Computer-navigated total knee arthroplasty

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC's advice does not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Contents

Tables

Figures

Glossary

AHMAC	Australian Health Ministers' Advisory Council
APAIS	Australian Public Affairs Information Service
AR-DRG	Australian Refined Diagnosis Related Groups
ARTG	Australian Register of Therapeutic Goods
BMI	Body Mass Index
CNTKA	Computer-Navigated Total Knee Arthroplasty
CT	Computed Tomography
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
KSS	Knee Society Score
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NSAID	Non-Steroidal Anti-Inflammatory Drugs
OA	Osteoarthritis
PICO	Population, Intervention, Comparator, and Outcome
RA	Rheumatoid Arthritis
QALY	Quality Life Adjusted Year
RCT	Randomised Controlled Trial
TGA	Therapeutic Goods Administration
TKA	Total Knee Arthroplasty
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Executive summary

The procedure

Total knee arthroplasty is a surgical procedure to replace the damaged knee with a prosthesis. The procedure involves removal of the condyles of the femur and tibia and replacing these with either metal or plastic components.

The procedure is performed through an initial anterior midline incision and one of three (medial parapatellar retinacular, subvastus or midvastus) secondary incisions. Rods are used to internally (intramedullary) or externally (extramedullary) align the femur and tibia.

The femoral and tibial prostheses are inserted following treatment of any bone deficiencies and after ligamentous balancing has been achieved using a cemented or cementless technique.

Success of total knee arthroplasty depends on the surgeon creating a kinetically stable, solidly fixed and well functioning knee using the prosthesis through accurate bony resection, good fixation techniques, soft tissue balancing and restoration of the mechanical axis. Restoration of the mechanical axis of the knee joint is particularly important as malalignment may affect postoperative complication and revision rates.

The conventional method of achieving correct limb alignment includes the use of special jigs provided with the knee prosthesis. Computer-navigated total knee arthroplasty provides an alternative method of achieving correct limb alignment. Computer navigation for the purposes of total knee arthroplasty requires a system consisting of a computer, a tracking device (eg an infrared camera) and arrays which are attached to the patient's bone (allowing the bone's position to be tracked in virtual space).

There are two types of computer navigation systems; image-free or image-based. Image-free systems, which form the subject of this report, use information for registration obtained intra-operatively by digitising various anatomical landmarks with a navigated pointer. Information can also be acquired through kinematic means. Image-based systems for computer navigation can be computed tomography-based, fluoroscopy-based, or robotic.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Commonwealth Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Commonwealth Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) was engaged to conduct a systematic review of the literature on computer-navigated total knee

arthroplasty. An Advisory Panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of computer-navigated total knee arthroplasty

Clinical need

Knee arthroplasty is a common surgical option for patients suffering from painful, deformed or unstable knees resulting from degenerative, inflammatory, traumatic or other causes. During 2007, there were 29,965 knee arthroplasties performed in Australia. Given the ageing population and the obesity epidemic facing Australia, it is likely that the number of knee arthroplasty procedures performed each year will increase.

Safety

Both comparative and case series data were included for safety. In total, 31 studies with a total of 4,513 patients overall were available. Safety was poorly and inconsistently reported in the studies identified for this report. Furthermore, long-term safety data was not available. No deaths were associated with the use of computer-navigated total knee arthroplasty and few serious adverse events were reported.

The data suggests that the occurrence of clinical adverse events between computer-navigated and the conventional total knee arthroplasty technique is comparable, with low complication rates reported. Rates of infection and deep vein thrombosis were similar for both procedures (approximately 1% and 1.7% respectively).

Although technical adverse events were only reported for the computer-navigated technique, preventing a comparison between techniques, the reported rates were low. Conversion from the computer-navigated technique to the conventional method was required in 12 out of 995 knees (1.3%).

In terms of blood loss, two out of eight studies reported significantly less blood loss using computer navigation.

The safety data available for this report suggests comparable safety between computer-navigated and conventional total knee arthroplasty.

Effectiveness

Fifteen randomised comparative trials and 28 level II comparative studies were included for effectiveness outcomes.

Radiological outcomes

The majority of the studies identified for this review reported radiological outcomes as a measure of effectiveness. Outcomes related to the postoperative mechanical axis were selected as the primary radiological outcomes for this review. Radiologically, computer navigation resulted in increased accuracy in the implantation of the knee prostheses. Meta-analysis of the degree of deviation in the postoperative knee comparative studies showed that there was an overall mean difference of -0.74° (95% CI: -0.89° to -0.59°) in favour of computer navigation ($P < 0.00001$).

Clinical and peri-hospital outcomes

Unlike the radiological results, few studies reported clinical outcomes. The two most commonly reported clinical outcomes included range of motion and the Knee Society Score, both of which were comparable between the computer-navigated and conventional total knee arthroplasty. Similarly, for the other clinical outcomes reported, results were comparable between the two techniques.

In terms of peri-hospital outcomes, both duration of surgery and tourniquet time were slightly increased through the use computer navigation. Computer navigation resulted in a mean additional 11.99 and 14.38 minutes for surgery (10 studies) and tourniquet times (five studies) respectively.

Long-term linking data

Analysis of the long-term outcomes of total knee arthroplasty provided little support for a link between postoperative limb alignment and long-term success. Therefore, at this stage further evidence is required to establish a relationship between optimal postoperative limb alignment, such as that provided by computer navigation, and long-term successful clinical outcomes.

Cost-effectiveness

The objective of the economic evaluation was to compare the cost-effectiveness of computer-navigated total knee arthroplasty with the conventional manual technique. The absence of long-term data supporting improved clinical effectiveness of computer-navigation meant that a Markov model was applied, with the rationale being that improved alignment may lead to a reduction in the total knee arthroplasty revision rate.

Model inputs, including costs, effectiveness and transition probabilities, were obtained from a review of the literature. Four scenarios were tested:

1) no improvement in the 10-year revision rate (approximately 6%)

2) a 1 percentage point improvement in the ten year revision rate

3) a 2 percentage point improvement

4) a 3 percentage point improvement (ie a 50% reduction).

Based on a number of estimates and assumptions:

- The incremental cost of receiving computer-navigated total knee arthroplasty rather than conventional manual total knee arthroplasty was $1029 per procedure. The additional cost is associated with the capital cost of buying the computer navigation equipment, the higher estimated procedural fee and the disposables required. These costs are offset somewhat by a reduction in the number of trays required during the procedure.

- If computer-navigated total knee arthroplasty is no more effective or only modestly effective at reducing the probability of a revision total knee arthroplasty (scenarios 1 and 2), then this technique is unlikely to be cost-effective.

Computer-navigation surgery is potentially a cost-effective treatment for total knee arthroplasty in the long term, provided the corresponding improvement in the 10-year revision rate of total knee arthroplasty improves by 2 percentage points or more (scenarios 3 and 4).

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of computer-navigated total knee arthroplasty. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including input from clinical experts.

MSAC's terms of reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

An advisory panel with expertise appropriate to this evaluation was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. Membership of the Advisory panel is provided at Appendix B.

This report summarises the assessment of current evidence for computer-navigated total knee arthroplasty.

Background

Knee joint failure

Knee joint failure commonly results from osteoarthritis, but other causes include inflammatory arthritis, most commonly rheumatoid arthritis (Australian Orthopaedic Association National Joint Replacement Registry 2008). Osteoarthritis is characterised by cartilage degeneration. Loss of cartilage results in friction between the leg bones, which can lead to deformity, pain and impaired joint mobility (AAOS 2003; Shiel et al 2007). Primary osteoarthritis is related to the ageing process whereas secondary osteoarthritis is caused by other conditions, including obesity, repeated trauma or surgery to the joint structures, or abnormal joints at birth (congenital abnormalities) (Shiel et al 2007). Rheumatoid arthritis, which is the most common form of inflammatory arthritis, is characterised by joint swelling, pain, heat and destruction caused by the immune system attacking the tissues lining the joints (Australian Bureau of Statistics 2007). Systemic lupus erythematosus and psoriatic arthritis are other conditions where joint inflammation and secondary degeneration takes place.

Other causes of knee joint failure include trauma (often resulting from motor vehicle accidents and sporting injuries), osteochondritis dissecans, osteonecrosis or ligamentous injuries.

Total knee arthroplasty

In total knee arthroplasty, the damaged knee is replaced with a prosthesis. The procedure involves removing sections of the tips (condyles) of the thighbone (femur) and shinbone (tibia) and replacing these with metal or plastic components. Following the initial 12 cm to 18 cm skin incision along the anterior midline, there are three different approaches the surgeon can take for secondary incision: the medial parapatellar retinacular, the subvastus 'Southern' or the midvastus (Canale 2003). The latter two methods have been suggested to reduce patellofemoral complications and hasten the return of the quadriceps function. Bone shaping and femoral component rotation then occurs with the use of 'posterior' or 'anterior referencing' instrumentation used to measure the thickness of bone removed. Rods are used to align either internally (intramedullary) or externally (extramedullary) the femur and the tibia. The posterior cruciate ligament can either be retained or substituted using a post and cam mechanism (Canale 2003). In some patients, the patellar may also be resurfaced (Forster 2004).

Once bone deficiencies have been treated and ligamentous balancing achieved to allow accurate bone cuts for depth and angle, the prosthesis can be inserted. In the cemented technique, the tibial and femoral prostheses are inserted and cement is applied to a depth of 2 mm to 5 mm in the cancellus bone to secure the prosthesis (Canale 2003). Alternatively, a cementless prosthesis may be fixed in place with rods, pegs or screws, which provide additional stability for bone in-growth and long-term prosthesis fixation (Canale 2003).

Total knee arthroplasty has been shown to benefit mobility, well-being and emotional status, social isolation and pain relief (Ethgen et al 2004). For total knee arthroplasty to be successful the surgeon needs to create a kinetically stable, solidly fixed and well-functioning knee using the prosthesis. This is achieved with accurate bony resection,

good fixation techniques, soft tissue balancing and restoration of the mechanical axis. Thus, correct limb alignment (ie restoring the mechanical axis of the knee joint) is essential during total knee arthroplasty as this affects postoperative complications and revision rates (Siston et al 2007). The conventional method of guiding correct limb alignment includes the use of special jigs provided with the knee prosthesis to be used. Two long rods, one reaching up to the hip joint area at the centre of the hip joint and the other reaching down to the ankle joint at the centre of the ankle joint meet above the knee joint area in a cutting jig. The cutting jig is therefore theoretically placed in line with the mechanical axis of the knee joint. A range of error between three and seven degrees from the ideal cutting plane is associated with the use of these rods.

Complications

In addition to the risk of the general anaesthetic, other potential complications of total knee arthroplasty include deep peri-prosthetic infection, deep vein thrombosis (DVT), pulmonary embolus and, in patients over 80 years of age, myocardial infarction and stroke (St.Clair et al 2006; Rodriguez-Merchan 2007). Stiffness of the knee and arthrofibrosis is a further significant issue associated with knee arthroplasty procedures. DVT 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 or, as a last resort, amputation (Canale 2003). In the United States, total knee arthroplasty is associated with a survival of 91 per cent at 10 years, 85 per cent at 15 years and 78 per cent at 20 years (St.Clair et al 2006). However, it is unclear to what degree these figures reflect the age of the patients receiving the intervention.

Contraindications

There are several absolute contraindications to total knee arthroplasty (TKA), including active systemic and skin infection, open wounds, neuropathic joints and adverse reactions to anaesthesia. (St.Clair et al 2006; Rodriguez-Merchan 2007).

Computer-navigated total knee arthroplasty

Computer-navigated total knee arthroplasty may reduce complication rates associated with total knee arthroplasty by providing better mechanical limb alignment (Siston et al 2007). For the purposes of this review, the navigation systems require the use of a computer, a tracking device such as an infrared camera, and arrays that are attached to the patient's bone by which the patient can be tracked in virtual space. The most frequently used devices employ optical tracking, but electro-magnetic tracking is also available.

Computer-navigated total knee arthroplasty can be divided into two types of systems: image-free or image-based.

Image-free systems

Image-free computer-navigated total knee arthroplasty systems use information for registration obtained intra-operatively by digitising various anatomical landmarks with a navigated pointer. There is also acquisition of information by kinematic means. Total

knee replacement performed using this method can allow for ligament and gap balancing as well as correct sizing and positioning of the components.

Image-based systems

Computed tomography (CT)

Image based computer-navigated knee replacements are performed using a technique where pre-operative CT scans of the individual patient are performed. Registration of key anatomical points required to navigate the knee are matched to the patient's CT scans. This does not allow for intra-operative kinematic data to be obtained.

