870)	1375 (61–4215)	.036
Chaiyakit 2009	638 ± 222	690 ± 288	ns
Ek 2008	33 g/L	32 g/L	ns

CN-TKA: computer navigated total knee arthroplasty; CONV-TKA: conventional total knee arthroplasty;

NR: not reported; NS: not statistically significant.
*Studies with statistically significant findings controlled for baseline data and possible confounding factors.

4.3.2. UKA versus TKA, Safety

No deaths and few complications were reported in one RCT and nine cohort studies.

Thromboembolic events, UKA vs. TKA (Table 25)
Newman et al[117] in a RCT reported a lower proportion of patients having a DVT following UKA (2.2%) compared with TKA (10.2%), though this was not statistically significant. Among the nonrandomized trials, DVT risk ranged from 0% to 5% in the UKA group and from 2% to 6.7% in the TKA group. With respect to pulmonary embolism, one cohort study reported 2 cases (7.1%) of pulmonary embolism in the UKA group and none (0/104) in the TKA group[164] while a second study identified no cases in the UKA group (0/20) and 1 case (5%) in the TKA group[172].

Wound Complications, UKA vs. TKA (Table 25)
There were no reports of wound infections. Delayed wound healing was reported in one RCT and one cohort study. There were no instances of delayed wound healing in the UKA groups in either study while 1.9%[117] and 3.5%[93] of patients inthe TKA groups experienced delayed healing.

Other Complications, UKA vs. TKA (Table 25)
Other complications varied across studies but did not differ statistically between groups. Two studies reported that no patients required manipulation under anesthesia (MUA)in the UKA group while 7.7% (4/52)[117] and 2.4% (3/130)[164] received MUA in the TKA group.

Operative time, blood loss and length of hospital stay, UKA vs. TKA (Table 25)
Safety outcomes of operative time, blood loss and length of hospital stay trended towards better outcomes for the UKA group, with several significant results. Rougraff et al.[135]found that significantly fewer patients required blood transfusion following UKA versus TKA (1% versus 67%, respectively, $P< .01$). Yang et al.[172] found a significantly lower amount of post-op drainage in the UKA group as compared with the TKA group (203 ± 131 ml versus 333 ± 229 ml, respectively, $P< .01$). The same authors also found less of a drop in post-op haemoglobin levels in the UKA group compared with the TKA group (1.8 ± 0.8 g/dl versus 2.6 ± 1.4 g/dl, respectively, $P< .01$). Hospital stay also trended towards fewer days for the UKA group compared with the TKA group, with one author[164] reporting 10.6 days versus 14.4 days, respectively, ($P< .01$) and another[172] reporting and 5.9 ± 1.5 days and 9.4 ± 3.0 days, respectively, ($P < .01$).

Table 25. Safety outcomes from one RCT and nine cohort studies comparing UKA and TKA

Outcome	UKA	TKA	*P*-value
THROMBOEMBOLIC EVENTS (%, N/N)			
Deep vein thrombosis*			
Newman 1998	2.2% (1/45 pts)	10.2% (5/49 pts)	ns
Cameron (1988)	5% (1/20 knees)	5% (1/20 knees)	NR
Weale (2001)	3.6% (1/28 pts)	6.7% (7/104 pts)	NR
Yang (2003)	0% (0/50 pts)	2% (1/50 pts)	NR
Pulmonary embolism			
Cameron (1988)	0% (0/20 pts)	5% (1/20 pts)	NR
Weale (2001)	7.1% (2/28 pts)	0% (0/104 pts)	NR
WOUND COMPLICATIONS (n/N)			
Delayed wound healing			
Newman 1998	0% (0/50 knees)	1.9% (1/52)	ns
Lombardi (2009)	0% (0/115 knees)	3.5% (4/115 knees) ‡	NR
OTHER COMPLICATIONS(%, N/N)			
Femoral condylar crack fracture			
Cameron (1988)	5% (1/20 knees)	0% (0/20 knees)	NR
Tibial eminence avulsion			
Cameron (1988)	5% (1/20 knees)	0% (0/20 knees)	NR
Neuroma of infrapatellar branch of saphenous nerve			
Cameron (1988)	10% (2/20 knees)	0% (0/20 knees)	NR
Drop foot			
Cameron (1988)	0% (0/20 knees)	5% (1/20 knees)	NR
Postoperative pneumonia			
Yang (2003)	0% (0/50)	2% (1/50)	NR
Persistent varus/valgus subluxation (source of moderate pain)			
Laurencin (1991)	0% (0/23 knees)	4.3% (1/23 knees)	NR
Complications treated with arthroscopy			
Lombardi (2009) §	2.6% (3/115 knees)	0% (0/115 knees)	NR
Loosening of femoral component with no surgery			
Weale (2001)	6.5% (2/31 knees)	0% (0/130 knees)	NR
Knee pain with no surgery			
Weale (2001)	0% (0/31 knees)	0.7% (1/130 knees)	NR
Manipulation under anesthesia†			
Newman 1998	0% (0/50 knees)	7.7% (4/52)	ns
Weale (2001)	0% (0/31 knees)	2.4% (3/130 knees)	NR
OPERATIVE TIME, BLOOD LOSS AND LENGTH OF HOSPITAL STAY			
Operating time (mean minutes)			
Yang (2003)	90 ± 24 (50–135)	87 ± 22 (60–160)	ns
Blood transfusion required			
Rougraff (1991)	1% (1/98)	67% (52/78)	< .01
Total post-op drainage (ml)			
Yang (2003)	203 ± 131 (100–380)	333 ± 229 (60–910)	< .01
Fall in post-op haemoglobin (g/dl)			
Yang (2003)	1.8 ± 0.8 (0.5–3.2)	2.6 ± 1.4 (0.8–5.9)	< .01

Outcome	UKA	TKA	*P*-value
Prolonged hospital stay >20 days			
Newman 1998	6.7% (3/45 pts)	22.4% (11/49 pts)	.043
Hospital stay (mean days)			
McAllister (2008)	2.2	3.9	NR
Robertsson (1999)	10.7 ± 4/4	12.3 ± 5.2	NR
Weale (2001)	10.6	14.4	< .01
Willis-Owen	5.9	8.3	NR
Yang (2003)	5.9 ± 1.5 (3–11)	9.4 ± 3.0 (6–19)	< .01

*Authors did not routinely perform venography or isotope scans.
†Reason not specified.
‡Incision and drainage for wound dehiscence (n = 1), incision and drainage for superficial sepsis (n = 3).
§Arthroscopy for removal of loose body (n = 2) and arthroscopy for synovectomy and chondroplasty of the patellar due to pain (n = 1).

4.3.3. UKA versus HTO

Complications after treatment, UKA vs. HTO (Table 26)
Three studies reported complications after treatment. In two of the studies, the HTO groups experienced more total complications than the UKA group, 28.1% versus 6.7% (P = .044)[153] and 24.3% versus 9.6% (*P* = .055)[25], respectively. There were five deaths in the study reported by Stukenborg-Colsman (two in the HTO group, 3 in the UKA group), all reported to be unrelated to the operation. One patient in the Broughton study in the HTO group had a cardiac rest, recovered, and then died 15 days after surgery. Reports of DVT varied among studies ranging from 0% to 9.4% in the HTO group, and from 0% to 2.8% among those receiving UKA. Superficial wound infection reported in two studies ranged from 4.3% to 6.3% in the HTO group compared with 0% in the UKA group. Manipulation under anesthesia occurred from 0% to 2.9% in the HTO group in two studies compared with a range of 3.8% to 6.7% in the UKA group. Other complications reported infrequentlyin the HTO and UKA groups, respectively, includepulmonary embolism (1.5% versus 0.0%), fracture (6.3% versus 0%), delayed union (3.1% versus 0%), aseptic loosening (0% versus 2.8%) and wound problems (7.1% versus 1.9%).

Table 26. Safety comparing HTO with UKA.

Complications	UKA	HTO	*P*-value
DEATH			
Stukenborg-Colsman	10.7% (3/28 pts)*	6.3% (2/32 pts)*	ns
Broughton	0.0% (0/43 pts)	1.5% (1/66 pts)†	ns
THROMBOEMBOLISM			
Deep vein thrombosis			
Stukenborg-Colsman	0.0% (0/30 knees)	9.4% (3/32 knees)	ns
Weidenhielm (Borjesson)	2.8% (1/36 knees)	0.0% (0/23 knees)	ns
Broughton	0.0% (0/43 pts)	4.5% (3/66 pts)	ns
Pulmonary embolism			
Broughton	0.0% (0/43 pts)	1.5% (1/66 pts)	ns
WOUND COMPLICATIONS (n/N)			
Superficial wound infection			
Stukenborg-Colsman	0.0% (0/30 knees)	6.3% (2/32 knees)	ns
Weidenhielm (Borjesson)	0.0% (0/36 knees)	4.3% (1/23 knees)	ns
Wound problems			
Broughton	1.9% (1/52 knees)	7.1% (5/70 knees)	ns
OTHER COMPLICATIONS			
Fracture			
Stukenborg-Colsman	0.0% (0/30 knees)	6.3% (2/32 knees)	ns
Staple loosening			
Stukenborg-Colsman	0.0% (0/30 knees)	3.1% (1/32 knees)	ns
Aseptic loosening			
Weidenhielm (Borjesson)	2.8% (1/36 knees)	0.0% (0/23 knees)	ns
Pneumonia			
Weidenhielm (Borjesson)	2.8% (1/36 knees)	0.0% (0/23 knees)	ns
Broughton	7.0% (3/43 pts)	0.0% (0/66 pts)	ns
Delayed union			
Stukenborg-Colsman	0.0% (0/30 knees)	3.1% (1/32 knees)	ns
Manipulation under anesthesia			
Stukenborg-Colsman	6.7% (2/30 knees)	0.0% (0/32 knees)	ns
Broughton	3.8% (2/52 knees)	2.9% (2/70 knees)	ns
Broughton	4.7% (2/43 pts)	3.0% (2/66 pts)‡	ns
TOTAL COMPLICATIONS§			
Stukenborg-Colsman	6.7% (2/30 knees)	28.1% (9/32 knees)**	.044
Weidenhielm (Borjesson)	8.3% (3/36 knees)	4.3% (1/23 knees)	ns
Broughton	9.6% (5/52 knees)	24.3% (17/70 knees) ††	ns

NR: Not Reported; ns: not significant.
*Cause unrelated to operation.
†Cardiac arrest and recovery; died at 15 days.
‡Includes patient with cardiac arrest and recovery.
§Patients could have more than one complication.
**Does not include deaths unrelated to operation.
††Includes death.

4.3.4. Bi-UKA versus TKA

Complications, bi-UKA vs. TKA

No cases of radiological loosening or infection were seen in either the bi-UKA or TKA groups in the one retrospective cohort. Two cases (9%) of intraoperative fracture of the tibial spine block occurred in the bi-UKA group but did not have any adverse effect on the outcome at last follow-up in either case.

4.3.5. Bicompartmental knee arthroplasty versus tricompartmental TKA

Complications were not reported for the two registry studies comparing bi- and tri-compartmental TKA.

4.4. Key Question 4
What is the evidence that TKA or partial knee arthroplasty has differential efficacy or safety issues in sub populations?

4.4.1. Study Selection Criteria

Total Knee Arthroplasty Selection Criteria
The Agency for Healthcare Research and Quality (AHRQ) published an evidence report on TKA in 2003[7] in which potential prognostic factors were evaluated. Eleven studies were identified that directly examined the correlation of patient variables with functional outcomes; all studies evaluated primary total knee arthroplasty in at least 100 knees.

We also included six additional studiespublished after 2003 in order to include data that has become available since the AHRQ report was conducted: one systematic review[104], two prospective studies[22,48], and three retrospective studies[58,122,142].

CN-TKA Selection Criteria
We only identified one study by Millar[113] evaluating prognostic factors after CN-TKA that met our study criteria. Three studies were identified that evaluated factors during and after surgery (e.g., post-surgical component alignment) but these were excluded. Only obesity was evaluated and outcomes were limited to blood loss and post-operative infection. No implant failure rates or functional outcomes were reported.

Partial Knee Arthroplasty Selection Criteria
We included all prospective cohort studies or peer-reviewed registry studies with prospective data collection methods that reported prognostic factors for outcome after unicompartmental knee arthroplasty (UKA). We excluded case series (prospective and retrospective) that did not report prognostic factors and/or evaluated only patients with the prognostic factor of interest (e.g., only patients <65 years of age with no comparison group). We excluded retrospective cohort studies with less than 100 procedures due to limited study power. We excluded studies that evaluated factors during and after surgery (e.g., implant type and post-surgical component alignment). No randomized trials were identified with a risk factor sub-analysis. Primary outcomes of interest included survival or revision rates. The following prognostic factors were identified and described in this section: age, obesity, sex, multicompartment disease (e.g., rheumatoid versus osteoarthritis), and provider/facility characteristics. Suggested prognostic factors not identified in the literature included psychological or psychosocial comorbidities, evidence based selection criteria, payer systems, and bilateral procedures. Level of evidence tables are found in Appendix F. Summary and detailed tables are found in Appendix H.

4.4.2. Differential Characteristics, Total Knee Arthroplasty

Age and TKA (Table 27)

AHRQ HTA (summary up to 2003)
While one study reported that older age was significantly associated with improvements in SF-36 physical health scores, no relationship was found between patient age and WOMAC scores in three studies and KS scores in another study. The AHRQ report concluded that age was not a significant predictor of outcomes following TKA, however the extremes of age were not tested.

Cohort Studies Published After 2003
Four studies[22,48,58,142] evaluated whether age predicted outcome following primary TKA.

- WOMAC**:** Two studies reported the effect of older age on WOMAC scores. Bourne et al (2007)[22] (N = 728) reported that patients over the age of 80 years had significant less improvements in WOMAC scores at a mean follow-up of 9.5 years compared with other age groups; no significant changes from preoperative scores were found for any other age group. Gandhi et al (2010) (N = 551) conducted a retrospective study, and using multivariate longitudinal modeling found that older age was significantly associated with less sustained improvement over time (mean f/u: 3.0 years (range, 1–8))[58].

- SF-12 OR SF-36**:** The same two studies described above (WOMAC) found similar effects of age on outcomes from the SF-12 or SF-36 questionnaires: Bourne et al (2007) found that those over 80 years of age had significantly less improvement in SF-12 scores compared with other age groups; Gandhi et al (2010) reported that older patients had less sustained improvements in SF-36 physical function and role physical scores over time.

- KNEE SOCIETY SCORE**:** Bourne et al (2007) found that younger patients (< 50 years) had greater improvements in KS Clinical Rating scores than other age groups at a mean of 9.5 years over baseline.

- PERIPROSTHETIC INFECTION:Dowsey et al (2009)[48] (N = 1214) reported no relationship between age group and the risk of developing periprosthetic infection by 12 months.

- MODERATE TO SEVERE POSTOPERATIVE PAIN:At two years follow-up (N = 5290),Singh et al (2008)[142] found that compared with those 60 years of age and under, patients between the ages of >60 and 70 had a significantly lower rate of moderate to severe pain (no differences were found between other age groups). In contrast, there were no significant differences in the rate of moderate to severe pain between younger patients (≤ 60 years) and any other age group at five years (N = 2602).

Sex and TKA (Table 27)

AHRQ HTA (summary up to 2003)[7]
- No association between patient sex and patient outcomes was found in four studies, three of which used WOMAC scores and the fourth used Knee Society scores.

Cohort Studies Published After 2003
Five studies[22,48,58,122,142] evaluated whether patient sex predicted outcome following primary TKA.

- WOMAC:Two studies reported the effect of sex on WOMAC scores with mixed results. Bourne et al (2007)[22] reported no relationship between patient sex and change in WOMAC scores at a mean follow-up of 9.5 years. In contrast, Gandhi et al[58] found the female sex was associated with less sustained improvements over time according to multivariate longitudinal modeling (mean f/u: 3.0 years, range, 1–8).

- SF-12 OR SF-36**:** The same two studies described above (WOMAC) reported no significant relationship between patient sex and change in SF-12[22] or SF-36 physical function and role physical scores over time[142].

- KNEE SOCIETY SCORE**:** Two studies reported the effect of sex on Knee Society cores with mixed results. Bourne et al (2007) found that females had significantly less improvements in KS Clinical Rating scores than males at a mean of 9.5 years over baseline, while Parsley et al[122](N = 698) reported no relationship between patient sex and change in KS knee or function scores at a mean follow-up of 1.56 years.

- PERIPROSTHETIC INFECTION:Dowsey et al[48] found that females had a lower risk of developing periprosthetic infection by 12 months versus males.

- MODERATE TO SEVERE POSTOPERATIVE PAIN:At 2 years follow-up,Singh et al[142] reported that females had a significantly higher rate of moderate to severe pain compared with males; no significant differences were found at 5 years follow-up.

Obesity/BMI and TKA (Table 27)

AHRQ HTA (summary up to 2003)
- Six studies evaluated whether BMI was a predictor of outcome following TKA. Three studies used the WOMAC outcome measure and had conflicting results; one small study found that obese patients had greater improvements in ten-year HSS scores; and two studies employed the KS outcome measure and reported conflicting results. The authors of the AHRQ concluded that obesity was not significantly correlated with outcomes following TKA, but noted that the extremes were not specifically tested.

Cohort Studies Published After 2003

Three studies[22,48,58] assessed whether BMI was predictive of patient outcomes following primary TKA.

- WOMAC: Two studies reported the effect of obesity/BMI on WOMAC scores with mixed results. Bourne et al[22] reported that patients with Class III (which was not defined) and Class IV obesity had greater improvements in WOMAC scores at a mean follow-up of 9.5 years compared with other groups (underweight, normal weight, Class I obesity, and Class II obesity). Gandhi et al[58] did not find a relationship between BMI and differences in WOMAC scores over time according to multivariate longitudinal modeling (mean f/u: 3.0 years, range, 1–8).
- SF-12 OR SF-36:The same two studies described above (WOMAC) reported no significant relationship between obesity/BMI and change in SF-12[22] or SF-36 physical function and role physical scores over time[142].
- KNEE SOCIETY SCORE**:** Bourne et al[22]reported no relationship between obesity/BMI and change in KS Clinical Rating scores at mean of 9.5 years over baseline.
- PERIPROSTHETIC INFECTION:Dowsey et al[48]reported that patients with BMI ≥ 40 had significantly higher rates ofperiprosthetic infection by 12 months compared to patients with BMI < 30; however, patients with BMI 30–39 were not at increased risk of infection compared to those with BMI < 30.

Type of Arthritis and TKA (Table 27)

AHRQ HTA (summary up to 2003)

- Three studies reported improved outcomes for patients with rheumatoid arthritis (RA) compared with patients with osteoarthritis (OA); two of these studies employed the Knee Society outcome measure, and the third used the Hospital for Special Surgery outcome measure. However, the authors of the AHRQ noted that RA patients may have had worse pain and function preoperatively as they tended to have worse preoperative scores than those with OA.

Cohort Studies Published After 2003

Two studies [22,48] evaluated whether the type of arthritis underlying the need for knee replacement was predictive of patient outcomes following primary TKA.

- WOMAC, SF-12, KS**:** Bourne et al [22] found no relationship between diagnosis (osteoarthritis versus other) and change in WOMAC, SF-12 physical health, or KS Clinical Rating scores at mean of 9.5 years over baseline.
- PERIPROSTHETIC INFECTION**:**Dowsey et al [48] reported that diagnosis (osteoarthritis versus rheumatoid arthritis) was not associated with periprosthetic infection rates at 12 months.

Comorbidities and TKA (Table 27)

AHRQ HTA (summary up to 2003)

- One study reported that a greater number of comorbid conditions was significantly associated with greater improvements in WOMAC function but not pain scores.

Cohort Studies Published After 2003

Two studies [48] evaluated the relationship between comorbidities and outcomes following primary TKA.

- WOMAC: Gandhi et al[58] reported no correlation between comorbidity and differences in WOMAC scores over time according to multivariate longitudinal modeling (mean f/u: 3.0 years (range, 1–8)).
- SF-36: Gandhi et al[58] found that patients with greater comorbidity had less sustained improvements in SF-36 physical function and role physical scores over time.
- PERIPROSTHETIC INFECTION: Dowsey et al[48]determined that patients with diabetes mellitus (DM) were at significantly higher risk of developing periprosthetic infection compared to patients without DM; there was no relationship between either respiratory disease or smoking status and the development of periprosthetic infection.

Preoperative pain levels and TKA (Table 27)

AHRQ HTA (summary up to 2003)

One study reported that preoperative bodily pain was significantly associated with both WOMAC pain and function outcomes; preoperative joint pain was correlated with WOMAC function scores (the relationship with pain was not reported).

Cohort Studies Published After 2003

One cohort study[142] found no relationship between moderate to severe preoperative pain levels and the risk of having moderate to severe pain at 2 and 5 years follow-up.

Hospital/surgeon volume and TKA (Table 27)

AHRQ HTA (summary up to 2003)

No summary on hospital/surgeon volume was reported in the AHRQ HTA.

Cohort Studies Published After 2003

One systematic review[104] of 11 studies assessed whether hospital or surgeon volume was predictive of patient outcome following primary TKA.The mean patient number was N = 102,947 (range, N = 734–295,473); follow-up information was not reported. Heterogeneity between studies prevented pooling of data or meta-analysis. For each study, Marlow et al reported how the hospital or surgeon volumes were defined, the relevant outcomes evaluated, and whether the study reported a statistically significant difference between the lowest and highest volume hospital or surgeon; specific data were not included in this review. The numerical definitions of the various categories of volume varied by study; furthermore, these definitions represented patient numbers in some studies and measures such as quartiles in others (details not reported).

Hospital volume

- MORBIDITY: Seven studies evaluated whether hospital volume was associated with morbidity rates. When comparing hospitals with the lowest volume to those with the highest volume (again, definitions varied), five found that increased hospital volume was significantly correlated with decreased morbidity rates, while two studies found no statistical difference.
- MORTALITY: Six studies evaluated the relationship between hospital volume and patient mortality. Increased hospital volume was significantly associated with decreased mortality rates in two studies, and another study conducted a logarithmic examination and similarly found that increased hospital volume was associated with decreased mortality. Three studies found no difference in the mortality rates between hospitals with the highest and lowest volumes.
- LENGTH OF STAY: Four studies assessed the effect of hospital volume on length of stay. Three studies found that increased hospital volume was significantly correlated with decreased length of stay; another study did not evaluate results for statistical significance (no other information given).

Surgeon volume

- MORBIDITY: Surgeon volume was evaluated as a prognostic factor for morbidity rates in three studies. Two studies found that surgeons with the highest volume had significantly decreased morbidity rates compared with those with the lowest volume (definitions varied). One study found no statistical difference.
- MORTALITY: Two studies reported no statistically significant difference in patient mortality rates between surgeons with the highest and the lowest volumes.
- LENGTH OF STAY: One study found that increased surgeon volume was significantly correlated with decreased length of hospital stay (low volume: <14; high volume: >42).

Other factors and TKA (Table 27)

AHRQ HTA (summary up to 2003)

- One study reported that increased length of hospital stay was associated with greater improvements in WOMAC function but not pain scores at 6 months follow-up; the same study found no effect of increased waiting time on WOMAC function or pain scores.

Cohort Studies Published After 2003

Gandhi et al[58] used multivariable longitudinal regression model to assess whether year of follow-up, education, and SF-36 mental health scores were predictive of WOMAC or SF-36 physical function or role physical scores at a mean follow-up of 3.0 years.

Year of follow-up

- WOMAC: Year of follow-up was correlated with less sustained improvement in WOMAC scores as analyzed using multivariable longitudinal regression models[58].

- SF-36: Year of follow-up was associated with less sustained improvement in SF-36 role physical scores; no relationship was found between year of follow-up and SF-36 physical function scores[58].

Education

- WOMAC: Education level was not predictive of WOMAC scores as analyzed using multivariable longitudinal regression models[58].
- SF-36: Lesser education was correlated with less sustained improvement in SF-36 physical function (but not role physical) scores[58].

SF-36 mental health

- WOMAC, SF-36: Poorer preoperative SF-36 mental health scores were associated with significantly less sustained improvement in WOMAC, SF-36 physical function, and SF-36 role physical scores over time according to multivariable longitudinal regression modeling.

Table 27. Summary of risk factors associated with revision after unilateral TKA

Risk Factor	Reference	Study Type	Level of Evidence	Outcomes (see supplemental table ## for details)
Age	AHRQ	SR/HTA	n/a	**WOMAC**: No relationship between age and scores (4 studies; f/u = 6 months for 3 studies, f/u = NR for 1 study) **SF-36:**Older age: better SF-36 physical health scores (1 study; f/u = 2 years) **KS:** No relationship between age and scores (KS knee pain, KS knee) (1 study; f/u = 2 years)
	Bourne (2007)	Prospective cohort	II	**WOMAC**: Age > 80 years: greater improvement in change in scores from baseline (versus other age groups) (mean change: 19 ± 2; *P* = .01); mean f/u = 9.5 years). **SF-12:** Age > 80 years: greater improvement in change in scores from baseline (versus other age groups) (mean change: 7 ± 1; *P* = .01). **KS:** Age < 50 years: greater improvement in change in scores from baseline (versus other age groups) (KS Clinical Rating scores) (mean change: 29 ± 5; *P* = .03).
	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: Older age: less sustained improvement by multivariable longitudinal regression modeling (*P*< .001); mean f/u = 3.0 years). **SF-36:** Older age: less sustained improvement in the physical function and role physical scores by multivariable longitudinal regression modeling (*P* = .002, *P* = .001; respectively); mean f/u = 3.0 years).
	Dowsey (2009)	Prospective cohort	I	**Periprosthetic infection:** No relationship between age group and periprosthetic infection rate (f/u = 12 months).
	Singh (2008)	Retrospective cohort	III	**Moderate/severe postoperative pain:** ***2 years:*** Age >60 to 70 years: lower rate of pain they would describe as moderate to severe (versus age ≤ 60 years) (6.3% versus 10.3%; multivariate analysis: OR = 0.49 (95% CI, 0.31, 0.77); *P* = .002). No significant relationship in outcome for patients >70 to 80 years (rate = 11.4%) or > 80 years (rate = 11.4%). Five ***5 years***: No significant differences between age groups (age ≤ 60 years versus others, as described above).
Sex	AHRQ	SR/HTA	n/a	**WOMAC**: No relationship between patient sex and scores (4 studies; f/u = 6 months to 7 years) **KS:** No relationship (KS knee pain, KS knee) (1 study; f/u = 2 years)
	Bourne (2007)	Prospective cohort	II	**WOMAC**: No relationship between patient sex and change in scores from baseline (mean f/u = 9.5 years) (males had significantly better preoperative scores). **SF-12:** No relationship between patient sex and change in SF-12 physical or mental health scores from baseline (males had significantly better preoperative scores). **KS:** Female sex: lower improvement in change in KS Clinical Rating score (versus males) (21 ± 24 versus 25 ± 22; *P* = .01) (males had significantly better preoperative scores). Male sex: no relationship in change in KS knee subscale score (versus females)
	Parsley (2010)	Retrospective cohort	III	**KS:** No relationship between patient sex and change in KS knee or function scores (males had significantly better