Fluoroscopy-based systems

Fluoroscopy-image intensified systems consist of a specific frame that is attached to the fluoroscopy machine and allows automatic registration of the patient. While this method is widely employed for the use of computer-navigation in trauma surgery, its use is not currently widespread in knee arthroplasty.

Robotics/navigation

Total knee arthroplasty using navigation and robotic surgery is practised in some countries but not used in Australia currently. It requires pre-operative CT Scans and the use of tracking devices as per routine navigation, but this information is fed into a robot. The robot has boundaries which are set by the navigation. The surgery can either be performed automatically by the robot or, more commonly, by the surgeon working with the tools under the constraints provided by the robot and navigation. This technique is not currently used in Australia.

Clinical need/burden of disease

Patients suffering from painful, deformed or unstable knees resulting from degenerative, inflammatory, traumatic or other causes, require a treatment option to effectively relieve pain and restore joint function. Knee replacement (knee arthroplasty) is a common surgical option for patients in such circumstances. In Australia, 29,965 knee replacements were performed in 2007 (Australian Orthopaedic Association National Joint Replacement Registry 2008). The number of patients who have undergone total knee arthroplasty under the MBS is also shown in Table 2.

Whilst no knee arthroplasty specific cost information is available, the estimated total cost of both hip and knee replacement procedures performed in Australia in the year ending June 2002 was above $500 million (Graves et al 2004). A combination of factors affecting the Australian population, such as ageing and the obesity epidemic, will place pressure to increase the number of knee arthroplasties performed each year. The number of knee arthroplasty procedures (including patellar/trochlear, unicompartmental, primary total and revision procedures) in Australia increased 152 per cent between 1994/95 and 2005/06, indicating a trend of increased number of knee arthroplasties performed each year (Australian Orthopaedic Association National Joint Replacement Registry 2007). It is likely that this trend will continue.

Alternative treatments

Non-pharmacological treatments, such as exercise and physiotherapy, are first-line options for reducing pain and improving physical function in patients with osteoarthritis

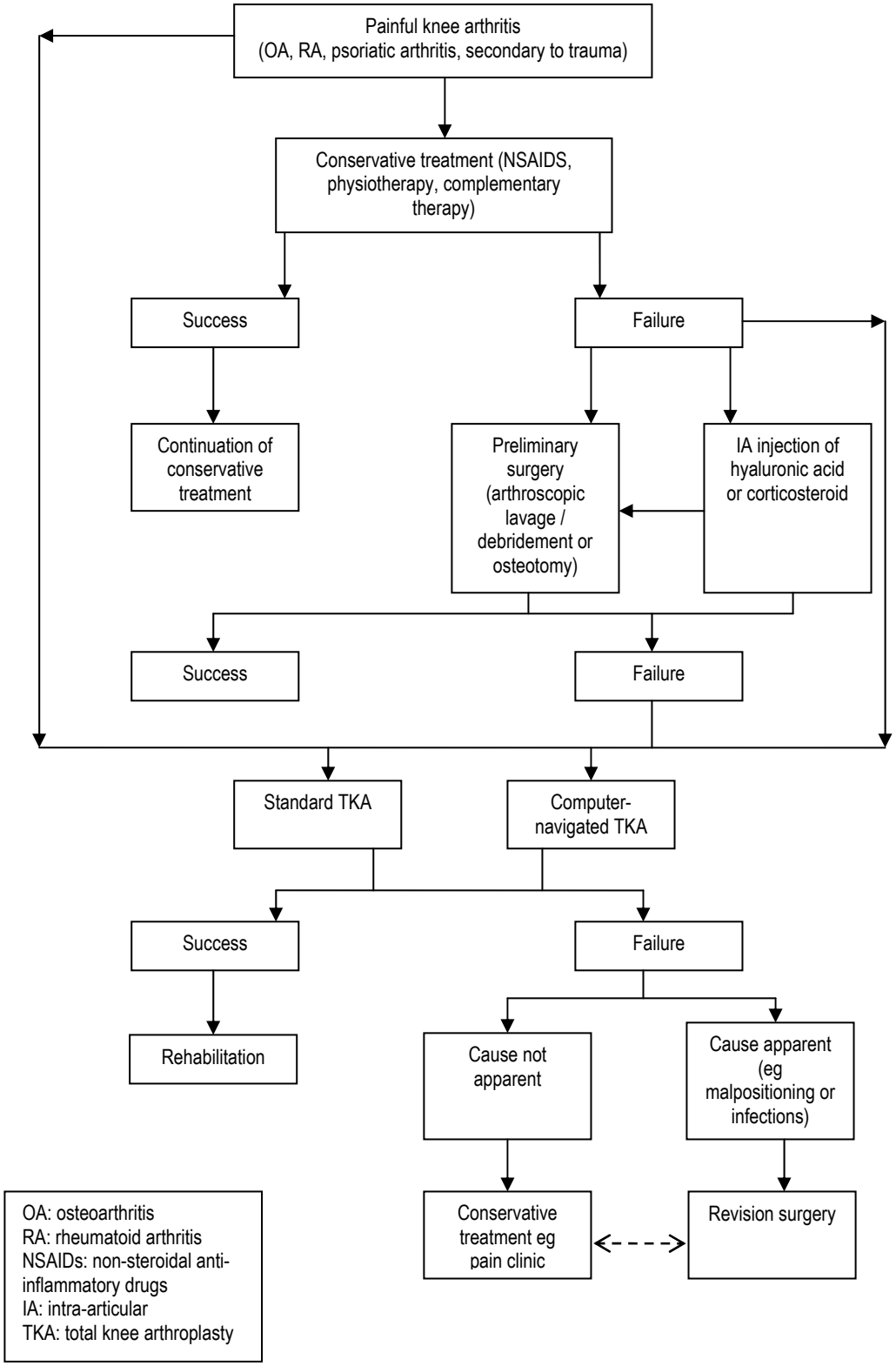
(Fransen et al 2003; Walker-Bone 2003). Pharmacological treatment for arthritis includes paracetemol, non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular injection of hyaluronic acid or corticosteroids, and dietary supplements such as fish oil, glucosamine and chondroitin (Gailer et al 2004). Second-line pharmacotherapy for rheumatoid arthritis and systemic lupus erythematosus includes hydroxychloroquine, an antimalarial medication that is particularly effective for joint symptoms, and immunosuppressive medications such as leflunomide, cyclosporin, etanercept, abatacept and adalimumab (Shiel et al 2007).

If first-line therapies fail to improve symptoms, surgical intervention may be required. Surgical options include arthroscopic debridement and osteotomy, osteochondral transplantation and patellectomy. The choice of intervention (surgical or pharmacological) is dependent on the specific indication and the severity of the damage. In the event that preliminary interventions fail and benefits outweigh risks, total knee arthroplasty may be required.

Comparator

The comparator for computer-navigated total knee arthroplasty is conventional, manual, jig-based total knee arthroplasty.

Figure 1 Clinical decision-making pathway



Marketing status of the technology

According to the applicant, the TGA listing for computer assisted total knee replacement is 'AUST L 12859 Stryker Surgical Instruments and Accessories powered (Stryker instruments USA)'.

Through scoping of the literature, four other manufacturers have been identified: Brainlab/DePuy, Orthosoft, Orthopilot and Medtronic. Table 1 lists the devices related to this application listed on the ARTG database.

Table 1 Devices related to this application on the ARTG

ARTG number	Product ID	Descriptor	Sponsor
127497	211649	Robot*, surgical, navigation unit	Stryker Australia Pty Ltd
128421	212752	Robot* software, surgical, navigation	Stryker Australia Pty Ltd
132150		CAS INSTRUMENTATION FOR USE WITH PFC SIGMA AND LCS TOTAL KNEE SYSTEM - Orthopaedic prosthesis implantation instrument	Johnson & Johnson Medical Pty Ltd T/A Depuy Australia
132269		CAS INSTRUMENTATION FOR USE WITH PFC SIGMA AND LCS TOTAL KNEE SYSTEM - Tray, instrument	Johnson & Johnson Medical Pty Ltd T/A Depuy Australia
132270		CAS INSTRUMENTATION FOR USE WITH PFC SIGMA AND LCS TOTAL KNEE SYSTEM - Driver/extractor	Johnson & Johnson Medical Pty Ltd T/A Depuy Australia

NOTES: ARTG = Australian Register of Therapeutic Goods; * = The term 'robot' does not refer to robotic systems as defined in this report.

Current reimbursement arrangement

Currently, the Medicare Benefits Schedule (MBS) lists seven items relating to total knee arthroplasty, described in Table 2.

Table 2 Current MBS listing of TKA procedures

MBS Item Number	Therapeutic Procedure	Fee as at 06/11/07	Adjusted Fee (additional premium of 25%)	Number of MBS Items by Financial Year
49518	Total knee replacement, arthroplasty of	Fee: $1190.15 Benefit: 75% = $892.65	$1487.69	2003/2004: 10 427 2004/2005: 11 534 2005/2006: 11 965 2006/2007: 12 935
49519	Total knee replacement, arthroplasty of, including associated minor grafting, if performed- bilateral	Fee: $2090.90 Benefit: 75% = $1568.20	$2613.63	2003/2004: 710 2004/2005: 792 2005/2006: 761 2006/2007: 920
49521	Total knee replacement, arthroplasty of, requiring major bone grafting to femur or tibia, including obtaining of graft	Fee: $1445.50 Benefit: 75% = $1084.15	$1806.88	2003/2004: 716 2004/2005: 765 2005/2006: 906 2006/2007: 1013
49524	Total knee replacement, arthroplasty of, requiring major bone grafting to femur and tibia, including obtaining of graft	Fee: $1700.45 Benefit: 75% = $1275.35	$2125.56	2003/2004: 288 2004/2005: 329 2005/2006: 332 2006/2007: 301
49527	Total knee replacement, arthroplasty of, revision procedure, including removal of prosthesis	Fee: $1455.50 Benefit: 75% = $1084.15	$1819.38	2003/2004: 724 2004/2005: 838 2005/2006: 822 2006/2007: 829

49530	Total knee replacement, arthroplasty of, revision procedure, requiring bone grafting to femur or tibia, including obtaining of graft and including removal of prosthesis	Fee: $1785.60 Benefit: 75% = $1339.20	$2232	2003/2004: 197 2004/2005: 188 2005/2006: 216 2006/2007: 248
49533	Total knee replacement, arthroplasty of, revision procedure, requiring bone grafting to both femur and tibia, including obtaining of graft and including removal of prosthesis	Fee: $2040.60 Benefit: 75% = $1530.45	$2550.75	2003/2004: 213 2004/2005: 202 2005/2006: 232 2006/2007: 255

Approach to assessment

Search strategy

PICO (population, intervention, comparator, and outcome) criteria were developed with the assistance of the Advisory panel to assist in specifying the search strategy (Table 3).

Table 3 PICO criteria

Population	Intervention	Comparator	Outcomes
1. Patients requiring primary total knee arthroplasty for any underlying indication 2. Patients requiring primary unicompartmental knee arthroplasty for any underlying indication All indications will be reported as pooled data. Subgroups: • Knock-knee/valgus • Post-osteotomy surgical patients	Computer-navigated total knee arthroplasty using passive, image-free, infra-red based systems.	1. Conventional, manual, jig-based total knee arthroplasty. Minimally invasive total knee arthroplasty will be considered if identified. 2. Conventional, manual, jig-based unicompartmental knee arthroplasty (both standard and minimally invasive will be considered).	*Effectiveness:* • Postoperative limb alignment • Length of time to revision • Recovery times/length of stay in hospital • Patient satisfaction: *Western Ontario* and McMaster Universities Osteoarthritis Index (WOMAC) functional knee score; Oxford knee score; Crosby & Insall score; Knee Society Score; Short-Form-36 (SF-36) Health Survey; Bartlett Patellar Score; pain (Visual Analogue Scale); quality of life *Safety:* • Infection/fracture through pin site • Complication rates • Blood loss • Thromboembolic effect • Revision rate *Economics:* • Duration of surgery/case
Clinical questions			
Is computer-navigated total knee arthroplasty as effective as, or more effective than, conventional jig-based arthroplasty for any or all of the patient populations considered above? Is computer-navigated total knee arthroplasty as safe as, or safer than, conventional jig-based arthroplasty for any or all of the patient populations considered above?			