Risk Factor	Reference	Study Type	Level of Evidence	Outcomes (see supplemental table ## for details)
				preoperative scores) (mean f/u: 1.56 years, minimum 1 year)
Sex (cont.)	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: Female sex: less sustained improvement by multivariable longitudinal regression modeling (P = .006; mean f/u = 3.0 years). **SF-36:** No relationship between patient sex and physical function or role physical scores by multivariable longitudinal regression modeling (P = .40, P = .59; respectively; mean f/u = 3.0 years).
	Dowsey (2009)	Prospective cohort	I	**Periprosthetic infection:**Female sex: lower risk of developing periprosthetic infection (versus males) (OR = 5.93; 95% CI, 1.95, 18.04; P = .002) (f/u = 12 months).
	Singh (2008)	Retrospective cohort	III	**Moderate/severe postoperative pain:** ***2 years***: Female sex: higher rate of pain described as moderate to severe (versus males) (9.0% versus 6.6%; multivariate analysis: OR = 1.45; 95% CI, 1.01, 2.08; P = .04). ***5 years***: No significant differences between sexes in rate of moderate to severe pain (7.9% versus 6.5%; multivariate analysis: OR = 1.23; 95% CI, 0.74, 2.02; P = .42).
Obesity/ BMI	AHRQ	SR/HTA	n/a	**WOMAC**: Mixed results (3 studies). Improvements in WOMAC scores correlate with increasing body max, difference between pts with BMI < 25 versus > 40 was not significant (1 study; f/u = 1 year); no relationship between BMI and WOMAC (1 study, f/u = 6 months); improvements in WOMAC scores associated with lower BMI (1 study, data and f/u = NR) **HSS:** BMI > 30: significantly better HS scores versus BMI < 30 (1 study, f/u = 10 years) **KS:** Mixed results (2 studies) BMI correlated with function (1 study, no details give, f/u = 2 years); no relationship between age and KS knee pain or knee scores (1 study; f/u = 1 year)
	Bourne (2007)	Prospective cohort	II	**WOMAC**: Class III (BMI not defined) and Class IV (BMI >40) obesity: Greater improvement in WOMAC scores from baseline compared with the other groups (Normal: 20 ± 2 versus Class III: 25 ± 3 and Class IV: 26 ± 7; P< .05 for both), but Class IV sample size was very small (n = 15) (mean f/u = 9.5 years). **SF-12:** No relationship between obesity/BMI and change in SF-12 physical or mental health scores from baseline. **KS:** No relationship between increasing obesity/BMI and change in KS Clinical Rating Function scores from baseline.
	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: No relationship between BMI and WOMAC scores by multivariable longitudinal regression modeling (P = .64); mean f/u = 3.0 years). **SF-36:** No relationship between BMI and physical function or role physical scores by multivariable longitudinal regression modeling (P = .73, P = .95; respectively); mean f/u = 3.0 yrs).
	Dowsey (2009)	Prospective cohort	I	**Periprosthetic infection:**BMI > 40: higher risk of developing periprosthetic infection (versus BMI < 30) (multivariate analysis: OR = 8.96 (95% CI, 1.59, 50.63); P = .013) (f/u = 12 months); BMI 30–39: similar risk in developing infection

Risk Factor	Reference	Study Type	Level of Evidence	Outcomes (see supplemental table ## for details)
				(versus BMI < 30) (multivariate analysis: OR = 2.2 (95% CI, 0.64, 8.14); *P*= .201).
Type of arthritis	AHRQ	SR/HTA	n/a	**KS:** RA patients: greater % improvement versus OA patients (KS knee, KS function) (2 studies; mean f/u = 4.5 – 9.8 years) **HSS:** RA patients: greater % improvement versus OA patients (1 study; mean f/u = 6.7 years).
	Bourne (2007)	Prospective cohort	II	**WOMAC**: No relationship between diagnosis (OA versus other) and change in WOMAC scores (mean f/u = 9.5 years). **SF-12:** No relationship between diagnosis (OA versus other) and change in SF-12 physical health scores. **KS:** No relationship between between diagnosis (OA versus other) and change in KS Clinical Rating Function scores from baseline.
	Dowsey (2009)	Prospective cohort	I	**Periprosthetic infection:** No relationship between diagnosis (OA versus RA) and risk of developing periprosthetic infection (f/u = 12 months).
Co-morbidities	AHRQ	SR/HTA	n/a	**WOMAC:**Number of comorbid conditions: more comorbidities was associated with greater improvements in WOMAC function (but not pain) scores (*P* = .01; *P* = .31, respectively)(1 study; f/u = 6 months).
	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: No relationship between comorbidity and WOMAC scores by multivariable longitudinal regression modeling (*P* = .100); mean f/u = 3.0 years). **SF-36:** Greater comorbidity: less sustained improvement in physical function and role physical scores by multivariable longitudinal regression modeling (*P* = .013, *P* = .005; respectively); mean f/u = 3.0 years).
	Dowsey (2009)	Prospective cohort	I	**Periprosthetic infection:**Diabetes mellitus (DM): significantly higher risk of developing periprosthetic infection (vs no DM) (OR = 6.87 (95% CI, 2.42, 19.56); *P*< .001) (f/u = 12 months). Respiratory disease or smokers: no relationship to risk of developing infection.
Pre-operative pain levels	AHRQ	SR/HTA	n/a	**WOMAC:**Greater bodily pain: associated with greater improvements in WOMAC pain and function scores (*P*< .001; *P* = .003, respectively)(1 study; f/u = 6 months); Greater joint pain: associated with greater improvements in WOMAC function scores (*P*< .001)(1 study; f/u = 6 months)
	Singh (2008)	Retrospective cohort	III	**Moderate/severe postoperative pain:** ***2 years and 5 years***: No relationship between preoperative pain levels (moderate to severe) and the risk of having moderate to severe postoperative pain (multivariate analysis: *P* = .53; *P* = .14 at 2 and 5 years, respectively).
Hospital volume	Marlow (2010)	SR	n/a	**Morbidity:**Lowest versus highest volume (definitions varied): Mixed results (7 studies total): 5 studies: increased hospital volume associated with decreased morbidity rates; 2 studies reported no relationship. **Mortality:** Lowest versus highest volume (definitions varied): Mixed results (6 studies total): 3 studies: increased hospital volume associated with decreased mortality rates; 3 studies

Risk Factor	Reference	Study Type	Level of Evidence	Outcomes (see supplemental table ## for details)
				reported no relationship. **Length of stay:** Lowest versus highest volume (definitions varied): Mixed results (4 studies total): 3 studies: increased hospital volume associated with decreased length of stay; 1 study reported no relationship.
Surgeon volume	Marlow (2010)	SR	n/a	**Morbidity:**Lowest versus highest volume (definitions varied):Mixed results (3 studies total): 2 studies: increased surgeon volume associated with decreased morbidity rates; 1 study reported no relationship. **Mortality:** Lowest versus highest volume (definitions varied): 2 studies reported no relationship. **Length of stay:** Lowest versus highest volume (definitions varied): 1 study: increased surgeon volume associated with decreased length of stay.
Length of hospital stay	AHRQ	SR/HTA	n/a	**WOMAC:**Increased length of stay: associated with greater improvements in WOMAC function (but not pain) scores (*P* = .03; *P* = .05, respectively)(1 study; f/u = 6 months).
Waiting time	AHRQ	SR/HTA	n/a	**WOMAC:**Increased waiting time: no relationship with improvements in WOMAC function or pain scores (*P* = .86; *P* = .40, respectively)(1 study; f/u = 6 months).
Year of follow-up	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: Greater year of follow-up: less sustained improvement by multivariable longitudinal regression modeling (*P* = .048); mean f/u = 3.0 years). **SF-36:** Greater year of follow-up: no relationship with physical function but less sustained improvement in role physical scores by multivariable longitudinal regression modeling (*P* = .37, *P* = .002; respectively); mean f/u = 3.0 years).
Education	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: No relationship by multivariable longitudinal regression modeling (*P* = .43); mean f/u = 3.0 years). **SF-36:** Lesser education: less sustained improvement in physical function but no relationship with role physical scores by multivariable longitudinal regression modeling (*P*< .001, *P* = .58; respectively); mean f/u = 3.0 years).
SF-36 mental health	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: Poorer mental health: less sustained improvement by multivariable longitudinal regression modeling (*P*< .001); mean f/u = 3.0 years). **SF-36:** Poorer mental health: less sustained improvement in physical function and role physical scores by multivariable longitudinal regression modeling (*P* = .031, *P* = .007; respectively); mean f/u = 3.0 years).
Ethnicity (white)	Gandhi (2010)	Retrospective cohort	III	**WOMAC**: No relationship between ethnicity (white or other) and WOMAC scores by multivariable longitudinal regression modeling (*P* = .074); mean f/u = 3.0 years). **SF-36:** No relationship between BMI and physical function or role physical scores by multivariable longitudinal regression modeling (*P* = .76, *P* = .16; respectively); mean f/u = 3 years)

AHRQ: Agency for Healthcare Research and Quality
BMI: body mass index
CI: confidence interval
HSS: Hospital for Special Surgery
KS: Knee Society
OR: odds ratio
RA: rheumatoid arthritis
SF-12: Short-Form 12 (outcome measure)
SF-36: Short-Form 36 (outcome measure)
SR/HTA: systematic review/health technology assessment

n/a: not applicable
NR: not reported
OA: osteoarthritis
WOMAC: Western Ontario and McMaster Universities OA index

4.4.3. Differential Characteristics, CN-TKA

Obesity

Millar et al. retrospectively evaluated tourniquet time, mean hemoglobin loss, true blood volume loss and postsurgical infection after computer-assisted knee arthroplasty in a morbidly obese (BMI of > 40 kg/m^2) and non-obese (BMI of < 30 kg/m^2) population. The authors reported that the groups were similar at baseline with respect to important prognostic factors; however, the obese group had a higher baseline ASA than the non-obese group and this was not controlled for in the analysis. The true blood volume (ml) loss was greater in morbidly obese (22 ± 10) compared with non-obese (17 ± 6; *P* = .02). The mean hemoglobin loss (g/dl) was also greater among the morbidly obese (1105 ± 321) compared with non-obese (923 ± 276; *P* = .02). A significantly higher 1-year superficial infection rate was also reported (12.5% and 2.5% in morbidly obese and non-obese patients, respectively; *P*<.01). The difference in tourniquet time (minutes) was not statistically significant (*P*=.16). The time for surgery in the morbidly obese was 92 ± 5 and non-obese 90 ± 6 minutes. Rate of blood transfusion and maximum allowable blood loss were not significantly different.

4.4.4. Differential Characteristics, Partial Knee Arthroplasty

Age and UKA

Registry Data

- We identified five peer-reviewed articles summarizing prognostic factors using registry data[59,62,87,133,159] and one additional registry report. Two *Swedish National Joint Replacement Registry* manuscripts were identified. Robertsson et al.[132] summarized data from years 1986–1995 on 11,395 patients and Harrysson 2004 years 1988–1997 on 12,662 patients. It is likely that much of these data overlap. In the paper by Robertsson, younger patients (< 65 years) were more likely to undergo revision than older patients (≥ 65 years), **Figure 4**. Revision rates or adjusted hazards ratios (Adj HR) through multivariate analyses were not reported. Harrysson reported a higher cumulative all-cause revision rate among younger (< 65 years) patients (mean, 22% at 9.2 years) compared with older (≥ 65 years) patients (mean, 14% at 9.2 years). When controlling for year of operation and gender, the risk for revision in the older group was lower (RR, 0.55; 95% confidence interval, 0.45–0.65; *P*<. 0001) compared to the risk for younger patients. A similar, albeit smaller, risk ratio was observed when examining risk of revision attributable to loosening of components (risk ratio, 0.63; 95% confidence interval, 0.48-0.83; *P* = .001).

- The study by W-Dahl 2010 examined data from the *Swedish National Joint Replacement Registry* years 1998–2007 reporting 7-year revision rates by four age categories (< 55 years, 55–64 years, 65–74 years, ≥ 75 years). Cumulative revision rates decreased with each increase in age category (19%, 13%, 8.6%, and 5.7%, respectively). Patients less than 65 years of had a significantly higher risk of revision than patients who were 65 years or older (cumulative revision rate at 7 years was 14% and 7.5%, respectively). This difference increased with time after surgery; Adj HR at 0–6 months = 1.23 (.95–1.6). *P* =.1; Adj HR at 6 months to 1.5 years = 1.8 (1.6–2.1), *P*< .001); Adj HR at ≥ 1.5 years = 1.96 (1.7–2.2), *P*< .001). Patients less than 55 years had a greater risk of revision than patients 55-64 years for the entire follow-up period (Adj HR = 1.52 (1.4–1.7), *P*< .001). This was observed in both males and females.

Figure 4. Revision rate of UKA in Sweden from 1986-1995 depending on age of patients.

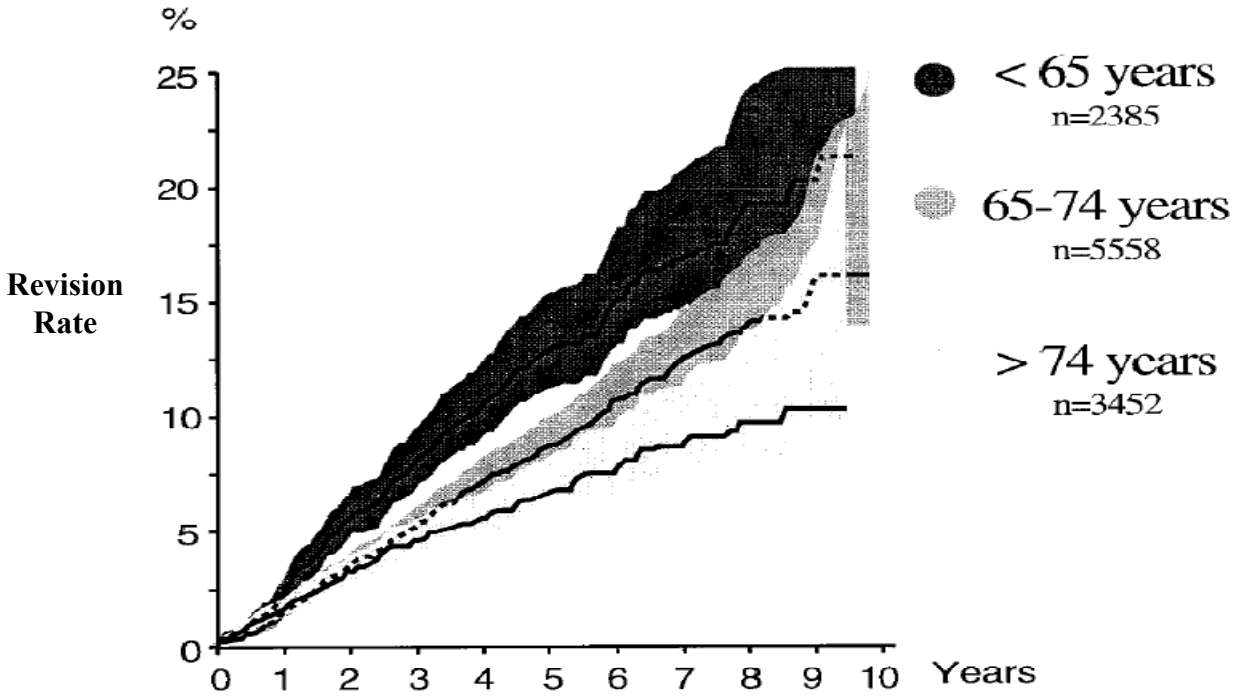


Figure used with permission.

- No peer reviewed articles summarizing UKA data from the *English/Wales National Joint Replacement Registry* were identified; therefore, we summarized data from their 2009 annual report which was based on patients undergoing UKA during the years 2003–2008[5]. Three year survival rates among those <65 years of age were 90.4% (95% confidence interval, 89.3–91.3). This was lower than those ≥ 65 years of age (95.3%, 95% confidence interval, 94.5–96.0), **Figure 5**. There were no analytical statistics reported (e.g., log rank test), or multivariate analyses producingAdj HRs for this comparison.

Figure 5. All implant-type 3- year survival stratified by younger (<65 years) and older (≥65 years) age.

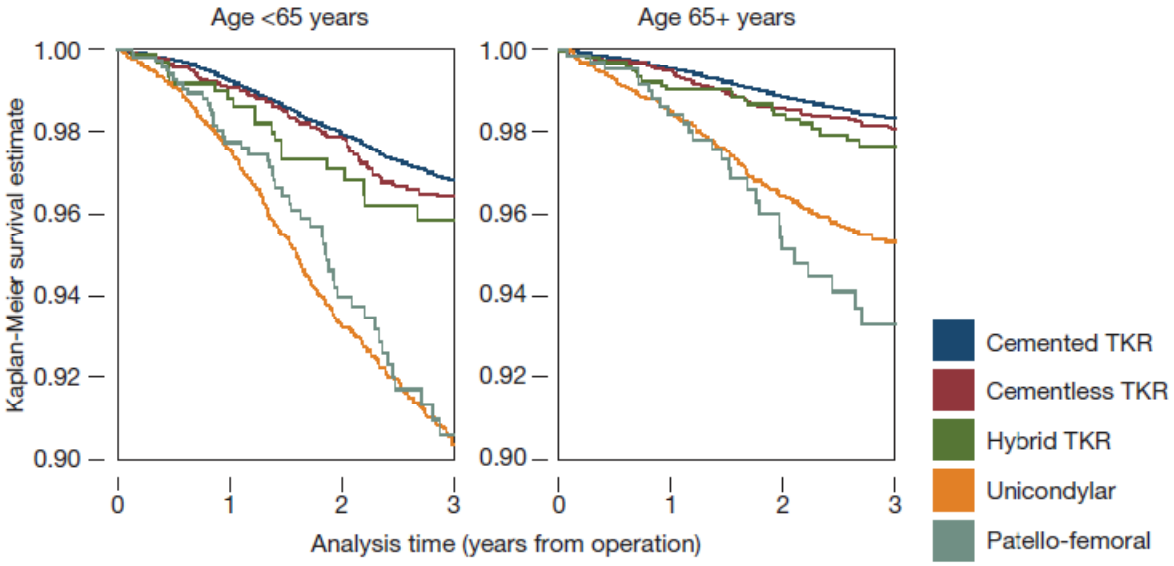


Figure used with permission from National Joint Registry of England and Wales.

- Koskinenet al.[87]reported data from the *Finnish Arthroplasty Register* on patients undergoing UKA during the years 1985–2003. Cumulative revision rates by age group were not reported; however, results from the Cox regression analysis demonstrated that younger patients (≤ 65 years of age) were at higher risk of revision than patients > 65 years of age, controlling for sex and brand of UKA (risk ratio, 1.5, 95% confidence interval, 1.1–2.0; *P* = .04).

- Gioeet al.[60] reported data from a community implant registry in Minnesota (Health East Hospital). Cumulative revision rates by age group were not reported; however, the authors reported age groups by category (< 65 years, 65–74 years, and ≥ 74 years) and found that age had "no effect" on revision rate (*P* = .11). No further data were presented to evaluate these findings.

Retrospective cohort studies

- Kuipers et al.[88] retrospectively reviewed survival rates in 437 patients with osteoarthritis (OA) at a mean of 2.6 years following UKA. Mean patient age was 63 years (range, 39–85) and 32% were male. The survival rate for patients < 60 years was 77.2% and ≥ 60 years was 89.4%. The hazard ratio for revision rates comparing younger age to older age was 2.2 (95% confidence interval, 1.1–4.4; *P* = .03), controlling for presence of patellofemoral joint OA, body mass index, gender, clinic, individual surgeon, and surgical caseload.

- Tabor et al.[155] retrospectively reviewed survival rates in 100 UKAs in 82 patients with OA. Mean patient age was not reported, 32% were male, and the mean follow-up was

146 (3–307) months. Five, 10, 15, and 20 year survival rates were reported for patients < 60 years of age and 60 years or older. These rates were 92%, 92%, 83%, and 77% for the < 60 year old group, respectively, and 95%, 89%, 85%, and 85% for the ≥ 60 year old group, respectively. The authors reported that survival was "comparable at all intervals"; however, no analytical statistics were reported.

- Price et al.[126] retrospectively reviewed revision rates in 447 OA patients with 564 UKAs with an unknown follow-up period. Mean patient age was 70 (35–96) years and 42% were male. The 10-year survival was 91% and 96% for patients < 60 years of age those ≥ 60 years of age, respectively (P = .6). The mean Hospital for Special Surgery (HSS) score for the younger group at 10 years was higher (94 points) than the older group (86 points), P = .001. The mean pre-surgical scores were 52 and 57 in the younger and older groups, respectively.

Obesity and UKA

Registry Data

- None of the previously reviewed registry studies evaluated obesity as a risk factor for revision after UKA.

Retrospective cohort studies

- Kuipers et al.[88] reported on the effects of obesity in addition to age (see demographic description above). A body mass index (BMI) of > 30 kg/m^2 did not predict implant survival after UKA in this population, controlling for age, presence of patellofemoral joint OA, gender, clinic, individual surgeon, and surgical caseload (P = .08). Only the p-value from the final model was reported. Unfortunately, revision rates for each category and an Adj HR with confidence interval were not reported to better determine if there may appear be a potential effect that was simply not significant at P< .05.

- Tabor et al.[155] reported on the effects of obesity in addition to age (see demographic description above). Five, 10-, 15-, and 20-year survival rates among obese were 100%, 100%, 91%, and 91%, respectively. For non-obese, survival rates were 93%, 87%, 82%, and 77%, respectively. Survival rates were superior for obese at all intervals. Statistical significance was achieved for 20-year survival only (P = .02).

- Heck et al.[66] retrospectively reviewed 255 patients with 294 UKAs and a mean follow-up of 6 years (up to 14.8 years). The majority of the patients had OA (85%), followed by osteonecrosis (9%), post-traumatic arthritis (4%), and unknown diagnosis (2%). Mean patient age was 68.2 years (22–92) and 37% were male. The mean patient weight was 106 kg (range, 50–136) and BMI was 25.5 kg/m^2 (range, 18.9–36.7). The authors reported the mean weight of patients requiring revision was 90.4 kg and the mean weight of patients with successful arthroplasty was 67 kg (P = .0003). The mean BMIs were 24.7 kg/m^2 and 32.6 kg/m^2 in the success and failure groups, respectively (no P-value reported). Patients who were obese (defined by authors as ≥ 81 kg) were more likely to undergo revision than those less than 81 kg (P = .0001). No effect estimate

was reported and authors did not control for other potential confounding factors such as age.

Sex and UKA

Registry Data

- We identified three peer-reviewed articles[59,62,87] summarizing registry data and one additional registry report. Harrysson reported data from the *Swedish National Joint Replacement Registry* for years 1988–1997 on 12,662 patients. The focus of this report was to determine the association between age and revision (see above). However, the authors included sex (men compared to women) in their multivariate model and found the association between sex and all-cause revision was not significant (risk ratio, .98, 95% confidence interval, .85–1.1; *P* = .71), adjusting for age and year of operation. The association between gender and revision caused by loosening of components was also not significant (*P* = .23). The rates by gender were not reported.

- No peer reviewed articles summarizing UKA data from the *English/Wales National Joint Replacement Registry* were identified; therefore, we summarized data from their 2009 annual report which was based on patients undergoing UKA during the years 2003–2008. Three year survival rates among females were 93% (95% confidence interval, 91.1–93.0). Three year survival rates among males were 93.5% (95% confidence interval, 92.6–94.3),**Figure 6**. There were no analytical statistics reported (e.g., log rank test), or multivariate analyses producingAdj HRs for this comparison.

Figure 6. All implant-type 3- year survival stratified by sex (male and female).

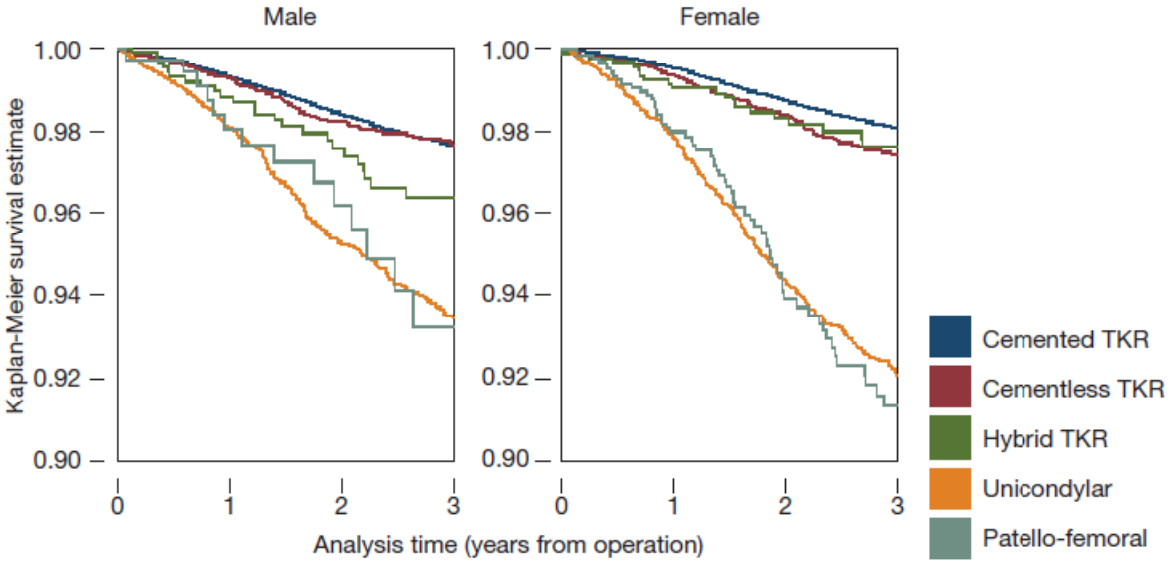


Figure used with permission from National Joint Registry of England and Wales.

- Koskinenet al.[86]reported data from the *Finnish Arthroplasty Register* on patients undergoing UKA during the years 1985–2003. Cumulative revision rates by age group were not reported, nor were effect estimates and confidence intervals; however, results from the Cox regression analysis demonstrated no significant difference in revision risk between males and females, adjusting for age and type of UKA.

- Gioeet al.[60]reported data from a Community Implant Registry in Minnesota (Health East Hospital). Cumulative revision rates by sex were not reported; however, the authors reported no significant association between sex and survival ($P = .90$).

Retrospective Cohort Studies

- Kuipers et al.[88] retrospectively reviewed survival rates on 437 patients with osteoarthritis (OA) at a mean of 2.6 years following UKA (demographics reported above). Survival rates by gender were not reported; however, results from a Cox regression analysis showed that gender was not associated with survival ($P = .11$), controlling for age, presence of patellofemoral joint OA, body mass index, clinic, individual surgeon, and surgical caseload.

- Tabor et al.[155]retrospectively reviewed survival rates on 100 UKAs in 82 patients with OA (demographics reported above). Five-, 10-, 15-, and 20-year survival rates among males were 87%%, 79%, 65%, and 56%, respectively. Survival rates among females were 97%, 95%, 92%, and 90%, respectively. Females had significantly higher survival rates than males at 10 years ($P = .03$), 15 years ($P = .04$), and 20 years ($P = .0007$). These analyses did not adjust for other potential confounding factors such as age.

- Heck et al.[66] retrospectively reviewed 255 patients with 294 UKAs and a mean follow-up of 6 years (up to 14.8 years). The demographics are reported above. The revision rate among men (2.4%) was lower than among women (3.9%), $P = .02$. No effect estimate was reported and authors did not control for other potential confounding factors such as age.

MulticompartmentDisease and UKA

Registry Data

- Robertsson et al.[133] summarized data from years 1986–1995 on 11,395 patients. The authors reported that patients with a multicompartment disease, such as rheumatoid arthritis, had much higher revision rates than those with one compartment OA, **Figure 7**. Rates per group or adjusted effect estimates were not reported.