The following statements provide further detail regarding the clinical questions outlined above:

Target population

- All patients who require TKA were included for assessment.
- Relevant patient sub-groups that were considered for assessment included knock-kneed/valgus and post-osteotomy patients.

- Other subgroup analyses were not required. All data could be grouped together, eg younger patients were not treated separately from older patients (< 60 years).

- Studies which reported on cadavers were excluded as they have no clinical outcomes.

- Patellofemoral arthroplasty was excluded.

- Unicompartmental arthroplasty was included as studies were identified, and have been reported separately to TKA.

Intervention

- If a study used a device that was not registered by the TGA for use in Australia, the study was not excluded. Passive, image-free, infra-red based computer navigation systems under consideration are similar enough to one another to include all devices within that category. The primary intervention is considered to be passive computer-aided, image-free, infra-red TKA.

- All devices (diagnostic systems and computer-navigation systems) were included, regardless of age.

- Electromagnetic tracking, a recent alternative to infra-red, was not considered. In addition, robotic knee arthroplasty and image-based systems were excluded.

General statements regarding total knee arthroplasty

- Subgroup analyses on specific prosthesis or fixation technique were not undertaken.

- Balancing of the posterior cruciate ligament was not considered.

- Patellar resurfacing or bone grafting was not reported.

Comparator

- The comparator was considered to be standard TKA. However, minimally-invasive TKA was included as a comparator where identified in the literature.

Outcomes

- All outcomes have been reported together, independently of the specific indication.

- The primary outcomes are alignment and length of time to revision. As long-term studies directly reporting on length of time to revision were unlikely to be identified for computer-navigated TKA, a linked evidence analysis was undertaken. Data regarding knee prosthesis alignment was taken from the included clinical studies. This has been linked to length of time to revision by undertaking a separate literature search to identify meta-analyses studies which provide evidence for time to revision surgery depending on knee alignment

following TKA. In this way the technical outcome of limb alignment has been linked to the clinical outcome of revision surgery.

- Rotation of the prosthesis was not included.
- All other technical outcomes were excluded.
- Soft tissue balancing was not considered.
- Long-term outcomes (between 5 and 10 years, depending on the intervention) have been used where possible.

Table 4 Overview of search terms utilised

Element of clinical question	MeSH and Keyword search terms
Target population	Arthritis, rheumatoid Osteoarthritis, knee
Intervention	Arthroplasty, replacement, knee Arthroplasty Knee joint; knee Knee prosthesis Surgery, computer-assisted Navigation Computer navigation Computer guided Computer assisted

Inclusion criteria

- As the first publications on computer-navigated knee arthroplasty were not published until 1997, expert opinion was that the searches could be limited to this date.
- Case series data were included for safety outcomes only.
- Abstracts were excluded.
- A separate search strategy was employed to identify meta-analyses which report on long-term revision rates and how this is linked to limb alignment. These studies have been used solely to inform these specific effectiveness outcomes.

Detailed inclusion and exclusion criteria applied to the identified citations for assessing the safety and effectiveness of computer-navigated knee arthroplasty are detailed in Appendix C.

Review of literature

Literature databases

Articles were retrieved if they were judged to possibly meet the inclusion criteria. Two reviewers independently applied the inclusion criteria and any differences were resolved by discussion. The bibliographies of all retrieved publications were hand-searched for any relevant references missed in the database search (pearling).

Data extraction

Data were extracted by one researcher and checked by a second using standardised data extraction tables developed a priori. Data were only reported if stated in the text, tables, graphs or figures of the article, or if they could be accurately extrapolated from the data presented. If no data were reported for a particular outcome then no value was tabulated. Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes in the individual studies, including numerator and denominator information.

Description and methodological quality of included studies

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000).

These dimensions (Table 5) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 5 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design.*
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *P*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

NOTES: *See Table 6

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 6.

Table 6 Designations of levels of evidence

Level of evidence*	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

NOTES: *Modified from NHMRC, 1999.

Included studies were critically appraised for study quality according to the guidelines in Chapter 6 of The Cochrane Reviewers' Handbook (Higgins and Green 2008). Included randomised controlled trials (RCTs) were examined with respect to the adequacy of allocation concealment and blinding (if possible), handling of losses to follow-up, and any other aspect of the study design or execution that may have introduced bias, with reference to the CONSORT Statement (Altman et al 2001). Two reviewers critically appraised each of the included studies, and any differences in interpretation were resolved through discussion. Individual quality scores were not assigned, rather the quality of the included studies was described in a narrative fashion, and any important quality issues highlighted in the discussion of outcomes.

Data analysis

Meta-analysis

Meta-analysis of sufficiently homogenous dichotomous and continuous variables was undertaken utilising Review Manager (RevMan) version 5.0 (The Cochrane Collaboration 2008).

For dichotomous variables, the odds ratio and 95 per cent confidence intervals were calculated using the Mantel-Haenszel method. If a high level of heterogeneity was detected amongst the studies ($I^2 > 50\%$), the random effects model was employed; in analyses involving greater homogeneity ($I^2 < 50\%$), the fixed effect model was utilised.

For continuous variables, the weighted mean difference and 95 per cent confidence intervals were calculated using the inverse variance method. If a high level of heterogeneity was detected amongst the studies ($I^2 > 50\%$), the random effects model was employed; in analyses involving greater homogeneity ($I^2 < 50\%$), the fixed effect model was utilised.

Where meta-analysis was not appropriate, the mean of the means and the pooled standard deviation was calculated. The pooled standard deviation was calculated by

$$s_p = \sqrt{\frac{\sum_{i=1}^{k}((n_i - 1)s_i^2)}{\sum_{i=1}^{k}(n_i - 1)}}$$

where s_p is the pooled standard deviation, n_i is the sample size of the i'th sample, s_i is the standard deviation of the ith sample, and k is the number of samples combined.

Where statistical pooling was not possible, narrative data reported was undertaken, with representative rates calculated where possible.

Included studies

The studies identified as fulfilling the review inclusion criteria are listed in Appendix E.

Current and recent clinical trials of computer-navigated total knee arthroplasty

Websites of clinical trials agencies were searched to identify all relevant ongoing or unpublished clinical trials related to computer-navigated total knee arthroplasty. These included the Australian New Zealand Clinical Trials Registry, United States National Institute of Health (clinicaltrials.gov) and the National Research Register (UK). As of October 2008, a total of seven trials investigating computer-navigated total knee arthroplasty were identified; these are detailed in Appendix F.

Expert advice

An Advisory panel with expertise in orthopaedics and consumer issues was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. In selecting members for advisory panels, MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the Advisory panel is provided at Appendix B.

Radiological long-term linking data: approach to assessment

The following section provides a description of the approach to assessment for the search for radiological long-term linking data, linking postoperative mechanical alignment with long-term follow-up outcomes of total knee arthroplasty.

Introduction

Due to the relatively recent adoption of computer-aided total knee arthroplasty into the treatment pathway of patients with painful knee arthritis, there are no studies included in the body of the report which describe long-term outcomes, such as revision surgery, for this procedure. Expert clinical opinion from the Advisory panel suggested that limb and mechanical axial alignments are significant to the long-term outcomes of total knee arthroplasty. Therefore a literature search was undertaken to identify studies which linked data concerning axial alignment following computer-navigated total knee arthroplasty studies with long-term outcomes.

Aim

To identify the highest quality evidence available, including meta-analyses and systematic reviews, in relation to mid- and long- term limb and axial alignment outcomes for total knee arthroplasty.

Methods

A number of literature searches were undertaken to identify relevant studies linking postoperative alignment with long-term treatment success following total knee arthroplasty. Studies identified by these searches were included if they fulfilled the inclusion criteria below.

Inclusion criteria

The study:

- reports postoperative limb alignment outcomes, including mechanical axis, tibiofemoral angle, femoral component alignment, tibial component alignment
- reports long-term effectiveness outcomes, including treatment failures, revision surgery and adverse event occurrence.

Exclusion criteria

The study:

- has insufficient mid- or long- term follow-up
- includes cadaveric subjects.

Literature searches

Studies of a higher level of evidence were favoured over lesser quality studies for inclusion due to the reduced level of bias and confounding associated with well-constructed meta-analyses, systematic reviews and randomised primary studies. However, a lack in their availability found case-series data to be the only source of evidence to

report the relationship between postoperative limb alignment and long-term effectiveness. The particular search modalities used for each level of evidence were as follows:

Level I evidence (Systematic reviews, Meta-analyses)

Systematic literature searches were conducted in March 2008 in order to identify relevant systematic reviews and meta-analyses, with no restriction on publication date. The medical databases searched included EMBASE (1980-2008), the Cochrane Database of Systematic Reviews and the York Centre for Reviews and Dissemination (United Kingdom).

Key search terms were identified using the PICO (population, intervention, comparator, and outcome) criteria from the main body of this review. The search strategy was as follows:

1. Arthroplasty, Replacement, Knee [MeSH]
2. Knee*
3. arthroplast* OR replace*
4. #3 AND #4
5. #2 OR #5
6. align* OR angle* OR mechanical axis OR varus OR valgus
7. #6 AND #8

A total of 152 publications was identified from this search, 143 from the Cochrane Database of Systematic Reviews, five from EMBASE and four from the York Centre for Reviews and Dissemination. The abstracts of the identified studies were examined to determine if they met the specified inclusion criteria. Whilst there were systematic reviews reporting mechanical axis, limb alignment and malalignment, these reviews focused on short-term outcomes only and were consequently excluded. **Therefore, the impact of alignment on long-term outcomes could not be found in any of the Level I evidence retrieved.**

Level II evidence (Randomised controlled trials)

A literature search of PubMed was conducted in April 2008 to identify relevant Level II evidence. There were no date restrictions. The search strategy used was as follows:

1. Arthroplasty, Replacement, Knee[MeSH]
2. Knee*
3. Knee Joint [MeSH] OR Knee [MeSH]
4. #2 OR #3
5. arthroplast* OR replace*
6. #4 AND #5
7. #1 OR #7
8. align*
9. angle*
10. mechanical axis
11. mechanical axes
12. varus
13. valgus
14. #8 OR #9 OR #10 OR #11 OR #12 OR #13

15. #7 AND #14
16. "Randomised Controlled Trial"[Publication Type]
17. randomized controlled trial
18. randomised controlled trial
19. #16 OR #17 OR #18
20. #15 AND #19
21. Search #7 AND #14 Limits: Humans, Randomised Controlled Trials

Using the above search strategy 97 publications were identified. The abstracts of these studies were examined and none were found to warrant inclusion. A second search of the same database was conducted using a broader search strategy (excluding terms concerning alignment and mechanical axis), returning 89 potential studies. From examination of the 89 identified studies' abstracts eight studies were retrieved in full text for data extraction and inclusion. Upon further review of the eight publications it was apparent that they had inadequate follow-up length and were excluded. **Therefore, there was no Level II evidence available concerning postoperative alignment and long-term outcomes.**

Level IV evidence (Case-series)

A literature search of PubMed to identify potentially relevant Level IV evidence was carried out in May 2008. The following search strategy was employed, with no limitation on publication date:

1. Arthroplasty, Replacement, Knee[MeSH]
2. Knee*
3. Knee Joint [MeSH] OR Knee [MeSH]
4. #2 OR #3
5. arthroplast* OR replace*
6. #4 AND #5
7. #1 OR #7
8. align*
9. angle*
10. mechanical axis
11. mechanical axes
12. varus
13. valgus
14. #8 OR #9 OR #10 OR #11 OR #12 OR #13
15. #7 AND #14

A total of 1664 publications were returned from this search. Extensive evaluation of these studies reduced the number of potential studies to 72. Of these, 19 studies were suitable for inclusion and were retrieved in full text for data extraction. Thirteen of the 19 included studies were excluded after extraction for reasons including insufficient follow-up and inappropriate outcomes. **A second reviewer concluded there were six studies suitable for inclusion; these studies form the majority of evidence.**

Hand searching

In addition to electronic searching, manual searching of reference lists was carried out. From this, five additional Level IV studies were identified for inclusion. These studies were retrieved in full text and extracted.

Results of assessment

Descriptive characteristics of included studies

Studies for assessment of safety

Thirty-one studies were identified for inclusion in the assessment of the safety of computer-navigated total knee arthroplasty. All studies compared computer-navigated total knee arthroplasty to the conventional technique. Sample sizes ranged from 24 to 1000 patients, with safety data reported for a total of 4513 patients overall.

Studies for assessment of effectiveness

A total of 43 comparative studies were identified and included to inform on the effectiveness of computer-navigated TKA. These studies allowed the assessment of the comparative effectiveness of the procedures within this review.

The systematic literature search revealed:

- a total of 15 randomised controlled trials that directly compared computer-navigated total knee arthroplasty to conventional total knee arthroplasty (Bejek et al 2007; Chauhan et al 2004; Chin et al 2005; Church et al 2007; Decking et al 2005; Ensini et al 2006; Kalairajah et al 2005; Kalairajah et al 2006; Kim et al 2008; Macule-Beneyto et al 2006; Matziolis et al 2007; Mombert et al 2007; Spencer et al 2007; Stockl et al 2004; Weinrauch et al 2006)

- seven pseudo-randomised controlled trials that directly compared computer-navigated total knee arthroplasty to conventional total knee arthroplasty (Bäthis et al 2004b; Böhling et al 2005; Kim et al 2007; Martin et al 2007; Oberst et al 2008; Song et al 2007; Sparmann et al 2003)

- twenty-one nonrandomised comparative studies (Anderson et al 2005; Bäthis et al 2004; Bolognesi et al 2005; Chang et al 2006; Confalonieri et al 2005; Daubresse et al 2005; Haaker et al 2005; Hart et al 2003; Jenny et al 2001; Jenny et al 2005; Kim et al 2005; Malik et al 2007; Matsumoto et al 2004; Molfetta et al 2008; Rosenburger et al 2008; Skowronski et al 2005; Stulberg et al 2006; Tingart et al 2008; Yau et al 2008; Zorman et al 2005; Zumstein 2006).

A subsequent section will examine these studies in greater detail and appraise their methodological quality.

Duplication of results

It is unlikely that duplication of the results has occurred across this dataset. There were various cases where the same patient population (or part of patient population) was used in multiple reports. In some cases, different outcomes were reported in those different reports. In cases where the same outcome was reported in more than one report, the most recent data was used for analysis.

Systematic reviews and health technology assessments

A list of electronic databases and websites of international health technology assessment (HTA) agencies can be found in Appendix C. A total of five health technology assessments, protocols for assessment and reviews were identified (Bäthis et al 2006; Bawens et al 2007; Brophy et al 2007; Luring et al 2006; Medical Advisory Secretariat 2004); these are presented in Appendix F.

An additional systematic review was also identified through the literature search (Mason et al 2007).

Bäthis et al (2006) identified 18 comparative studies examining the precision of implantation using computer navigation during total knee arthroplasty. As the article was published in German, only the English abstract was available. The abstract did not state whether imageless navigation was the focus of the article. Thirteen studies were able to be meta-analysed to determine the effectiveness of computer navigation in achieving mechanical axis alignment within ± 3° from neutral alignment. **The authors reported a statistically significant greater number of computer-navigated components were implanted within ± 3° compared to the conventional technique.** Unfortunately, the results for the postoperative mechanical axis alignment were not presented in the abstract. **The abstract did, however, report that no differences in the clinical course of the patients were observed.**

Bawens et al (2007) conducted a meta-analysis of 33 randomised and nonrandomised comparative studies comparing CT-based and imageless navigated knee arthroplasty with conventional unicompartmental or total knee arthroplasty. No differences in the number of complications, infection rates or thromboembolic events were reported between navigated and conventional knee arthroplasty. The results of the meta-analysis indicated that there was no evidence of a difference in the mean postoperative mechanical axis between navigated and conventional knee replacement, although navigation may lower the risk of malalignment greater than ± 3° compared to the conventional technique (P <0.001). The authors report an increased operation time of 17 minutes using navigation ($P < 0.001$). In the few studies that reported clinical outcomes, no statistically significant differences were stated between the two techniques.

The use of imageless computer-navigated total knee arthroplasty in 19 randomised and nonrandomised comparative studies was reported by Brophy et al (2007). The study reported a small average difference between conventional and navigated techniques in terms of the postoperative mechanical axis, and the femoral and tibial component alignments. Similar to the other reports, the authors reported that computer navigation may improve alignment by the avoidance of the occurrence of outliers. The study also stated that there was a lack of correlation between postoperative malalignment and clinical outcomes.

Six prospective and randomised clinical studies with more than 30 patients per group were included in a meta-analysis performed by Luring et al (2006) to investigate the differences between imageless computer-navigated and conventional knee arthroplasty. The analysis revealed a statistically significant greater number of patients with postoperative mechanical axis within ± 3° using computer navigation ($P < 0.001$). An increase in the operation time of 20 minutes was also reported. A matched pair analysis of 100 patients found no differences between groups in common clinical and functional parameters such as Knee Society Score, Western Ontario and McMaster Universities

Osteoarthritis index (WOMAC) score or patient satisfaction, although the navigated group demonstrated a superiority in terms of postoperative collateral stability. The authors state that no published studies showing significant differences between the conventional and navigated techniques with respect to clinical and functional parameters were available at the time the article was published.

A combined review of computer-navigated hip and knee arthroplasty using robotic and imageless navigation systems was prepared by the Medical Advisory Secretariat (2007) on behalf of the Ontario Health Technology Assessment Committee. The review included four knee-related studies. The findings on the use of imageless arthroplasty indicated that the use of computer navigation led to improved alignment outcomes, although it is unclear if this will lead to improved clinical outcomes in the short term.

The systematic review conducted by Mason et al (2007) identified 29 studies. The meta-analysis conducted indicated that the risk of greater than ± 3° malalignment was significantly less using computer navigation for the mechanical axis as well as the femoral and tibial components. The review included both randomised and nonrandomised comparative studies as well as uncontrolled case series. The review only considered studies reporting an optimal alignment measure in conjunction with an associated number of knees achieving this optimal alignment. Therefore, studies which reported a mean or mean deviation from an optimal alignment were not considered.

All of the health technology assessments and systematic reviews identified acknowledged that although computer navigation may result in a marginal benefit in terms of improved alignment outcomes, it is unclear whether or not this will translate to better long-term clinical outcomes. The most common benefit reported was the potential reduction of the number of patients with mechanical axis or component alignment outside the desired range of ± 3°.

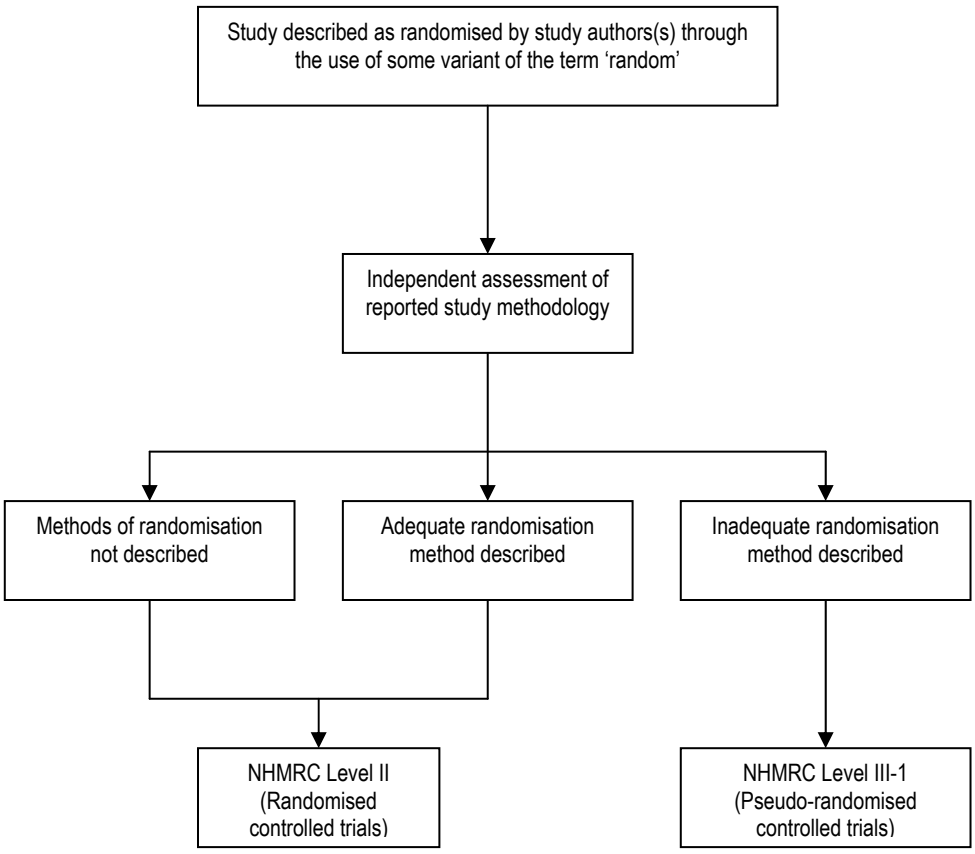
Critical appraisal of randomised controlled studies

Summaries of the quality of the 15 randomised controlled trials (RCTs) and seven pseudo-randomised controlled trials included in this review are reported in Table 36 and Table 37 in Appendix D and briefly described below.

Studies were classified utilising the National Health and Medical Research Council (NHMRC) Hierarchy of Evidence (NHMRC 2000) and allocated the classification of level II randomised controlled trial or level III-1 pseudo-randomised controlled trial based on the process outlined in Figure 2. Study quality was assessed according to the methods outlined in Section 6 of the Cochrane Reviewers' Handbook (Higgins & Green 2008) and the CONSORT Statement (Altman et al 2001).

A number of key appraisal parameters are applicable to both RCTs and pseudo-RCTs. Hence, for parameters where differentiation between the study designs is not relevant, these studies have been grouped together to better allow for the description of the higher-level evidence as a whole.

Figure 2 Method of assessing studies for assignment of NHMRC levels of evidence II & III-1



Study design details

Sample size

Across the 22 studies sample sizes ranged from 24 patients (24 knees) to 260 patients (420 knees). Only four studies had more than 100 patients in each study group. Studies did not differentiate well between unilateral and bilateral arthroplasty – there were frequent discrepancies between the number of patients treated and the number of knees treated that were not always explicitly accounted for.

Participants

Twelve of the 22 studies did not clearly describe their eligibility criteria for the recruitment of patients. The 10 studies that described inclusion and exclusion criteria considered a variety of factors when recruiting patients, including age, joint status, underlying pathology and comorbidities.

Study groups were reported to be generally well-matched at baseline, with age, gender and weight/body mass index (BMI) being the most frequently considered baseline characteristics. One pseudo-randomised controlled study reported on patients undergoing bilateral total knee arthroplasty acting as their own control, with one knee treated utilising computer navigation and the other the conventional technique (Kim et al 2007).

Randomisation, concealment and implementation

Of the 15 studies considered level II evidence, 10 employed adequate methods of randomisation, including sealed numbered envelopes, computerised random number generators and random number tables. Five of the 15 studies stated that the participants were randomised but provided no details on the randomisation methodology; as per the methods outlined in Figure 2, these have been considered as randomised controlled studies. Further prevention of selection bias through assignment concealment and/or independent implementation of the randomised assignment were reported in six of the 15 studies.

Of the seven studies considered level III-1 evidence, five utilised alternate allocation to assign patients to treatment and control groups. One study based treatment allocation according to the day of the operation (Bäthis et al 2004b) and another on patient codes (Martin et al 2007). Only one study reported rigorous allocation concealment and appropriate implementation of group assignments (Sparmann et al 2003).

Blinding

Half of the studies (11/22) did not report on blinding of outcomes assessors. Ten specifically reported employing some form of blinding, including blinding radiologists analysing postoperative radiographs, ward staff performing mental test scores and physiotherapists assessing functional outcomes. One pseudo-randomised controlled study specifically reported that it was not possible to blind the radiological assessors, as the drill holes for fixing of the rigid bodies (associated with the computer-navigated tracking system) were clearly visible on the films in the scout view (Oberst et al 2008).

Interventions and outcomes

Interventions were generally clearly detailed; the majority of studies defined primary outcomes. However, the majority of studies defined unvalidated surrogate endpoints, utilising radiological outcomes. Less frequently employed were clinical endpoints reporting on the function of the knee after arthroplasty.

Results reporting and analyses

Numbers analysed

The majority of studies did not report undertaking power calculations. Only five of the 22 studies reported undertaking power calculations on appropriate outcomes and recruiting the sample size necessary to detect statistically meaningful differences between the two groups.

Twenty studies did not report whether they undertook an intention-to-treat or per-protocol analysis. One study reported undertaking analysis by treatment intention, but provided no further details (Maculé-Beneyto et al 2006), while one study specifically stated that an intention-to-treat analysis was precluded by the short follow-up time (Kim et al 2008).