Figure 7. Revision rate of UKA in Sweden from 1986-1995 depending on diagnosis.

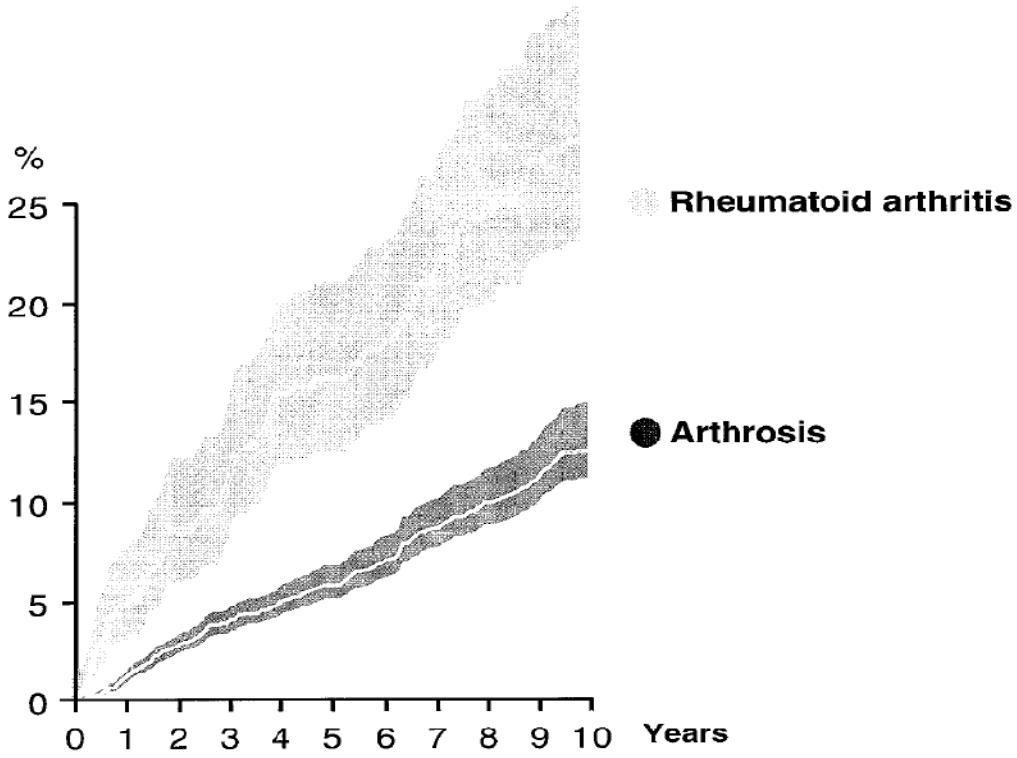


Figure used with permission

Retrospective Cohort Studies

- Kuipers et al.[88] reported from their multivariate analysis that the presence of patellofemoral OA was associated with decreased risk of revision (Adj HR = 0.3, 95% confidence interval, .11–.89; *P* = .03), controlling for age, body mass index, gender, clinic, individual surgeon, and surgical caseload. This amounts to an almost 70% reduction in revision risk over time. Two or more radiological features of patellofemoral OA were present in 98 of 437 procedures (22.4%). The agreement between observers for determining these features was fair (mean kappa = 0.39, standard error = 0.048).

Provider/Facility Characteristics and UKA

Retrospective Cohort Studies

Kuipers et al.[88] retrospectively evaluated the effects of different surgeons (n = 13), surgical caseload (≤10 or > 10 UKA per year), and different hospitals (n = 3) on UKA implant survival and did not find any significant associations (*P* =.53, .17, .78,

respectively). Revision rates for each category and an adjusted hazard ratio with confidence intervals were not reported.

Koskinenet al.[86]reported data from the *Finnish Arthroplasty Register* on patients undergoing UKA during the years 1985–2003. The authors reported no association with surgical caseload (≤10 or > 10 UKA per year). No revision rates per group or effect estimates were reported.

We found no articles evaluation differential characteristics in bicompartmental knee arthroplasty patients.

4.4.5. Simultaneous versus Staged Bilateral TKA

We found no randomized controlled trials comparing simultaneous versus staged bilateral knee arthroplasty. Eleven cohort studies were found making the comparison between simultaneous and staged bilateral TKA, and are summarized here. The study characteristics are found in Appendix F.

Effectiveness, Simultaneous vs. Stage Bilateral TKA (Table 28)

Knee pain

One cohort study reported on knee pain using a modified Knee Society Score (KSS). Mean pain scores were not significantly different for simultaneous (38.5) and staged (within 12 months) groups (39.3) after 3.9 years and 2.8 years follow-up, respectively[152].

Quality of Life Measures

One cohort study reported on SF-12 health-related quality of life scores. At 3.9 years and 2.8 years follow-up for thesimultaneous and staged (within 12 months) groups, respectively, no significant differences were found between the treatment groups regarding mean physical health scores (44.1 versus 43.3) or mean mental health scores (54.0 versus 54.5)[152].

Clinician Based Knee Scores

KNEE SCORE

Three cohort studies reported on knee scores using two clinician-based outcome measures: the KSS score (scale 0 100 points, lower score indicates greater disability) and the Hospital for Special Surgery (HSS) knee score (scale 0–100 points, lower score indicates greater disability). Forster et al.[55] found no significant difference in mean KSS Knee score between the simultaneous (92, 54–100), staged within one week (94, 58 – 100), and staged within 29 months (93, 49–100) groups at 4 year follow-up. Likewise, another study found no significant differences in KSS between the simultaneous and staged (within 1.4 years) groups at 3-, 5-, 7-, 10-, 12-, and 15-year follow-up[131]. With respect to the HSS, one study reported significantly higher mean HSS scores in those

staged within one week (94, 77–100) compared with the those staged within 29 months (91, 72–99) and those getting having bilateral TKA simultaneously (91, 73–100) (*P* = .02) at 4 year follow-up[55]. Another study found no significant difference in mean HSS score between the simultaneous (84.1, range 71–95) and staged (within 7.4 days) (85.3, range 74–94) group at a 31 month follow-up[92].

FUNCTION SCORE

Two studies reported on knee function using the KSS score (scale 0–100 points, lower score indicates lower functionality). One study reported a significantly lower mean functional score in the staged (within 29 months) group (84, 30–100) compared with the staged (within one week) group (89, 0–100) and the simultaneous group (90, 0–100) at 3.9 year, 4.1 year, and 4.8 year follow-up, respectively (*P* = .02)[55]. The other study also found significantly lower mean KSS Function score in the staged (within 12 months) group (69.9) than the simultaneous group (78.9) at 2.75 year and 3.86 year follow-up (*P* = NR)[152].

Revision and Prosthesis Survival

Two studies reported revisions after surgery. One study reported that the ten-year probability of survival of the prosthesis was not significantly different for the simultaneous group (98.3%, 95% CI: 97.5%, 99.1%) compared with the staged (within 1.4 years) group (99.5%, 95% CI: 98.6%, 100%)[131]. In the other study the simultaneous group had one revision (1.64%) compared with no revisions in the staged group after three years of follow-up[152].

Range of motion

Two studies reported on range of motion; neither study reported significant differences between treatment groups. In one study at 4.8 year, 4.1 year, and 3.9 year follow-up for the simultaneous, staged (within 1 week), and staged (within 29 months) groups, respectively, the mean flexion range was 122° (90°–145°), 123° (90°–145°), and 120° (85°–135°)[55]. Another study reported a mean postoperative ROM of 100° in the simultaneous group and 105° in the staged (7.4 days) group at the 31 month follow-up[92].

Table 28. Effectiveness Outcomes comparing Simultaneous with Staged Bilateral TKA

Outcome	Bilateral TKA: Simultaneous	Bilateral TKA: Staged [within time frame]	*P*-value	Follow-up [staged time frame]
PAIN				
American Knee Society Score (AKS) (mean)				
Stubbs 2005	38.5	39.3	ns	*Simultaneous*: 3.86 yrs *Staged*: 2.75 yrs
PATIENT-REPORTED HEALTH STATUS (mean)				
SF-12 Physical Score				
Stubbs 2005 (mean, range)	44.1	43.3	ns	*Simultaneous*: 3.86 yrs *Staged*: 2.75 yrs
SF-12 Mental Score				
Stubbs 2005 (mean, range)	54.0	54.5	ns	*Simultaneous*: 3.86 yrs *Staged*: 2.75 yrs
CLINICIAN BASED KNEE SCORES				
American Knee Society Score (AKS)				
Knee Score (mean, range)				
Forster 2006	92 (54–100)	94 (58–100)[1 wk] 93 (49–100) [ave. 29 mos]	ns	*Simultaneous*: 4.8 yrs*Staged:* 4.1 yrs[1 wk] 3.9 yrs [*ave. 29 mos]*
Ritter 2003	90.2 91.9 91.3 86.5 87.1 88.6	92.4 90.7 87.4 84.8 78.2 62.0	ns ns ns ns nsn s	3 yrs 5 yrs 7 yrs 10 yrs 12 yrs 15 yrs
Function Score (mean, range)				
Forster 2006	90 (0 – 100)	89 (0–100) [1 wk] 84 (30–100)[ave.29 mos]	ns .02	*Simultaneous*: 4.8 yrs*Staged:* 4.1 yrs[1 wk] 3.9 yrs [*ave. 29 mos]*
Stubbs 2005	78.9	69.9	<.05	*Simultaneous*: 3.86 yrs *Staged*: 2.75 yrs
Hospital for Special Surgery knee scale (HSS)				
Knee Score				
Forster 2006 (mean, range)	91 (73–100)	94 (77–100) [1 wk] 91 (72–99) [ave. 29 mos]	.02 ns	*Simultaneous*: 4.8 yrs*Staged:* 4.1 yrs[1 wk] 3.9 yrs [*ave. 29 mos]*
Liu 1998 (mean, SD, range)	84.1 (71–95)	85.3 (74–94)	ns	31 months
REVISION/PROSTHETIC SURVIVAL				
Revision (%, n/N)				
Stubbs 2005	1.64% (1/61)	0% (0/38)	ns	3 years
Survival (end point: revision)				
Ritter 2003 (probability of survival, 95% CI)	98.3% (97.5%, 99.1%)	99.5% (98.6%, 100%)	ns	10 years

All denominators = number of patients.
NR: Not reported.
ns: not significant.

Safety, Simultaneous vs. Staged Bilateral TKA (Table 29)

Mortality
Ten studies specifically reported mortality. Three studies reported no deaths in the perioperative period[92,152,173].

Four studies[101,103,129,151] reported on 30-day mortality. Mortality within 30 days is thought by some likely to be causally associated with surgery[151]. In one large study using a Medicare database, Ritter et al[129] reported a higher rate of mortality in the simultaneous group (0.99%) compared with four groups staged at time periods ranging from 6 weeks to 12 months (mortality rates ranged from 0.29% to 0.48%; cause of death was not reported). By the one- and two-year follow-ups, respectively, the mortality rates were similar (2.79% and 3.75% for the simultaneous group and 1.94% to 2.83% and 2.98% to 4.05% for the four staged groups). A second study reported higher mortality at 30 days post surgeryin the simultaneous group (0.97%) compared with the staged (within 12 months) group (0.15%) (HR = 7.53, 95% CI: 2.62, 21.69, after adjusting for differences in age, gender, and year of operation)[151]. The primary causes of death for the simultaneous group were diseases of the circulatory system and pulmonary embolism; cause of death was not reported for the staged group. The third study reported a higher 30-day mortality rate in the simultaneous group (7.4%) compared with the staged group (0%), however this was not statistically different[103]. All four deaths in the simultaneous group were cardiac-related and in patients over 75 years of age. The fourth study had small sample sizes and reported no deaths in the simultaneous (0/91), or staged (0/32) groups[101].

One registry study[160] compared mortality after 90 days following surgery and found no difference between groups, (OR: 0.70, 95% CI: 0.31, 1.55; $P = .48$). The length of time between staging for this study is unknown as any second replacement surgery was assumed to represent a planned, staged, bilateral procedure. No causes of death were reported.

Comparison of mortality rates in simultaneous versus staged bilateral TKA is difficult in non-randomized trials. Confounding by indication is one problem. In general, those who are sicker are more likely to have staged bilateral TKA, and hence, may be more likely to die following surgery. This bias would result in an overestimation of mortality in the staged group. On the other hand, some patients who are scheduled for staged bilateral TKA end up having a serious complication or die after the first surgery and before they receive the second. These patients should be counted as part of the staged cohort but are excluded. Those that are included are only patients that have survived the first operation,

and these may have certain survival characteristics that will make them more likely to survive the second operation. This could result in survival overestimates in favor of staged bilateral TKA.

Thromboembolic Events

DVT and PE were reported infrequently. There were no statistical differences between groups in risk of DVT and PE reported in six studies documenting venous thromboembolism[12,55,92,131,151,173].

Wound Complications

There were no statistical differences in deep wound infections between simultaneous and staged bilateral TKA as reported by three studies[92,131,152], risks ranged from 0% to 1% of the knees in each group. With respect to superficial infection, three studies reported no significant intergroup differences in the risk of superficial infection[92,131,173]. One large study[129] reported a statistically lower risk of superficial wound infection in patients receiving simultaneous bilateral TKA (0.05%) compared with those obtaining staged replacement (0.9% staged at 6 weeks or 3 months, 0.8% staged at 6 months and 1.1% staged at 12 months after index surgery). Prolonged wound drainage was reported by two studies, ranging from 0% to 1.3% and from 0% to 2.6% in the simultaneous and staged bilateral TKA groups, respectively, with no significant differences between groups[55,173].

Ischemic Events

Ischemic events, (with permanent or temporary consequences) included acute myocardial infarction, cerebrovascular accident and postoperative confusion. There was no statistical difference between groups in three studies reporting myocardial infarction (from 0% to 1.5% in simultaneous bilateral TKA and 0% to 1.3% in staged)[131,151,152] or in two studies reporting cerebrovascular accident (no cases in the simultaneous group and one case in the staged group)[55,131]. Postoperative confusion occurred at similar rates in three studies ranging from 1.7% to 14.6% in the simultaneous group and 0% to 11.8% in the staged group[55,152,173].

Prosthetic Complications

Reports of prosthetic complications were reported in two studies[55,92] and included aseptic loosen and anterior impingement. The occurrence of these complications ranged from 0% to 3.6% in the simultaneous group compared with 0% to 8.3% in the staged group, respectively. There were no reported statistical differences between treatment groups.

Other Complications

Other complications reported infrequently in the studies include GI-related complications (0.9%–24% versus 1.3%–27.5%), knee pain (0% versus 0%–2.8%), prolonged wound drainage (0%–1.3% versus 0%–2.6%), and urinary problems (0%–6.3% versus 0%–2.6%) for the simultaneous and staged groups, respectively.One study reported a significantly higher rate of surgical complications in all staged groups (3.4%–3.9%) compared with the simultaneous group (2.4%, $P< .001$)[129]. Another study reported a significantly higher rate of systemic complications (including pneumonia, confusion, acute renal failure, and mortality) in the simultaneous group (5.0%) compared with the staged (12 months) group (0.8%, $P< .05$), with most of the complications arising during the immediate postoperative period[173]. All systemic complications in the simultaneous group were in patients older than 70 years.

Total Complications

Total complications were reported inconsistently among studies. Some studies had a higher overall complication rate in the simultaneous group and other studies had a higher complication rate in the staged group(s).

Postoperative blood loss

Four studies reported on postoperative blood loss, with two of the studies reporting significantly less blood loss in the staged group. One study found significantly greater blood loss in the simultaneous group (3312 ml, 1280–4705) compared with the group undergoing TKAs staged one week apart (2578 ml, 720–4735; $P = .004$); however, blood loss was similar when compared to the other staged (29 months) group (3011 ml, 1335–4810)[55]. Another study also found significantly more blood loss in the simultaneous group (2744 ± 727.2, 1185–4700) compared with the staged (7.4 days) group (2403 ± 551.2 ml, 1565–3735; $P< .022$)[92].In one study the simultaneous group had an average blood loss of 1701.8 ml (480–4410) compared with 896 ml (160–3735) in the staged (within 12 months) group, but this difference was not tested statistically[152]. One study found no significant difference in mean blood loss in the simultaneous group (1299 ml, range 480–2625) compared with the staged (12 months) group (1302 ml, 130–2734 ml)[173].

Length of hospital stay, Simultaneous vs. Staged Bilateral TKA

Six studies reported on mean length of hospital stay, with five of the studies reporting a significantly shorter length of hospital stay in the simultaneous group. Length of hospital stays for the simultaneous and the staged groups, respectively, were: 7.5 days (range 5–15) versus 11.7 days (average for both hospital stays, range 8–18, staged within 12 months; $P< .0001$)[173]; 11 days (7–15) versus 15 days (12–23; staged within one week) and 14 days (10–24, staged within 29 months; $P< .0001$)[55]; 5.8 days (± 2.0) versus 9.4

days (± 2.29; staged within 184 days; $P< .0001$)[101]; 16.5 days (± 4.58, range 12–30) versus 20.9 days (± 3.47, range 1–37, staged within 7.4 days; $P< .00046$)[92]; and a median of 12 days compared with a range of 20–21 days all four staged groups ($P = .0001$)[129]. The sixth study reported that the simultaneous group had an average hospital stay of 11 days and the staged (within 12 months) group had an average of 8 days, but this difference was not tested statistically[152].

Summary, Simultaneous vs. Staged Bilateral TKA

There are no randomized controlled trials comparing simultaneous with staged bilateral TKA.

Effectiveness

- Data from four retrospective cohort studies suggest that there are similar pain and functional outcomes following bilateral TKA over varying follow-up periods whether patients receive simultaneous or staged replacement (staged within one year). However, the evidence for this is weak given the biases inherent in the study designs of those trials seeking to answer this question.

Safety

- Short term mortality is thought by some likely to be causally associated with surgery. In four studies reporting on this outcome, three reported a higher frequency of death with simultaneous bilateral TKA compared with staged TKA. Whether this association actually exists is difficult to determine given the likelihood of selection bias (e.g. only including those that survived the first surgery in the staged group).
- There is no evidence among six studies that venous thromboembolism occurs more frequently in either group.
- The risk of deep infection is reported similarly between groups. Superficial infections were more frequent in staged bilateral TKA in one very large study.
- In general, other complications were reported inconsistently among studies and occurred relatively infrequently in both groups.

Table 29. Safety comparing Simultaneous with Staged Bilateral TKA

	Bilateral TKA		
	Simultaneous	**Staged [within time frame]**	***P*-value**
MORTALITY			
Yoon (2010) (perioperative period)	0% (0/119)	0% (0/119)	ns
Stefansdottir (2008) (within 30 days)	0.97% (11/1139)	0.15% (5/3432)	.003
Forster (2006) (3 – 5 year f/u)*	7.1% (2/28)	0% (0/36) [1 wk]	ns
		2.6% (1/38) [ave. 29 mos]	ns
Stubbs (2005) (perioperative period)	0% (0/61)	0% (0/38)	ns
Macario (2003) (within 30 days)	0% (0/91)	0% (0/32)	ns
Ritter (2003) (within 12 months)	1.2% (25/2050)	0.7% (1/152)	ns
Mangaleshkar (2001) (within 30 days)	7.4% (4/54)	0% (0/34)	ns
Liu (1998) (perioperative period)	0% (0/64)	0% (0/24)	ns
Ritter (1997) (within 30 days)	0.99 % (128/12922)	0.48% (21/4354) [6 wks]	.0012
		0.29% (13/4524) [3 mos]	.000
		0.31% (30/9829) [6 mos]	.000
		0.36% (113/31401) [12 mos]	.000
Survival (end point: death) (probability of survival to 9 years, 95% CI)			
Ritter (2003)	80.9% (77.7%, 84.2%)	84.4% (72.8%, 95.9%)	ns
THROMBOEMBOLIC EVENTS (%, N/N)			
DVT			
Yoon (2010)	0% (0/119)	0% (0/119)	
Ritter(2003)	0.9% (18/2050)	0.7% (1/152)	ns
Liu (1998)	0% (0/64)	4.2% (1/24)	ns
PE			
Yoon (2010)	0% (0/119)	0% (0/119)	
Stefansdottir (2008)†	0.35% (4/1139)	NR	NR
Barrett (2007)§	1.44% (NR)	0.54% (NR)	NR
Forster (2006)	3.6% (1/28)	2.8% (1/36) [1 wk]	ns
		5.3% (2/38) [ave. 29 mos]	
Liu (1998)	0% (0/64)	0% (0/24)	ns
WOUND COMPLICATIONS			
Deep infection within knee joint			
Stubbs (2005)	0% (0/122 knees)	0% (0/76 knees)	ns
Ritter (2003)	0.8% (31/4100 knees)	1.0% (3/304 knees)	ns
Liu (1998)	0.8% (1/128 knees)	0% (0/48 knees)	ns
Superficial wound infection			
Yoon (2010)	1.3% (3/238 knees)	1.3% (3/238 knees)	NR
Ritter(2003)	0.3% (14/4100 knees)	0.3% (1/304 knees)	ns
Liu (1998)	0.8% (1/128 knees)	2.1% (1/48 knees)	ns
Ritter (1997)	0.05% (7/12922)	0.9% (39/4354) [6 wks]	< .001
		0.9% (41/4524) [3 mos]	
		0.8% (79/9829) [6 mos]	
		1.1% (345/31401) [12 mos]	
Prolonged wound drainage			
*Yoon (2010)***	1.3% (3/238 knees)	0.8% (2/238 knees)	ns
Forster (2006)	0% (0/28)	0% (0/36) [1 wk]	ns
		2.6% (1/38) [ave. 29 mos]	
ISCHEMIC EVENTS			
Acute myocardial infarction			
Stefansdottir (2008)†	0.35% (4/1139)	NR	NR
Stubbs (2005)	0% (0/61)	0% (0/38)	ns

	Bilateral TKA		
	Simultaneous	**Staged [within time frame]**	***P*-value**
Ritter (2003)	1.5% (31/2050)	1.3% (2/152)	ns
Liu (1998)	0% (0/64)	0% (0/24)	ns
Cerebrovascular accident			
Stefansdottir (2008)	0% (0/1139)	NR	
Forster (2006)	0% (0/28)	2.8% (1/36) [1 wk] 0% (0/38) [ave. 29 mos]	ns
Ritter(2003)	0.3% (6/2050)	0% (0/152)	ns
Confusion			
Yoon (2010)	1.7% (2/119)	0% (0/119)	ns
Forster (2006)	3.6% (1/28)	5.6% (2/36) [1 wk] 0% (0/38) [ave. 29 mos]	ns
Stubbs (2005)††	14.6% (9/61)	11.8% (9/76)	ns
PROSTHETIC COMPLICATIONS			
Anterior impingement requiring insert change to rotating platform			
Forster (2006)	3.6% (1/28)	8.3% (3/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Asceptic loosening			
Forster (2006)	0% (0/28)	0% (0/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Liu (1998)	0% (0/128 knees)	0% (0/48 knees)	ns
OTHER COMPLICATIONS			
Acute renal failure			
Yoon (2010)	0.8% (1/119)	0% (0/119)	ns
Anterior knee pain requiring secondary patellar resurfacing			
Forster (2006)	0% (0/28)	2.8% (1/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Arthrofibrosis			
Forster(2006)	7.1% (2/28)	5.6% (2/36) [1 wk] 18.4% (7/38) [ave. 29 mos]	ns
Bed sore			
Liu (1998)	7.8% (5/64)	4.2% (1/24)	ns
Cardiac problems (non-MI)			
Stubbs (2005)	26.2% (16/61)	28.9% (22/76)	ns
Congestive heart failure			
Liu (1998)	0% (0/64)	8.3% (2/24)	ns
Gastrointestinal tract complications			
Stefansdottir (2008)	0% (0/1139)	NR	
Stubbs (2005)††	24% (15/61)	27.5% (21/76)	ns
Ritter(2003)	0.9% (19/2050)	1.3% (2/152)	ns
Hypovolemic shock			
Yoon (2010)	0% (0/119)	0.8% (1/119)	ns
ICU care			
Yoon (2010)	0.8% (1/119)	0% (0/119)	ns
Macario (2003)	3.3% (3/91)	3.1% (1/32)	ns
Nosocomial infection			
Ritter (1997)	11.8% (1525/12922)	13.2% (575/4354) [6 wks] 10.9% (493/4524) [3 mos] 11.5% (1130/9829) [6 mos]	< .001

	Bilateral TKA		
	Simultaneous	**Staged [within time frame]**	***P*-value**
		13.2% (4145/31401) [12 mos]	
Other circulatory system diseases			
Stefansdottir (2008)†	0.18% (2/1139)	NR	NR
Patellar subluxation			
Liu (1998)	3.9% (5/128 knees)	2.1% (1/48 knees)	ns
Pneumonia			
Yoon (2010)	0.8% (1/119)	0% (0/119)	ns
Pseudo-obstruction			
Forster (2006)	0% (0/28)	2.8% (1/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Respiratory complications (including atelectasis, hypoxia, and pneumonia)			
Stefansdottir (2008)	0% (0/1139)	NR	
Stubbs (2005)††	3% (2/61)	13% (10/76)	ns
Return to surgery (reason not stated)			
Macario (2003)	1.1% (1/91)	0% (0/32)	ns
Severe chronic post-operative pain			
Forster (2006)	0% (0/28)	0% (0/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Surgical complications including wound dehiscence, infection, hemorrhage, mechanical complications of orthopedic device			
Ritter (1997)	2.4% (310/12922)	3.5% (152/4354) [6 wks] 3.5% (158/4524) [3 mos] 3.4% (334/9829) [6 mos] 3.9% (1225/31401) [12 mos]	< .001
Surgical removal of retained drain			
Forster (2006)	0% (0/28)	0% (0/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Uremic encephalitis			
Yoon (2010)	0.8% (1/119)	0% (0/119)	ns
Urinary retention or other unspecified urinary problems			
Stefansdottir (2008)	0% (0/1139)	NR	
Forster (2006)	0% (0/28)	0% (0/36) [1 wk] 2.6% (1/38) [ave. 29 mos]	ns
Ritter(2003)	1.2% (25/2050)	0% (0/152)	ns
Liu (1998)	6.3% (4/64)	0% (0/24)	ns
Vascular complications			
Ritter (1997)	5.7% (737/12922)	4.1% (179/4354) [6 wks] 4.5% (204/4524) [3 mos] 5.7% (560/9829) [6mos] 6.8% (2135/31401) [12 mos]	< .001
Total complications‡			
Yoon (2010)	10.1% (12/119)	9.2% (11/119)	NR
Stefansdottir (2008)	0.9% (10/1139)	NR	NR
Forster (2006)	17.9% (5/28)	30.6% (11/36) [1 wk] 44.7% (17/38) [ave. 29 mos]	ns
Stubbs (2005)††	68.9% (42/61)	81.6% (62/76)	NR
Macario (2003)	4.4% (4/91)	3.1% (1/32)	NR
Ritter (2003)	5.9% (121/2050)	4.6% (7/152)	NR

	Bilateral TKA		
	Simultaneous	**Staged [within time frame]**	***P*-value**
Liu (1998)	25% (16/64)	25% (6/24)	NR
Ritter (1997)	20.0% (2578/12922)	21.7% (945/4354) [6 wks] 19.8% (896/4524) [3 mos] 21.4% (2103/9829) [6 mos] 25.0% (7850/31401) [12 mos]	NR

Denominators = number of patients unless otherwise specified.
NR: Not Reported; ns: not significant.
*Deaths unrelated to surgery.
†Patient(s) died.
‡Patients could have more than one complication.
§Estimate of probability of pulmonary embolism in the first three months after surgery for patients who had a simultaneous bilateral TKA or the first of a planned staged bilateral TKA; based on actuarial life table techniques.
**Prolonged wound drainage defined as 4 or more days of postoperative discharge through the wound.
††Per hospital admission; GI and respiratory complications estimated from a graph.