Statistical methods

The descriptive and inferential statistics utilised were clearly stated in 20 of the 22 studies. Fifteen studies prospectively identified an alpha level for statistical significance, most frequently of 0.05.

Outcomes and estimation

The included studies were thorough in reporting the results of each primary outcome defined. The mean was the most frequently employed indicator of central tendency, with almost all studies including some measure of estimation; standard deviations, 95% confidence intervals (CI) and ranges were reported where appropriate.

Adverse events were not well reported. A number of studies described events only briefly for each study group, with less than half of the studies (9/22) not reporting on adverse events.

Follow-up and losses to follow-up

A wide variety of follow-up time was reported amongst the 22 studies, ranging from immediate postoperative observations to three-year postoperative radiological and functional assessment. However, most studies employed a relatively short follow-up period, focussing on short-term outcomes.

Losses to follow-up were poorly reported; this may be due to the relatively short period of follow-up undertaken in a number of studies, where patients were assessed during their hospitalisation and not followed up after discharge. Only four studies reported explicitly that no patients were lost to follow-up.

Critical appraisal of nonrandomised comparative studies

An appraisal of the quality of the 21 level III-2 and III-3 studies included in this review is reported in Appendix H, and briefly summarised below.

Eleven studies were classified as Level III-2 evidence, as they reported a concurrent control group. Six studies utilised historical control groups, resulting in them being classified as level III-3 evidence, as a range of biases may be engendered from this use of historical controls. Four studies did not report their study design methodology in enough detail to allocate an accurate level of evidence under the NHMRC Hierarchy (NHMRC 2000). These have been described as level III-2/3 studies and, for the purposes of critical appraisal, are considered grouped together with the level III-2 and level III-3 evidence wherever possible.

Study design details

Participants

Sample sizes across the 21 studies ranged from a total of 28 patients (14 in each study group) to 1000 patients (500 in each study group).

Blinding

Six studies reported undertaking blinding of outcomes assessors, while one study specifically reported that blinding was not undertaken. Fourteen studies did not report on blinding status.

Interventions and outcomes

Interventions were generally clearly detailed; primary outcomes were defined well overall, with a clear focus towards radiological outcomes. A number of studies briefly reported on safety outcomes, and five studies considered functional outcomes.

Results reporting and analysis

Statistical methods

The analysis techniques employed were consistently reported; 20 of the 21 studies explicitly listed the statistical tests employed. Sixteen studies also reported a pre-defined level alpha value that would be considered statistically significant.

Follow-up and losses to follow-up

A wide range of follow-up times was reported. However, there was a consistent focus on short-term follow-up, with seven studies undertaking immediate postoperative follow-up and the majority of studies undertaking follow-up within three months of arthroplasty.

Losses to follow-up were reported in only six studies. Of these, five reported that no patients were lost to follow-up, and one reported losing two patients from an initial study group of 60.

Is it safe?

Summary of safety data from level II and III studies

Included studies

Of the 44 comparative studies included (NHMRC level II and III evidence), 30 studies provided some information on adverse events. An additional comparative study using the OrthoPilot system, which did not provide any effectiveness outcomes of interest, was included as it reported adverse events (Clemens and Miehlke 2003). The remaining 14 studies presented no adverse events numerical data or statements; however, this does not necessarily indicate an absence of complications in these studies. Safety outcomes of interest were clinical adverse events, technical adverse events related to the navigation system, and blood loss. This summary does not take into account surgical time or length of hospital stay, as these are covered in the effectiveness section. The adverse events reported by each study are shown in Table 7. From the safety data, it was possible to calculate incidence rates of the various adverse events. While some studies did not report total patient numbers, all studies reported total number of knees; thus, incidence rates were calculated in terms of number of knees in the study group.

Table 7 Adverse events reported in studies providing level II and III safety evidence

Study	Conventional technique			Computer-navigated		
	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)
Level II studies						
Bejek 2007	63 or 69 (both numbers reported)	69	Delayed wound healing (1)	69	69	Septic complication (1) (required two-stage revision) Delayed wound healing (1) Deep vein thrombosis (1) Complications from screws temporarily fixing the transducer devices (0)
Chauhan 2004	35	35	Pulmonary embolus (1) Deep vein thrombosis (2) Superficial infection (2) Transient ischemia (1) Acute postoperative confusional state (10)	35	35	Deep venous thrombosis (1) Superficial infection (1) Stiff knee requiring manipulation under anaesthesia (1) Acute postoperative confusional state (1) Complications related to computer software or tracker pins (0)
Chin 2005	60	60	Mild stroke (1)	30	30	Wound complications (0) Major morbidity (0)
Church 2007	12	12	Wound infection (superficial or deep) (0) Chest infection (0) Pulmonary embolism (0) Deep venous thrombosis (0) Modified Mayo Clinic emboli score (mean (range)): 6.15 (4 to 8)	14	14	Wound infection (superficial or deep) (0) Chest infection (0) Pulmonary embolism (0) Deep venous thrombosis (0) Modified Mayo Clinic emboli score (mean (range)): 4.89 (3 to 7). Difference: *P* = 0.004
Decking 2005 & 2007*	25	25	Superficial postoperative wound infection with skin necrosis (2) (Both patients had revision surgery and secondary wound closure within two weeks. Both healed.) Clinically evident thrombosis (0) Deep infection (0)	27	27	Required switch to manual (0) Superficial postoperative wound infection with skin necrosis (2) (One had revision surgery three times within four weeks after implantation. One had conservative treatment. Both healed.) Clinically evident thrombosis (0) Deep infection (0)
Ensini 2006	60 NR/107)	60	Problems with screw fixation, positioning and moving of the trackers, digitization, and aligning procedures (0)	60	60	Problems with screw fixation, positioning and moving of the trackers, digitization, and aligning procedures (0) Navigation system failure (0)
Kalairajah 2006	10	10	Emboli detection (mean ± SD): 10.7 ± 13.5	14	14	Emboli detection (mean ± SD): 0.64 ± 0.74. Difference: *P* = 0.0003
Kim 2008	160 (60 had navigated on other knee)	210	≥ 1 fat globule emboli (109) ≥ 1 bone marrow cell emboli (31)	160 (60 had conventional on other knee)	210	≥ 1 fat globule emboli (102). Difference: *P* = 0.2674 ≥ 1 bone marrow cell emboli (36) Difference: *P* = 0.2591
Spencer 2007	36	36*	Anterior knee pain (14) Clinically significant pain (moderate to severe): (2)	35	35*	Anterior knee pain (14) Clinically significant pain (moderate to severe) (5). Difference: *P* = 0.427
Stökl 2004	32	32	…	32	32	Loosening of tibial tracker (1) (reverted to conventional, excluded)

Table 7 continued Adverse events reported in studies providing level II and III safety evidence

Study	Conventional technique			Computer-navigated		
	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)
Level III-1 studies						
Bäthis 2004b	80	80	…	80	80	Conversion to conventional technique (0)
Kim 2007	100 (also had computer-navigated on other knee)	100	Anterior femoral notching (1)	100 (also had computer-navigated on other knee)	100	Anterior femoral notching (6) Excessive resection of tibia (1) (required tibial insert) Complication rate not significantly different: *P* = 0.058
Martin 2007	100	100	Anterior knee pain (8)	100	100	Insufficient fixation of femoral dynamic reference base (2) (navigation failed, excluded) Navigation- related perioperative or postoperative clinical complications (0) Anterior knee pain (8)
Song 2007	46	46	…	46	46	Navigation system registration failure (2) (excluded)
Sparmann 2003	120	120	Deep infection (0) Thrombosis (1) Delayed would healing: (1) Manipulation under anaesthesia (4)	120	120	Deep infection: (1) Thrombosis: (1) Delayed would healing: (3) Manipulation under anaesthesia (1)
Level III-2 studies						
Bäthis 2004a	50	50	…	50	50	Conversion to conventional technique (0)
Chang 2006	29	29	Infection (0) Deep vein thrombosis (0) Pulmonary embolism (0) Anterior femoral notching (4)	43	50	Intraoperative fractures (2) Infection (0) Deep vein thrombosis (0) Pulmonary embolism (0) Anterior femoral notching (12). Difference: *P* = 0.414
Confalonieri 2005	77	77	Intraoperative complications (0)	38	38	Intraoperative complications (0)
Hart 2003	60	60	…	60	60	Complications related to the use of the computer navigation system (0)
Matsumoto 2006	30	30	Knee crepitus (2) Patellofemoral symptoms (patellar clunk syndrome, patellar subluxation or fracture) (0) Reported knee pain (0)	30	30	Complications related to the use of the device (0) Knee crepitus (1) Patellofemoral symptoms (patellar clunk syndrome, patellar subluxation or fracture) (0) Reported knee pain (0)

Table 7 continued Adverse events reported in studies providing level II and III safety evidence

Study	Conventional technique			Computer-navigated		
	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)	No. of patients	No. of knees	Adverse event (number of events) (resolution of adverse event, where reported)
Level III-2 studies						
Molfetta 2008	30	30	Intraoperative complications (0) Postoperative complications (0)	30	30	Replacement of femoral screw due to loosening (1) Intraoperative complications (0) Postoperative deep vein thrombosis (1) (resolved)
Tingart 2008	500	500	Infection rate, onset of thromboembolic events and wound healing data not reported.	500	500	Intraoperative loosening of femoral or tibial tracker (6) (converted to conventional technique and excluded) Other technical complications such as pin breakage (0) Infection rate, onset of thromboembolic events and wound healing data not reported. No evidence of difference.
Zumstein 2006	30	30	Wound healing problems (0) Infection (0)	30	30	Technical difficulties(1) (Conversion to conventional) Arthrofibrosis (1) (treated with manipulation, with patella ligament rupture during manipulation and reconstruction)
Level III-2/3 studies						
Bolognesi 2005	48	50	…	50	50	Complications (wound complications, fractures, soft tissue injury) associated with placement of trackers (0)
Jenny 2001	30	30	…	30	30	Interruption of navigation procedure (0)
Level III-3 studies						
Anderson 2005	51	51	Intraoperative complications (0)	116	116	Complications related to the use of the navigation system (0) Intraoperative complications (0)
Clemens 2003	30	30	Deep venous thrombosis (1)	60	60	Deep venous thrombosis (3) Navigation complication - Drill for fixation of the rigid body at the iliac crest broke during the procedure (1)
Daubresse 2005	50	50	Complications related to operative technique (0)	50	50	Complications related to operative technique (0)
Jenny 2005	235	235	Phlebitis (10) Pulmonary embolism (1) Haematoma (9) Skin necrosis (4) Infection (2) Delayed rehabilitation (6) Other (11)	235	235	Broken pelvic drill (1) Femoral screw forgotten (1) Phlebitis (4) Pulmonary embolism (2) Haematoma (2) Infection (1) Delayed rehabilitation (4) Other (4)
Rosenburger 2008	50	50	…	50	50	Broken Schanz Pin before procedure(1) Malfunction of Medtronic Treon plus™ spring paddle requiring exchange (1) Femoral or tibial fractures or infections related to the use of femoral or tibial pins (0)
Zorman 2005	62	62	…	72	72	Major complication related to the technique of navigation (0) Displacement of beacons leading to partial loss of data (8)

NOTES: SD = standard deviation; … = not reported; * study did not state if the arthroplasty was unilateral or bilateral. Unilateral arthroplasty was assumed.

Clinical adverse events

Few included studies reported statistical comparisons between the conventional and computer-navigated techniques in terms of adverse events. This may be due to the rare nature of many of these events.

Systemic emboli released during total knee arthroplasty have been implicated as a cause of peri-operative morbidity and neurological dysfunction (Church et al 2007). Three studies statistically compared the presence of emboli between the conventional and computer-navigated knee groups (Church et al 2007; Kalairajah et al 2006; Kim et al 2008). Church et al (2007) found the Modified Mayo Clinic emboli score to be significantly higher (corresponding to more emboli) in the conventional group ($P = 0.004$). Similarly, Kalairajah et al (2006) detected more emboli in patients who had undergone total knee arthroplasty using the conventional technique ($P = 0.0003$). The clinical significance of this improvement is not reported. In contrast, Kim et al (2008) found no statistically significant difference between the conventional and computer-navigated knee arthroplasty groups for the number of fat and bone marrow cell emboli detected ($P > 0.05$).