Summary, Simultaneous vs. Staged Bilateral TKA

There are no randomized controlled trials comparing simultaneous with staged bilateral TKA.

Effectiveness

- Data from four retrospective cohort studies suggest that there are similar pain and functional outcomes following bilateral TKA over varying follow-up periods whether patients receive simultaneous or staged replacement. However, the evidence for this is weak given the biases inherent in the study designs in those trials seeking to answer this question.

Safety

- Short term mortality (within 30 or 90 days of surgery) is thought by some likely to be causally associated with surgery. In four studies reporting on this outcome, three consistently report a higher frequency of death with simultaneous bilateral TKA compared with staged TKA. Whether this association actually exists is difficult to determine given the likelihood of selection bias and the bias inherent in including only the healthiest patients in the staged group (those that survive the first operation).
- There is no evidence among five studies that venous thromboembolism occurs more frequently in either group.
- The risk of deep infection is reported similarly between groups. Superficial infections were more frequent in staged bilateral TKA in one very large study.
- In general, other complications were reported inconsistently among studies and occurred relatively infrequently in both groups.

4.5. Key Question 5
What is the evidence of cost implications and cost effectiveness of CN-TKA and partial knee arthroplasty?

There is limited evidence on the cost-effectiveness of CN-TKA compared with CONV-TKA and UKA compared with TKA.

4.5.1. CN-TKA versus CONV-TKA, Cost Effectiveness

Australian HTA (2009):
This HTA examined the effectiveness and cost implications of CN-TKA compared withCONV-TKA surgery. The authors conducted a literature review to identify relevant economic studies, and then conducted a within-HTA cost-effectiveness analysis to determine what improvement in revision rate would be required to make CN-TKA cost-effective.

In the literature review, they identified three relevant economic evaluations[47,118,145]. Given the lack of long-term clinical trial data on CN-TKA, all three studies used modeling techniques to estimate cost-effectiveness. However, the lack of long-term data underscores this study as an early assessment of cost-effectiveness.

The Dong study (UK, 2006)[47] suggested that CN-TKA was associated with only a slight improvement in QALYs and reduced revision and complication rates; and that CN-TKA was potentially cost-saving in the long term (given the high initial investment in the technology).

The Novak study (USA, 2005)[118] conducted a cost-effectiveness model of CN-TKA using inputs from published literature, and suggested that computer-assisted technology is associated with increased cost (US$1500 per procedure) as well as improvement in coronal alignment precision with a ICER of US$45,554 per QALY. Technology cost, accuracy of alignment, and probability of revision with misalignment were the most sensitive variables.

Slover and colleagues (USA, 2008)[145] constructed a Markov decision model to estimate the impact of hospital volume on the cost-effectiveness of CN-TKA. Not surprisingly given the initial cost of purchasing and implementing the technology, the model suggests that CN-TKA becomes more cost-effective as hospital volume increases.

These studies suggest that there is limited data available on the effectiveness of CN-TKA, making economic models highly likely to change. Also, since CN-TKA requires an initial investment by a health care system, the cost effectiveness of the technology is dependent, at least in the short term, by the time horizon considered and the number of procedures conducted.

The CEA conducted by the authors of the HTA was designed to determine what improvement in revision rate would be necessary to make CN-TKA cost effective from a health care system perspective. They conducted a Markov model of four scenarios using a 10-year revision rate forCONV-TKA of 6%:
Scenario 1: no improvement in revision rate between CN-TKA and CONV-TKA (most conservative),
Scenario 2: a 1 percentage point reduction in the 10-year revision rate (17% improvement versus CONV-TKA)
Scenario 3: a 2 percentage point reduction in the 10-year revision rate (33% improvement versus CONV-TKA)
Scenario 4: a 3 percentage point reduction in the 10-year revision rate (50% improvement versus CONV-TKA)

The model suggested that CN-TKA would not likely be cost-effective (<$50,000 per QALY) for scenario 2, only cost-effective for scenario 3 after 15 years following surgery, and only cost-effective in scenario 4 after 10 years following surgery.

Sensitivity analysis demonstrated that the ICERs are driven by the capital cost of the CN equipment, the predicted reduction in revision rate and the utility weight "normal health after TKA revision".

4.5.2. UKA versus TKA, Cost Effectiveness

We found three peer-reviewed economic evaluations; two conducted in US settings. All three studies found that total knee and unicompartmental knee arthroplasty have small differences in costs and outcomes; in the US studies this translated to incremental cost effectiveness ratios favoring UKA; in the Singapore study favoring total knee replacement. All three studies highlight the lack of long-term data from randomized controlled trials; conclusions are subject to change as more evidence becomes available. Each study is summarized below and in Table 30.

Xie 2009
Xie et al (2009)[171] conducted a cost utility analysis comparing the costs and 2-year outcomes of total knee replacement (TKR) and unicompartmental knee arthroplasty (UKA). They used data from an observational prospective cohort study of patients at SingaporeGeneralHospital during 2003. Participants completed the OKS joint function scale and the SF36 and were used as the health outcome. Microcosting methods were used to estimate costs for each patient using hospital data and are presented in 2008 US dollars. The study used a societal perspective as the base case (total resources consumed, direct costs only) and also calculated incremental cost-utility ratios (ICUR) for a patient (copay cost) and government (subsidy cost) perspective.

At two years of follow up, costs were higher for TKR (US$8513 vs $6824, *P*<.001) and associated with slightly higher QALYs gained, though QALY difference was not

statistically significant and marked by a wide individual variation, especially for UKA (Table 30). The base case ICUR was $65,245/QALY for the societal perspective. A comparable ICUR was estimated using the patient perspective; but the ICUR from the government perspective was markedly lower, $4860/QALY. Bootstrapping sensitivity analysis suggested that in 15% of the base case samples, TKR was dominated by UKA. Their cost effectiveness acceptability curves suggested that the probability of TKR being <$50,000/QALY to be 0.4. The authors highlight the importance of the choice of perspective and conclude that they cannot conclude with 95% confidence that TKR is more costeffective than UKA.

We found this to be a reasonably well-conducted economic evaluation, and assigned it a QHES quality score of 77/100; deductions from a perfect score of 100 came from the unclear presentation of cost and outcome data and in the lack of discussion of direction of possible bias. The use of patient-level data, if not from a randomized controlled trial, is a main strength. However, as with many economic evaluations conducted outside of the US, for our purposes the generalizability, especially of cost data, is unknown and likely limited. In this case, patient and payer contributions to total cost may be very different than in the Xie study population. In addition, specific variables that would ease comparison with the other studies we assessed, such as revision rate and prosthetic survival, are not presented (though they appear to have been calculated in the measurement of resource use). We agree with the authors that the study highlights the importance of the perspective taken in any economic evaluation.

SooHoo 2006 (USA)

SooHoo and colleagues[146] conducted a cost utility analysis comparing UKA to TKA in a target population of 65 year olds with unicompartmental knee arthritis. The authors obtained clinical probabilities and utilities from a literature review and cost estimates from Medicare reimbursement schedules. Outcomes of the model were revisions/complications over an 18 year time horizon. TKA prosthetic was assumed to have a survival of 15 years; unicompartmental prosthetic 12 years. Sensitivity analyses provided model estimates for a range of implant survival and procedure cost.

The reference case analysis found similar costs and QALYs for both procedures, resulting in an ICER of $277/QALY. Sensitivity analyses suggested that if unicompartmental prosthetic survival is four or more years less than TKA prosthetic survival, TKA remains the dominant procedure (more effective and less costly). However, under base case assumptions, if the cost of unicompartmental knee arthroplasty was decreased by 25%, it became the dominant procedure. The authors conclude that there is potential for unicompartmental surgery to be a cost-effective intervention but that there is high uncertainty around prosthetic survival and procedure costs.

This is a reasonably well-conducted economic evaluation that conforms to current guidelines for economic evaluation methods. Our assessment of study quality using the QHES is 80/100. Its main weaknesses, as the authors acknowledge, is the paucity of long-term clinical trial data directly comparing total knee arthroplasty to unicompartmental arthroplasty. The study perspective is not clearly stated, but from the gross-costing methods employed using Medicare reimbursement rates we may infer a

payer perspective. Overall, the SooHoo evaluation suggests that unicompartmental knee arthroplasty is potentially cost-effective as long as prosthetic survival is within 4 years of that of TKA.

SLOVER 2006

Slover and colleagues (2006, USA)[144] conducted a cost utility analysis of UKA compared to conventionalTKA in a hypothetical cohort of 78 year old people with unicompartmental arthritis. A Markov model estimated transitions to a well health state, procedure revision, or death at 20 years post procedure. Clinical probabilities were extrapolated from the Norwegian Arthroplasty Register database, utilities were from published literature, and costs were obtained from Medicare reimbursement schedules. The base case analysis suggested similar average costs and QALY gains for both technologies; however, UKA was estimated at slightly less cost ($200) and slightly more QALYs (0.05) than TKA, making it the dominant technology. Sensitivity analyses suggested that implant survival rates, perioperative mortality, infection, and utility values could alter the results of the model and cause UKA to cease being dominant or cost-effective at the threshold of <$50,000/QALY or TKA to become more cost-effective. The authors conclude that UKA and TKA have similar cost and effectiveness profiles in the elderly population.

We found this to be an adequately conducted study generally consistent with current standards for economic evaluations (QHES score: 85). The study's main strengths were in its access to registry data, a good alternative if randomized trial data is lacking, and its attempt at comprehensive inclusion of relevant variables, including disutilities and perioperative mortality. The main weaknesses are in the lack of generalizability to a younger population and in its relatively unclear presentation of data sources and base case characteristics, including revision rates. Overall, this study suggests similar costs and outcomes for unicompartmental and total knee arthroplasty.

CONCLUSIONS, COST EFFECTIVENESS

CN-TKA versus CONV-TKA

- There is insufficient data to make strong conclusions about the long-term cost effectiveness of CN-TKA.
- Modeling suggests that CN-TKA is potentially a cost effective intervention compared withCONV-TKA if the 10-year revision rate is reduced by between 33 to 50%.

UKA versus TKA

- There is some evidence that UKA and conventional TKA have similar cost and quality-adjusted outcome profiles from a health care perspective
- Lack of data precludes assessment of the cost effectiveness of UKA in people under age 65.

Table 30. Summaries of economic studies comparing UKA with TKA.

Study	Design	Population & Model inputs	Methods of analysis/ strengths& limitations	Relevant results	Results of sensitivity analysis	Author conclusions

Study	Design	Population & Model inputs	Methods of analysis/ strengths& limitations	Relevant results	Results of sensitivity analysis	Author conclusions
Xie (2009) Singapore	Cost utility analysis Intervention: Total knee replacement (TKA) Comparator: Unicompartmental knee arthroplasty (UKA) Perspectives: 1 (base case)-Societal (total resources consumed) 2-Patient (copayment by patient) 3-Government (subsidy by government) Outcomes at 2 years discounted 3.5%	Resource use and outcomes from non-randomized 2-year prospective observational cohort study; hospital data (Singapore) Population: People with knee osteoarthritis choosing TKA (n=431) or UKA (n=102) in 2003 who had not undergone knee surgery in past 6 months Direct costs estimated using unit costing methods: -Health professional; test; prosthesis; other device; medication; physiotherapy; ward; and overhead Outcome: function measured by OKS (scale of procedure- and joint-specific function (measured at 6 mo and 2 years) Utility: SF-36 (generic health-related QOL measure) (measured at 6 mo and 2 years)	Calculation of total costs, QALYs gained 95% confidence interval estimated by nonparametric bootstrapping Cost-effectiveness acceptability curves showing the probability that the intervention is cost-effective at various levels of willingness to pay $/QALY Strengths: -Use of patient level data -Estimation of uncertainty -Use of societal, patient, and government perspectives Limitations: -Direct costs only -No sensitivity analysis for individual variables -Generalizability to US setting unknown	TKA and UKA pts comparable on all baseline characteristics but mean age (67 vs. 63; *P*=.01) Wide individual variation in outcome (~85% TKA favorable) Average length of stay: TKA 7.7 vs UKA 5.3 (*P*<.001) Total costs (2008 USD) Society: TKA $8513 UKA $6824 Difference $1689 (<.001) Patient: TKA $4165 UKA $2601 Difference $1564 (<.001) Government: TKA $4348 UKA $4223 Difference: $125 (NS) QALYs gained baseline to 2 years: TKA 0.053 UKA 0.028 Difference 0.026 (NS) **BASE CASE ICUR: $65,245/QALY** Pt perspective: $60,382/QALY Govt perspective: $4860/QALY	95% confidence interval could not be calculated since >15% of bootstrapped samples suggested that TKA is dominated by UKA (less effective, more costly) Probability of TKA being cost-effective at <$50,000/QALY =0.4 from society or patient perspective =0.7 from government perspective	"Based on 2-year data, TKA gained more QALYs at higher costs compared to UKA. However, we cannot conclude with 95% confidence that TKA is more cost effective than UKA due to notable individual variations." "…[this study] highlighted the importance of choosing a perspective from which a decision is made…"