Other statistical comparisons of clinical adverse events were performed by Spencer et al (2007) who found no significant difference in clinically significant pain between the conventional and computer-navigated knee arthroplasty groups, and by Chang and Yang (2006) who found no significant difference in the number of anterior femoral notching cases between the conventional and computer-navigated knee arthroplasty groups. Kim et al (2007) reported that the complication rate in general was not significantly different between the two groups.

Table 8 displays the incidence rates of the various reported clinical adverse events. There was no clear difference between the conventional and computer-navigated knee arthroplasty groups for any of the adverse events reported. Infection and deep vein thrombosis were the most commonly reported clinical adverse events, and both demonstrated small incidence rates of 0.8 per cent and 1.6 per cent respectively in the conventional technique population, and 1.1 per cent and 1.7 per cent in the computer-navigated technique population. Knee pain was reported in 13.3 per cent of knees, for both the conventional and computer-navigated technique groups. As reported by one study, the presence of fat globule emboli was high in both groups, with 51.9 per cent of conventional knees and 48.6 per cent of computer-navigated knees having fat emboli present.

Major morbidities were rare in both the conventional and computer-navigated knee groups, and there were no reported deaths as a result of the TKA procedure in either group. Long-term safety data was not available from the included studies.

Table 8 Summary of clinical adverse events in level II and III studies providing safety evidence

Clinical adverse event	Conventional technique		Computer-navigated technique	
	Incidence* n/N (%)	No. of studies reporting outcome	Incidence* n/N (%)	No. of studies reporting outcome
Infection (superficial or deep)	4/486 (0.8%)	7	6/550 (1.1%)	7
Deep vein thrombosis	4/251 (1.6%)	6	7/405 (1.7%)	8
Pulmonary embolism	2/311 (0.6%)	4	2/299 (0.7%)	3
Delayed wound healing	2/219 (0.9%)	3	4/219 (1.8%)	3
Reported knee pain	22/166 (13.3%)	3	22/165 (13.3%)	3
Anterior femoral notching	5/129 (3.9%)	2	18/150 (12.0%)	2
Skin necrosis	6/260 (2.3%)	2	2/27 (7.4%)	1
Haematoma	9/235 (3.8%)	1	2/235 (0.9%)	1
Chest infection	0/12 (0%)	1	0/14 (0%)	1
Acute postoperative confusional state	10/35 (28.6%)	1	1/35 (2.9%)	1
Mild stroke	1/60 (1.7%)	1	…	0
Transient ischemia	1/35 (2.9%)	1	…	0
Phlebitis	10/235 (4.3%)	1	4/235 (1.7%)	1
Knee requiring manipulation under anaesthesia	4/120 (3.3%)	1	3/185 (1.6%)	3
Knee crepitus	2/30 (6.7%)	1	1/30 (3.3%)	1
Patellofemoral symptoms (patellar clunk syndrome, patellar subluxation or fracture)	0/30 (0%)	1	0/30 (0%)	1
Delayed rehabilitation	6/235 (2.6%)	1	4/235 (1.7%)	1
Fat globule emboli	109/210 (51.9%)	1	102/210 (48.6%)	1
Bone marrow cell emboli	31/210 (14.8%)	1	36/210 (17.1%)	1
Major morbidity	…	0	0/30 (0%)	1
Intraoperative fractures	…	0	2/50 (4%)	1
Excessive resection of tibia, requiring tibial insert	…	0	1/100 (1%)	1

NOTE: *Incidence is reported in terms of number of knees rather than number of patients; … = not reported

Technical adverse events

The included studies generally only reported technical adverse events associated with the computer navigation system, and not with the conventional technique. Table 9 displays the incidence rates of the various reported technical adverse events. From 10 studies, the rate of conversion to the conventional manual technique due to technical failure of the computer navigation system was 12/955 knees (1.3%). The most common technical problem was difficulty with tracker fixation or loosening of the tracker. This occurred in 18/794 knees (2.3%). Other technical adverse events reported included pin breakage, drill breakage, malfunctioning of a spring paddle, and a forgotten screw. All of these events were relatively rare. Ten studies specifically reported that no complications occurred in relation to the navigation system.

Non-specified intra-operative, postoperative and 'other' complications were reported for the conventional technique in five studies and for the computer-navigated technique in four studies. Of the studies reporting non-specified intra-operative complications, a 0% complication rate was reported for both techniques. Non-specified postoperative complications were reported by one study for the conventional technique only, reporting a complication rate of 0%. Finally, under 'other' non-specified complications, one study reported a complication rate of 11/235 (4.7%) for the conventional technique, and one study reported a complication rate of 4/235 (1.7%) for the computer-navigated technique.

Table 9 Summary of technical adverse events in level II and III studies providing safety evidence

Technical adverse event	Conventional technique		Computer-navigated technique	
	Incidence* n/N (%)	No. of studies reporting the event	Incidence* n/N (%)	No. of studies reporting the event
Difficulty with tracker fixation/ loosening	N/A	-	18/794 (2.3%)	6
Pin breakage	N/A	-	1/550 (0.2%)	2
Broken drill	N/A	-	2/295 (0.2%)	2
Malfunctioning of spring paddle	N/A	-	1/50 (2%)	1
Complications from screw/tracker placement (fracture/infection/ screw forgotten)	N/A	-	1/404 (0.2%) (screw forgotten)	4
Non-specified complications related to navigation system	N/A	-	0/363 (0%)	6
Non-specified complications related to navigation system, requiring conversion to manual technique	N/A	-	3/323 (0.9%)	7
Total reported conversions to manual technique due to technical failure of navigation system	N/A	-	12/955 (1.3%)	10

NOTES: *Incidence is reported in terms of number of knees rather than number of patients. N/A = not applicable; ... = not reported

Blood loss

Eight of the included studies provided measures of the amount of blood lost during the TKA procedures (Table 10). Kalairajah et al (2005) found that blood loss (drainage) and haemoglobin drop was significantly less in the computer-navigated group compared to the conventional group ($P = 0.001$ and $P < 0.00001$, respectively). Chin et al (2005) also reported blood drainage to be significantly ($P = 0.046$) less in the computer-navigated group. The other six studies either found no significant difference between the conventional and computer-navigated groups, or did not report on statistical significance.

Table 10 Blood loss during TKA in the conventional and computer-navigated groups

Study	Measure	Conventional technique Mean ± SD (range)	Computer-navigated technique Mean ± SD (range)	*P* value
Chin 2005	Drainage (mL)	EM: 400.5 (50.0 to 990.0) IM: 396.3 (105.0 to 770.0)	290.3 (0.0 to 650.0)	0.046
	Hb loss (g/dL)	EM: 2.94 (0.2 to 8.8) IM: 3.14 (1.3 to 6.2)	2.56 (0.1 to 5.3)	0.176
Kalairajah 2005	Total blood loss (mL)	1747 (1100 to 3030)	1351 (715 to 2890)	0.001
	Hb loss (g/dL)	52.6 (95%CI 46.4 to 58.7)	36.5 (95%CI 33.2 to 39.8)	< 0.00001
Matziolis 2007	Blood loss (mL)	520 ± 295 (50 to 1015)	469 ± 327 (50 to 1120)	NS
Weinrauch 2006	Hb level post-op (g/L)	105.7	103.2	…
	Transfusion requirement (units)	0.54	0.36	…
Kim 2007	Blood loss (mL)	264.7 (40 to 850)	277 (80 to 700)	0.714
	Drainage (mL)	750 (60 to 1440)	783.3 (52 to 1410)	0.633
Martin 2007	Blood loss (mL)	394 ± 350 (30 to 1910)	434 ± 272 (30 to 1080)	…
	Hb level (mg/dL)	10.9	11.3	…
	Transfusion requirements (units)	2.64 ± 1.28 (1 to 7)	2.38 ± 0.98 (1 to 6)	…
Stulberg 2006	Blood transfused (units)	0.4 ± 0.76 (0-4)	0.6 ± 0.82 (0-3)	…
Anderson 2005	Blood loss (mL)	103	105	…

NOTES: SD = standard deviation; EM = extramedullary guide; Hb = haemoglobin; IM = intramedullary guide; … = not reported; NS = non-significant

Summary of safety data from level IV studies

Included studies

Six level IV studies reported safety data on computer-navigated total knee arthroplasty. Additionally, three nonrandomised comparative studies and one randomised controlled study with inappropriate comparisons have been treated as level IV studies and their study arms included for safety data only (Jenny et al 2008; Lampe et al 2007; Martin 2006, Mullaji et al 2007). Where studies compared outcomes of computer-navigated total knee arthroplasty between study centres, or compared different types of imageless computer navigation software or different surgical approaches (minimally invasive versus conventional), these cohorts were combined. A summary of included studies is displayed in Table 11 below. Where reported, follow-up was longer than from the comparative studies and ranged from three months to two years. Studies which did not report safety data were excluded.

Table 11 Characteristics of studies providing level IV safety evidence

Study	Evidence level	Study period	Patient allocation	No. of patients	No. of knees	Age (years) Mean ± SD (range)	Male / female	Length of follow-up	Lost to follow-up/ excluded from outcome data
Alan 2007	IV	2005-2006	Consecutive	60	60	70 (43-86)	22/38	…	3
Catani 2008	IV	…	Consecutive	91	91	69.2 ± 9.4	27/64	…	1
Hernandez-Vaquero 2007	IV	2002-2006	Consecutive	…	151	…	…	…	…
Jenny 2008	III-2	2002-2003	Consecutive	368	368	67.8 ± 8.9 (35-88)	118/250	…	…
Lampe 2007	III-2	…	…	50	50	72 ± 11 (41-84) 71 ± 9 (53-84)	23/27	…	…
Martin 2006	III-3	2001-2002	Consecutive	22	22	70.6 ± 5.1 (62-81)	6/16	2 years	1
Mullaji 2007	II	2004-2006	Consecutive	282	282	65.5	67/215	1 year	33/500 (full study cohort)
Seon 2007	IV	…	Consecutive	46	46	…	2/40 (after exclusion of 4 cases)	1 year	4
Sikorski 2005	IV	…	Unclear	192	232	74.2 ± 8.8 72.5 ± 7.6 73.7 ± 9.4	112/80	1 year then 'yearly intervals'	…
Walde 2005	IV	…	Consecutive	60	…	68 (44-83)	27/33	3 months	0

NOTES: SD = standard deviation; … = not reported

The five studies which reported study periods covered the years 2001 to 2006 inclusive. The total number of patients was 1171 (excluding one study which only reported number

of knees rather than patients), and the total number of knees was 1302 (excluding one study which only reported number of patients). The mean age across the studies ranged from 65 to 74 years (excluding two studies which did not report mean age data). There were more females than males. Five of the 10 studies did not specify their follow-up period, and four studies did not report losses to follow-up. Table 12 shows the prostheses and navigation systems used in the included studies. The OrthoPilot was the most commonly used navigation system.

Table 12 Prosthesis and system used in studies providing level IV safety evidence

Study	Prosthesis	Navigation system
Alan 2007	…	Electromagnetic Navigation (manufacturer not reported)
Catani 2008	Scorpio (Stryker, Allendale, New Jersey)	Stryker (Stryker Navigation, United States)
Hernandez-Vaquero 2007	…	Stryker-Leibinger, Freiburg, Germany
Jenny 2008	E-Motion TKR (Aesculap, Germany) (posterior-cruciate retaining total knee replacement)	OrthoPilot (Aesculap, Germany)
Lampe 2007	Columbus CR (B. Braun Aesculap, Germany)	OrthoPilot TKA 4.2 navigation system (B. Braun Aesculap, Germany)
Martin 2006	NexGen (MBK, Zimmer Inc, United States) Legacy constrained condylar knee prosthesis (Zimmer Inc)	Vector Vision knee navigation system (Brain-LAB Inc, Germany)
Mullaji 2007	PFC Sigma (DePuy Inc, United States)	Ci-Navigation System (BrainLab, Germany)
Seon 2007	E-Motion (Aesculap, Germany)	OrthoPilot (ver. 4.08, Aesculap, Germany)
Sikorski 2005	Duracon monogram (Stryker Corp.) Genesis II (Smith & Nephew Inc.)	Stryker (versions 1.1 & 2.0) (Stryker Corp., Leibinger, United States) Vector Vision system Brain-LAB (versions β1, β2, β3, β4 & 1.5) (Smith & Nephew)
Walde 2005	Columbus (B. Braun-Aesculap, Germany)	OrthoPilot (B. Braun-Aesculap, Germany)

NOTES: … = not reported

Clinical and technical adverse events

The 10 included studies reported intra-operative and/or postoperative adverse events, as well as complications that resulted in exclusions from the studies. These adverse events are detailed in Table 13. Complications have been divided into either technical or clinical events for clarity, and are summarised in Table 14. There were a total of 28 technical adverse events and 27 clinical adverse events reported in the studies. Given the fact that these events occurred across more than 1171 patients (or more than 1302 knees), the incidence of reported adverse events was relatively uncommon. As the studies did not report number of patients or number of knees, the incidence rates of the various adverse events were not calculated. Of the technical events, difficulty with tracker fixation or loosening of the tracker was the most common adverse event, followed by the navigation system providing incorrect data. There were 13 reports of technical adverse events leading to abandonment of the navigation technique, resulting in a reversion to conventional manual TKA. These cases were often excluded from the outcome data reported in the study. Infection and nerve injury were the most common clinical adverse events reported. There were no reports of any deaths as a result of the computer-navigated total knee arthroplasty procedure. Long-term safety data was not available from the included studies, and the long term morbidity of adverse events such as nerve damage could not be determined.

Table 13 Adverse events reported in studies providing level IV safety evidence

Study	No. of patients	No. of knees	Adverse events (number of events) (resolution of adverse event, where reported)	Total complications
Alan 2007	60	60	Electromagnetic surveillance abandoned because data from navigation grossly incorrect (3) (excluded)	3
Catani 2008	91	91	Fixation of a tracker of the navigation system was lost (1) (excluded)	1
Hernandez-Vaquero 2007	…	151	Painful scarring found in tibial tracker hole (3) (disappeared after two months) Technical complication related to fixing trackers (9) Major complications (fractures, infections or vascular-nervous damages) (0)	12
Jenny 2008	368	368	Difficulty with hip registration (2) Interruption of the software (2) Loosening of tibia localiser (2) Loosening of femoral localiser (1) Non plausible axis measurement (2) Femoral fracture through hole of reference screw (1) (reoperated with satisfactory result)	10
Lampe 2007	50	50	Femoral notching (2) Haematoma (1) (uncomplicated revision) Deep vein thrombosis (1) (uncomplicated) Wound healing or septic complications (0)	4
Martin 2006	22	22	Loosening of dynamic reference base (1) (excluded) Anterior knee pain (1) Help required to undertake the step test because of pain (1)	3
Mullaji 2007	282	282	Acute deep infection (1) (debridement and change of insert, now asymptomatic) Supracondylar fracture after a fall, at site of hole for array (1) (treated surgically, healed uneventfully)	2
Seon 2007	46	46	Navigation system registration failure (resulting in a switch to conventional TKA) (2) (excluded)	2
Sikorski 2005	192	232	Injury to the lateral cutaneous nerve of the thigh with numbness (6) Pin track infections (7) Peri-prosthetic fractures (2, including one through site of screw for array and one through medial femoral condyle away from screw site)	15
Walde 2005	60	…	Complications with navigation process - blood contamination leading to tracking problems (3) (system cleaned and surgery finished without further problems)	3
Total	1171 (excluding one study which did not report number of patients)	1302 (excluding one study which did not report number of knees)		55

NOTES: … = not reported

Table 14 Summary of adverse events reported in studies providing level IV safety evidence

Technical adverse event	No. of cases	Clinical adverse event	No. of cases
Difficulty with tracker fixation/ loosening	14	Infection (severity not reported)	7
Navigation data incorrect	5	Nerve injury/ numbness	6
Blood contamination caused tracking problems	3	Painful scarring in tracker hole	3
Difficulty with hip registration	2	Fracture through hole of reference screw	3
Software interruption	2	Femoral notching	2
Non-specified navigation system registration failure	2	Knee pain	2
Total	28	Deep vein thrombosis	1
Total reported conversion to manual technique due to technical failure of navigation system (for reasons detailed above)	13	Haematoma	1
		Deep infection	1
		Other peri-prosthetic fracture	1
		Total	27
TOTAL REPORTED ADVERSE EVENTS			55

Expert opinion

The clinical experts of the Advisory panel consider the reported complication rates from the included studies to be lower than might be expected from their clinical experience with any knee replacement. It was acknowledged that the studies investigated effectiveness outcomes (such as postoperative mechanical axis or component alignment) as the primary outcome, rather than complications and adverse events from knee replacement procedures. This study bias may have lead to an under-reporting of safety issues.

Summary of safety outcomes

In general, among the 31 comparative and 10 case series studies included for safety, few serious adverse events and no deaths were reported as a result of computer-navigated total knee arthroplasty. Safety data was separated into three categories: clinical adverse events, technical adverse events (resulting from the use of computer navigation) and blood loss.

Comparative data demonstrates that clinical adverse events were relatively uncommon and almost identical in occurrence between computer-navigated and conventional total knee arthroplasty. The release of systemic emboli during total knee arthroplasty, which has been implicated as a cause of peri-operative morbidity and neurological dysfunction, was reported in three studies. Two studies reported significantly more emboli in patients who had undergone total knee arthroplasty using the conventional technique, while one study found no statistically significant difference between the two techniques. For other clinical adverse events, no significant differences between the conventional and computer-navigated technique in terms of clinically significant pain, number of anterior femoral notching cases, and general complication rate were reported, although in each case these were only reported by one study. Infection and deep vein thrombosis were the most common reported clinical adverse events and demonstrated a rate of 0.8 per cent and 1.6 per cent respectively in the conventional technique and 1.1 per cent and 1.7 per cent in the computer-navigated group. These differences were not statistically significant.

Technical adverse events, reported for the computer-navigated technique only, were also relatively low amongst the 10 comparative studies reporting these outcomes. The rate of conversion to the conventional technique was reported as 1.3 per cent. The most common technical problem reported was difficulty with tracker fixation or loosening of the tracker which occurred in 2.3 per cent of cases. Ten studies specifically reported that no complications occurred in relation to the navigation system.

Blood loss during the total knee arthroplasty procedure was reported in eight comparative studies. Two studies reported significantly favourable results using computer navigation while the remaining six did not report any statistically significant differences.

Level IV evidence from 10 studies provided longer follow-up data than comparative data, but no long-term adverse events were reported. In absolute terms, tracker fixation/loosening and infection were the most common complications. The rate of resolution of these events was not reported in the studies; however, given the type of adverse events it may be safe to assume that the majority of complications resolved with little or minor intervention.

In summary, it appears that computer-navigated total knee arthroplasty is as safe as conventional total knee arthroplasty.

Is it effective?

Radiological results

The radiological results are presented in two sections. This has been done due to the wide variety in outcomes reported by the included studies, and also by the non-standard angles and reference standards utilised by the authors. There are two sections to the effectiveness results:

- radiological results, and
- clinical results and peri-hospital results.

Where possible, data analysis has been undertaken according to study level of evidence (NHMRC 2000).

The radiological results section presents the reported frontal plane radiological outcomes of the entire limb as reported by the overall mechanical axis alignment (angle created between femoral and tibial mechanical axes) and the tibiofemoral angle (angle created between shaft of the tibia and shaft of the femur). Additionally, the alignment of the femoral and tibial components with reference to either the mechanical axis of the leg or the mechanical axis of the bone is reported.

Mechanical axis alignment

Postoperative deformity

Sixteen studies (four randomised controlled trials, three pseudo-randomised controlled trials and nine comparative studies) were identified that compared computer-navigated total knee arthroplasty with conventional total knee arthroplasty in the postoperative deformity achieved (Daubresse 2005; Decking 2005; Ensini 2006; Jenny 2005; Kim 2005; Malik 2007; Martin 2007; Mombert 2007; Oberst 2008; Rosenburger 2008; Song 2007; Stökl 2004; Stulberg 2006; Yau 2008; Zorman 2005; Zumstein 2006).

Mechanical axis alignment is a bi-directional outcome measure, as it can be represented as either a positive value (indicating a valgus alignment) or a negative value (indicating a varus alignment) or vice versa. As such, meta-analysis of the weighted mean differences in postoperative mechanical axis alignment between the conventional and computer-navigated total knee arthroplasty groups was meaningless, as it gave no information on the absolute magnitude of the postoperative deviation from the ideal mechanical axis; nor could information on the direction (varus or valgus) be obtained.

As an alternative measurement, the mean of the mean postoperative deformities and the pooled standard deviation were calculated to illustrate the difference in postoperative deformity achievement between conventional and computer-navigated total knee arthroplasty.

Three separate analyses, one including only the four randomised controlled trials, one including the four randomised controlled trials and three pseudo-randomised controlled trials, and one including all sixteen identified studies were performed (Table 15).

The mean of mean postoperative deformities among the four included randomised controlled studies was calculated in Microsoft Excel and slightly favoured the conventional technique with conventional patients (n = 138) achieving an angle of 1.20° varus and navigated patients (n = 140) achieving an angle of 1.25° varus. The pooled standard deviation on the other hand slightly favoured the navigated technique with navigated patients achieving a smaller pooled standard deviation than conventional patients (2.27° versus 2.99°).

The addition of three pseudo-randomised studies into the above analysis more than doubled the number of patients available for analysis in each group and in contrast to the RCT-only analysis, demonstrated a slight favour towards computer navigation. Patients in the computer-navigated group (n = 314) achieved a mean postoperative deformity of 1.10° varus while patients in the conventional group (n = 316) achieved a postoperative deformity of 1.33° varus. However, as per the RCT-only analysis, the pooled standard deviation favoured computer navigation (1.94° versus 2.61°).

Analysis of all 16 identified studies approximately tripled the number of patients available for analysis in each group and demonstrated a slightly better postoperative deformity and pooled standard deviation in patients who had undergone computer-navigated total knee arthroplasty. In the computer-navigated group (n = 928), patients achieved a mean postoperative deformity and pooled standard deviation of 0.79° varus and 2.21° respectively. In comparison, patients who underwent the conventional technique achieved a mean postoperative deformity of 0.90° and pooled standard deviation of 2.95°.

In all three postoperative deformity analyses performed, the mean postoperative deformity achieved was similar and in the same direction (varus). Similarly in all three analyses, the pooled standard deviation achieved was smaller in the computer-navigated group indicating greater overall accuracy with computer navigation. However, in all cases the standard deviation was larger than the mean deformity.

Table 15 Postoperative deformity achievement

	Number of studies	Sample size	Mean of mean postoperative deformities (degrees)	Pooled standard deviation (degrees)
Level II RCTs				
Conventional TKA	4	138	1.20	2.99
Computer-navigated TKA		140	1.25	2.27
Level II & III-1: RCTs & pseudo-RCTs				
Conventional TKA	7	316	1.33	2.61
Computer-navigated TKA		314	1.10	1.94
Level II – Level III-3: all comparative studies				
Conventional TKA	16	924	0.90	2.95
Computer-navigated TKA		928	0.79	2.21

NOTE: positive values indicate varus alignment; TKA: Total knee arthroplasty.

Deviation

Deviation from the mechanical axis alignment was defined as the deviation in degrees from the target angle of 180°, regardless of whether the deviation was in the varus or valgus direction. Eight studies (one randomised controlled study, one pseudo-randomised and six nonrandomised comparative studies) reporting this outcome were identified and considered suitable for meta analysis (Bäthis et al 2004a; Chang et al 2006; Haaker et al 2005; Jenny et al 2005; Matziolis et al 2007; Molfetta et al 2008; Oberst et al 2008; Tingart et al 2008).

All studies reported a postoperative varus deviation. **Amongst the individual studies, the mean deviation was consistently larger in the conventional TKA groups when compared to the computer-navigated groups.**

Meta-analysis[1] under a fixed-effects model revealed an overall mean difference of 0.74° (95% CI: -0.89° to -0.59°) in favour of computer navigation (Figure 3). **This suggests that the use of computer navigation reduces the amount of deviation in the postoperative knee by a mean of 0.74° when compared to the deviation resulting from conventional navigation. This result was statistically significant ($P < 0.00001$).** No study crossed the line of no effect, and the narrow confidence intervals of the overall effect indicate the precision of the result. The studies were homogeneous ($P = 0.31$, $I^2 = 16\%$).

[1] A meta-analysis combines the results of several studies and is graphically represented by a forest plot.

The left hand side of the forest plot lists the studies included in the meta-analysis. For each study, the number of patients in each treatment group, as well as the mean and standard deviation of the outcome of interest in each treatment group. The meta-analyses performed in this report use the inverse variance (IV) method in which the average effect size across all studies is computed as a weighted mean, whereby the weights reflect the inverse variance of each studies effect estimator. For comparative studies with continuous outcomes, the standardised mean difference (standard score equivalent to the difference between means) is the effect size indicator. For studies where the outcome is dichotomous, the odds ratio is the effect size indicator used.