Study	Design	Population & Model inputs	Methods of analysis/ strengths& limitations	Relevant results	Results of sensitivity analysis	Author conclusions
Slover (2006) USA	Cost utility analysis Intervention: unicompartmental knee arthroplasty (UKA) Comparator: conventional total knee arthroplasty (TKA)	Hypothetical cohort of 78 year old people with unicompartmental arthritis Time horizon: 20 years post procedure Probabilities: Norwegian Arthroplasty registry; literature Utilities: quality well-being scores from published literature Disutilities (pain, mobility, complications) set by authors Costs: Medicare reimbursement schedules 2005 calculated from procedure lengths from authors' institution	Markov decision model One-way sensitivity analysis of all variables; ICER of $50,000/QALY used in threshold analysis Strengths: Methods consistent with standards for economic evaluation Use of registry data Weaknesses: Sources of all variables not clearly stated Multivariate sensitivity analysis not performed Generalizability to younger populations unknown	Base case: Average cost (USD 2005): UKA: $13,100 TKA: $13,300 Difference: -$200 Average QALYs gained: UKA: 5.66 TKA: 5.61 Difference: 0.05 ICER: UKA is dominant (less costly, more effective)	For UKA to become less cost effective (>$50,000 per QALY) : - revision rate would have to be >4% than TKA -UKA cost would have to be >$13,500 -revision cost would have to be >$116,000 -perioperative mortality would have to be >0.34% -infection probability >2.6% -utility value <0.672 -disutility <-0.113	UKA has similar cost-effectiveness profile to TKA in elderly population Prosthetic survival, costs, perioperative mortality, infection rates, and utilities can alter the cost effectiveness of UKA.
SooHoo (2006) USA	Cost utility analysis Unicompartmental (UKA) versus total knee arthroplasty (TKA)	Target population: People age 65 years with unicompartmental arthritis Time horizon: 18 years (based on life expectancy of 65 year old patients) Reference case assumptions/ probabilities: Survival/durability:	Primary analysis: Decision tree model, perspective not stated Discounting in reference case = 3% per year Sensitivity analysis: Performed by varying the assumed values for key variables	Reference case: Incremental costs ($): UKA versus TKA: +$5 Incremental effectiveness (QALY): UKA versus TKA: +0.02 Incremental cost-effectiveness ratio:	Model sensitive to procedure costs, survival, and utilities. TKA becomes dominant if unicompartmental prosthetic survival is ≥4 years less than TKA prosthetic survival.	UKA is a cost-effective alternative to TKA for unicompartmental arthritis assuming comparable survival and function. To be cost-

Study	Design	Population & Model inputs	Methods of analysis/ strengths& limitations	Relevant results	Results of sensitivity analysis	Author conclusions
SooHoo (2006) USA (cont)		UKA: 12 years TKA: 15 years Implant failure: 1% Mortality: 0.5% Data source: Nine published studies* Costs: Direct lifetime (18 yrs) costs (hospitalizations and physician services): Medicare reimbursement schedule (1998) Utility values† for reference case: UKA: 0.9 TKA: 0.9 Treatment of infection: 0.5 Postop recovery: 0.5 Death: 0.0 Revision TKA: 0.85 Resection KA: 0.6 Data source: Nine published studies*	(durability, functional utility, and cost) Strengths: Study design consistent with accepted methods of design for economic evaluations Weaknesses: Costs and QALYs in final model not given (just ratio)	UKA versus TKA: $277/QALY	UKA becomes dominant if procedure cost is decreased by 25%.	effective, survival of unicompartmental knee arthroplasty must be at least 3-4 years less than that of TKA.

QALY: quality-adjusted life year
TKA: total knee arthroplasty
UKA: unicompartmental knee arthroplasty
NS: not statistically significant

* Soohoo (2006): Data based on nine studies: 1 RCT, 6 prospective cohort and 2 retrospective cohort studies; published between 1994–2004; median N = 124 (mean N = 1738) (range, 56–14,772); median f/u = 7.6 yrs based on 8 studies (mean f/u = 9.2 yrs); mean age = 69.6 years.
† Soohoo (2006): utility continuum defined as follows: 1.0 = perfect health; 0.0 = death; arthritis assumed to have a utility value of 0.7.

5. Summary by Key Question

Key Question 1: What is the evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA (CONV-TKA)?					
	Strength of evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
Knee Pain, Function and Quality of Life	**High evidence (up to 2 years post surgery)**	• Several randomized controlled trials reported similar results in pain, function and quality of life outcomes when comparing patients receiving either CN-TKA or CONV-TKA at various follow-up times ranging from 3 months to 2 years . • The data are similar with respect to nonrandomized cohort studies with 1 to 3 year follow-up. • No comparative data are available for these outcomes past 2 to 3 years. *There is high evidence that CN-TKA results in similar clinical and functional outcomes as CONV-TKA in the short term.*	+	+	+
Revision	**Low evidence**	• Two RCTs and two cohort studies reported similar, low rates between CN-TKA AND CONV-TKA groups of less than 2%. A third RCT reported half as many revisions following CN-TKA (3.7% vs.8.0%) after 3 years though the study numbers were small. *The small sample sizes, short follow up, and inconsistent rate of revision among the RCTs renders low evidence concerning the relative short term revision rates between surgeries.Conclusions on whether CN-TKA affects long term revision rates are premature.*	+	-	–
Alignment	**High Evidence**	• Evidence from 2 metaanalyses of several RCTs and cohort studies demonstrate that the risk of unsatisfactory alignment by more than 3º is significantly less using CN-TKA compared with CONV-TKA. *There is high evidence that the risk of unsatisfactory alignment (> 3º) is significantly less following CN-TKA.However, this has not been shown to translate into better functional outcomes.*	+	+	+

Key Questions2: What is the evidence of efficacy and effectiveness of using partial knee arthroplasty compared with TKA?					
	Strength of evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
UKA vs. TKA *Knee Pain and Function*	**Moderate evidence**	•Knee pain and function were comparable between UKA and TKA in one RCT and 14 cohort studies over a variety of follow up times ranging from 3 months to 15 years. •Range of motion was consistently higher in the UKA group in the studies comparing mean motion and the proportion of patients achieving ≥120º of flexion at a variety of follow up times. *The low quality of studies renders the evidence for function between UKA and TKA moderate.*	-	+	+
Revision, prosthesis survival	**Low evidence**	•Revision rates were comparable between UKA and TKA in one RCT at 5 and 15 year follow up. •In 9 cohort studies the rates of revision were slightly higher in the UKA compared with TKA group in 8, mean follow up between 2 and 10 years. Survival of the arthroplasty in two large studies at 10 and 14-15 years slightly favored TKA. *It is unclear whether long term revision risks differ between UKA and TKA. This evidence is low.*	-	+	+/-
UKA vs. HTO *Knee Pain, Function and Revision*	**Moderate evidence**	•Knee pain, function and revision rates were comparable in 3 small RCTs assessing UKA and HTO for patients with isolated medial compartment arthritis. Follow up ranged from 1 to 10 years. *This evidence is moderate.*	+	-	+
Bi-UKA vs. TKA *Knee Pain, Function and Revision*	**Very low evidence**	•Only one small retrospective cohort study compared bi-UKA with TKA. No difference was found in functional scores at a minimum of 4 year follow up. No revisions were recorded in either group. *Lack of the number of studies renders this evidence very low.*	-	-	-
Bicompartmental knee arthroplasty vs. TKA *Revision*	**Very low evidence**	•Two large registry studies comparing revision between bicompartmental knee arthroplasty and tricompartmental TKA found similar revision rates and 2 to 4 year implant survival. *Lack of the number of studies renders this evidence very low.*	-	-	+

Key Question 3: What is the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty?					
	Strength of evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
CN-TKA *Thromboembolic events, wound and other complications*	**High evidence**	•Several RCTs and cohort studies report no significant differences between CN-TKA and CONV-TKA with respect to thromboembolic events, infection or all other complications other than ischemic events (see below). *The evidence is high that CN-TKA is as safe as CONV-TKA when considering these safety parameters.*	+	+	+
Ischemic events	**Low evidence**	•One RCT reported no significant differences in acute myocardial infarction and one reported no difference in transient ischemia following CN-TKA vs. CONV-TKA. Confusion was reported by two RCTs at different rates (0% in the CN-TKA group, 4% in the CONV-TKA group in one, and 3% in the CN-TKA group vs. 28% in the CONV-TKA group.) *The infrequent reporting of these outcomes renders the evidence for ischemic events low.*	+	–	-
UKA vs. TKA	**Low evidence**	•Complications were infrequent, and the risk of complications was similar between UKA and TKA in one RCT and nine cohort studies. *The paucity of higher quality studies renders the evidence for the safety of UKA compared with TKA as low.*	-	+	+
UKA vs. HTO	**Very low evidnece**	•The incidence of total complications was similar between UKA and HTO in two studies (1 RCT, 1 cohort) and slightly higher in the HTO group in another RCT. *Few higher quality studies and the inconsistency of the findings render the evidence that UKA is similar to HTO with respect to safety as very low.*	-	+	-
Bi-UKA vs. TKA	**Very low evidence**	•One small cohort study reported 2 cases (9%) of intraoperative fracture of the tibial spine in the bi-UKA group. No other complications reported. *The lack of literature in general render the evidence for the safety of bi-UKA compared with TKA as very low.*	-	-	-
Bi- vs. tricompartmental TKA	**No evidence**	•Complications not addressed in two registry studies.	none	none	none
Simultaneous vs. staged bilateral TKA	**Low evidence**	•Four cohort studies reported 30 day mortality rates following either staged or simultaneous TKA. Three of the four report significantly higher rates in the			

Key Question 3: What is the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty?					
	Strength of evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
Mortality		simultaneous group. *Despite the consistency of the findings, the potential for bias due to study design renders this evidence low.*	–	+	+
Thromboembolic events, wound and other complications	**Low evidence**	• From nine cohort studies, there are no significant differences in thromboembolic events, wound complications, or other complications between simultaneous and staged bilateral TKA. *The lack of higher quality studies renders the evidence for safety following simultaneous compared with staged bilateral TKA as low.*	-	+	+

Question 4: What is the evidence that TKA or partial KA has differential efficacy or safety issues in sub populations?					
	Strength of Evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
CONV-TKA					
Age, sex, obesity, comorbidity	**Very low evidence**	• Evidence from one HTA and studies published after the HTA reported inconsistent results as to whether age, sex, obesity or comorbidity significantly affected outcomes. *The low quality and inconsistency render very low evidence for or against age, sex, obesity or comorbidity as factors affecting success or failure of TKA.*	–	+	–
Type of arthritis	**Moderate evidence**	• One HTA reported greater improvement in baseline functional scores among RA patients compared with OA patients. One prospective study published after the HTA no difference in function/quality of life outcomes based on type arthritis type. *There is some evidence to suggest that patients with RA have greater improvement in function after TKA than those with OA; however, this may be related to their lower function at baseline. Given that and this difference and the lack of consistency, this evidence is moderate.*	+	+	–
Hospital and surgeon volume	**Very low evidence**	• One systematic review of several studies reported mixed results with respect to morbidity, mortality and length of hospital stay *Low study quality and inconsistency render very low evidence for a trend towards increased hospital volume and lower morbidity and length of hospital stay.*	–	+	–
Other characteristics	**Very low evidence**	• One study each either in the HTA or published after the HTA reported on possible associations between preoperative pain levels, length of hospital stay, waiting time, year of follow-up, education, SF-36 mental health scores and ethnicity and outcomes. *The low quality and/or the small number of studies render very low evidence for or against these other characteristics as factors influencing outcomes.*	–	–	–
CN-TKA					
Obesity	**Very low evidence**	• One retrospective study reported that morbidly obese patients experienced a significantly greater mean total blood loss, mean hemoglobin loss, and superficial infection rate compared with those of normal weight. *The low quality, low number of studiesand inconsistency render very low evidence for or against obesity as a risk facture for increased complications following CN-TKA.*	–	–	–

Question 4: What is the evidence that TKA or partial KA has differential efficacy or safety issues in sub populations?					
	Strength of Evidence	**Conclusions/Comments**	**Quality**	**Quantity**	**Consistency**
UKA					
Age	**High evidence**	• Five of six registry studies reported a statistically significant higher revision rate among patients < 65 years of age versus those >65 years of age. . *The higher quality studies consistently found a greater risk among patients < 65 years of age; therefore, there is high evidence that younger patients are at greater risk of failure after UKA than older patients.*	+	+	+
Obesity	**Very low evidence**	• Among three retrospective cohort studies evaluating obesity as a risk factor, one found higher rates among obese, one found lower rates among obese, and the 3rd found no statistically significant difference. *The low quality and inconsistency render low evidence for or against obesity as a risk factor for UKA failure.*	–	+	–
Sex	**High evidence**	• Five of seven published studies found no association between sex and UKA failure. Among the two that found an association, both were LoE III retrospective cohort studies. One reported a higher revision rate among males, the other a higher revision rate among females. *The higher quality studies consistently found no association between sex and revision rates; therefore, there is high evidence that sex is not a risk factor for UKA failure.*	+	+	+
Multi-compartment	**Very low evidence**	• One LoE II registry study reported higher rates of revision among patients with RA compared to those with OA *There is very low evidence that patients with RA are at greater risk of UKA failure than patients with OA.*	-	–	–
Provider facility	**Low evidence**	• Two LoE II studies found no statistically significant difference in revision rates among caseloads ≤10 or >10 UKAs per year; and one study did not find an association between different surgeons or different hospitals on revision rates. *The limited quantity of reports evaluating these factors renders low evidence for or against different surgeons or hospitals as risk factors for UKA failure.*	+	–	–

Question 5: What is the evidence of cost implications and cost effectiveness ofCN-TKA or partial knee arthroplasty?					
	Strength of evidence	**Conclusions/Comments**			
CN-TKA	**Low evidence**	• There is insufficient data to make strong conclusions about the long-term cost effectiveness of CN-TKA. • Modeling suggests that CN-TKA is potentially a cost effective intervention compared with CONV-TKA if the 10-year revision rate is reduced by between 33 to 50%.			
UKA vs. TKA	**Moderate**	• There is some evidence that UKA and TKA have similar cost and quality-adjusted outcome profiles from a health care perspective • Lack of data precludes assessment of the cost effectiveness of UKA in people under age 65.			

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