On the right hand side of a forest plot, there is a plot of the measure of effect for each of the studies included in the meta-analysis, represented by a square (the weight given to each study is reflected by the size of the square) and demonstrating the confidence intervals in the form of horizontal lines. The overall measure of effect is represented by a diamond with flanking horizontal lines representing the confidence intervals.

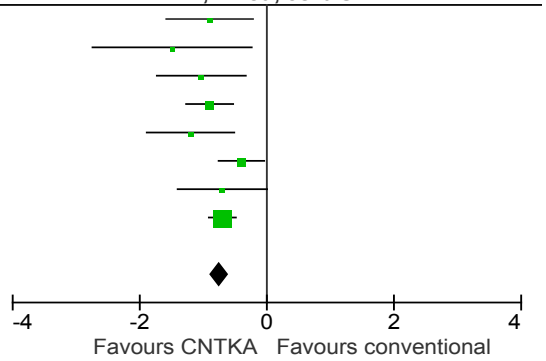
The forest plot has a vertical line at zero (when the mean difference is the measure of effect) or at one (when the odds ratio is the measure of effect) representing the line of no effect. Crossing of this line by individual studies or the overall result indicates that at the given level of confidence, the effect size does not differ from no effect.

Legend for forest plots
■ Each square represents the effect of the individual studies. The size of each square reflects the weight a particular study has in the overall analysis.
— The horizontal lines flanking the squares represent the 95% confidence intervals of each study. Generally, studies given smaller weights have larger confidence intervals than those with larger weights.
◆ The diamond represents the overall pooled effect. The width of the diamond represents the confidence intervals of the overall effect.
Line of no effect: The line of no effect is the vertical line located at 0 (when the mean difference is the measure of effect) or 1 (when the odds ratio is the measure of effect). Crossing this line indicates that the result is not significant.

Figure 3 Mechanical axis postoperative deviation (all studies)

	Computer-navigated TKA			Conventional TKA				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Bathis 2004a	1.3	1.1	50	2.2	2.2	50	4.6%	-0.90 [-1.58, -0.22]
Chang 2006	1.89	2.19	43	3.38	2.93	29	1.4%	-1.49 [-2.74, -0.24]
Haaker 2005	0.77	1.91	100	1.8	3.01	100	4.4%	-1.03 [-1.73, -0.33]
Jenny 2005	1.5	1.6	235	2.4	2.4	235	15.9%	-0.90 [-1.27, -0.53]
Matziolis 2007	1.4	0.8	32	2.6	1.7	28	4.6%	-1.20 [-1.89, -0.51]
Molfetta 2008	0.2	0.6	30	0.6	0.8	30	16.8%	-0.40 [-0.76, -0.04]
Oberst 2008	1.8	1.3	32	2.5	1.6	34	4.4%	-0.70 [-1.40, 0.00]
Tingart 2008	1.6	1.5	500	2.3	1.9	500	47.9%	-0.70 [-0.91, -0.49]
Total (95% CI)			**1022**			**1006**	**100.0%**	**-0.74 [-0.89, -0.59]**

Heterogeneity: Chi² = 8.31, df = 7 (P = 0.31); I² = 16%
Test for overall effect: Z = 9.86 (P < 0.00001)



NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Satisfactory alignment and outliers

Satisfactory postoperative alignment of the mechanical axis in the frontal plane was defined as postoperative deviation of three degrees or less from the target angle of 180°, regardless of whether the deviation was in the varus or valgus direction. In total, twenty-five studies using this standard outcome were identified and suitable for meta-analysis.

Five randomised controlled trials reporting this outcome were identified (Chauhan et al 2004; Ensini et al 2006; Matziolis et al 2007; Mombert et al 2007). Heterogeneity was low ($I^2 = 0\%$), so meta-analysis under a fixed effects model was undertaken. This showed a statistically significant total odds ratio (non-event) of 2.88 (95% CI: 1.85 to 4.49) in favour of computer navigation ($P < 0.00001$). **This indicates that the odds of having a knee with satisfactory postoperative alignment are 2.88 times greater with computer navigation than with conventional TKA (Figure 4).**

Six pseudo-randomised controlled trials were added to the meta-analysis and given the resultant increase in heterogeneity ($I^2 = 57\%$), a random effects model was employed (Bäthis et al 2004b; Böhling et al 2005; Kim et al 2007; Martin et al 2007; Oberst et al 2008; Sparmann et al 2003). The results show a statistically significant total odds-ratio (non-event) of 4.04 (95% CI: 2.37 to 6.88) in favour of computer navigation ($P < 0.00001$). **This indicated that the odds of having a knee with satisfactory postoperative alignment are 4.04 times greater with computer navigation than with conventional TKA (Figure 5).**

A further 14 nonrandomised comparative studies were added to the meta-analysis (Anderson et al 2005; Bäthis et al 2004a; Chang et al 2006; Confalonieri et al 2005; Daubresse et al 2005; Haaker et al 2005; Jenny et al 2001; Jenny et al 2005; Kim et al 2005; Matsumoto et al 2006; Skowronski et al 2005; Stulberg et al 2006; Tingart et al 2008; Zumstein et al 2006). Heterogeneity was slightly higher than the previous meta-analysis of randomised and pseudo-randomised controlled studies ($I^2 = 58\%$), so meta-analysis under a random effects model was employed. This showed a statistically significant total odds ratio (non-event) of 4.14 (95% CI: 3.03 to 5.66) in favour of computer navigation ($P < 0.00001$). **This indicates that the odds of having a knee with satisfactory postoperative alignment are 4.14 times greater with computer navigation than with conventional total knee arthroplasty (Figure 6).**

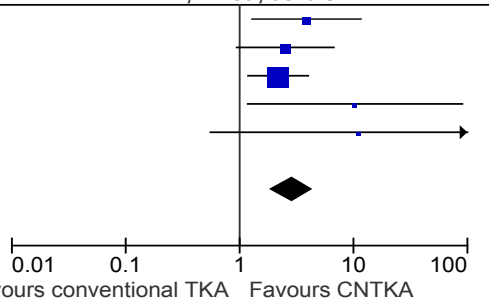
The cumulative meta-analysis undertaken demonstrates that computer-navigated total knee arthroplasty provides a significantly greater chance of achieving a postoperative knee that is within three degrees of the target angle on radiological examination than conventional arthroplasty.

This finding is robust, with the significance of this result maintained across all comparative study designs.

Figure 4 Mechanical axis satisfactory postoperative alignment (RCTs)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Fixed, 95% CI
Chauhan 2004	20	36	29	35	14.1%	3.87 [1.29, 11.59]
Ensini 2006	45	60	53	60	21.9%	2.52 [0.95, 6.73]
Macule-Beneyto 2006	25	84	49	102	59.4%	2.18 [1.19, 4.01]
Matziolis 2007	21	28	31	32	2.9%	10.33 [1.18, 90.26]
Mombert 2007	17	21	21	21	1.7%	11.06 [0.56, 219.68]
Total (95% CI)		**229**		**250**	**100.0%**	**2.88 [1.85, 4.49]**
Total events	128		183			

Heterogeneity: Chi² = 3.26, df = 4 (P = 0.52); I² = 0%
Test for overall effect: Z = 4.67 (P < 0.00001)

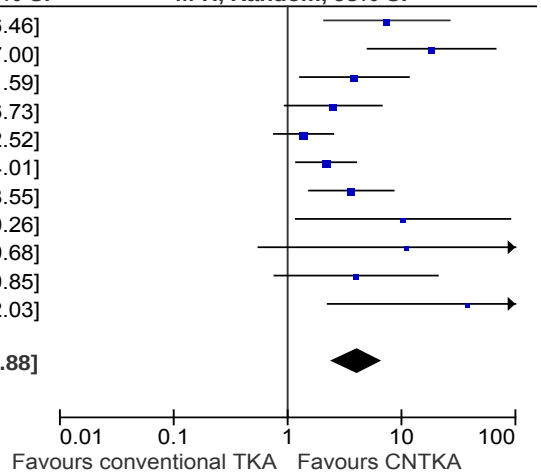


NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 5 Mechanical axis satisfactory postoperative alignment (RCTs & pseudo-RCTs)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004b	62	80	77	80	9.1%	7.45 [2.10, 26.46]
Bohling 2005	23	50	47	50	8.9%	18.39 [5.05, 67.00]
Chauhan 2004	20	36	29	35	10.5%	3.87 [1.29, 11.59]
Ensini 2006	45	60	53	60	11.5%	2.52 [0.95, 6.73]
Kim 2007	65	100	72	100	15.2%	1.38 [0.76, 2.52]
Macule-Beneyto 2006	25	84	49	102	15.1%	2.18 [1.19, 4.01]
Martin 2007	76	100	92	100	12.7%	3.63 [1.54, 8.55]
Matziolis 2007	21	28	31	32	4.6%	10.33 [1.18, 90.26]
Mombert 2007	17	21	21	21	2.7%	11.06 [0.56, 219.68]
Oberst 2008	28	35	32	34	6.7%	4.00 [0.77, 20.85]
Sparmann 2003	104	120	120	120	3.0%	38.05 [2.26, 642.03]
Total (95% CI)		**714**		**734**	**100.0%**	**4.04 [2.37, 6.88]**
Total events	486		623			

Heterogeneity: Tau² = 0.39; Chi² = 23.47, df = 10 (P = 0.009); I² = 57%
Test for overall effect: Z = 5.14 (P < 0.00001)

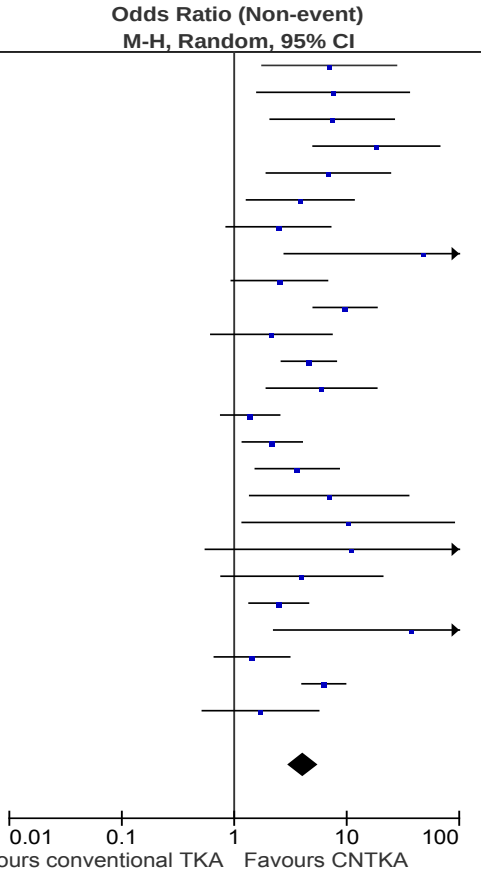


NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 6 Mechanical axis satisfactory postoperative alignment (all studies)

Study or Subgroup	Conventional TKA Events	Total	Computer-navigated TKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Anderson 2005	43	51	113	116	3.2%	7.01 [1.78, 27.65]
Bathis 2004a	38	50	48	50	2.7%	7.58 [1.60, 35.93]
Bathis 2004b	62	80	77	80	3.5%	7.45 [2.10, 26.46]
Bohling 2005	23	50	47	50	3.4%	18.39 [5.05, 67.00]
Chang 2006	17	29	39	43	3.5%	6.88 [1.94, 24.43]
Chauhan 2004	20	36	29	35	4.1%	3.87 [1.29, 11.59]
Confalonieri 2005	56	77	33	38	4.2%	2.48 [0.85, 7.19]
Daubresse 2005	34	50	50	50	1.0%	48.30 [2.80, 832.24]
Ensini 2006	45	60	53	60	4.6%	2.52 [0.95, 6.73]
Haaker 2005	28	100	79	100	6.1%	9.67 [5.05, 18.52]
Jenny & Boeri 2001	21	30	25	30	3.6%	2.14 [0.62, 7.39]
Jenny 2005	170	235	217	235	6.6%	4.61 [2.63, 8.06]
Kim 2005	57	78	65	69	4.0%	5.99 [1.94, 18.47]
Kim 2007	65	100	72	100	6.4%	1.38 [0.76, 2.52]
Macule-Beneyto 2006	25	84	49	102	6.3%	2.18 [1.19, 4.01]
Martin 2007	76	100	92	100	5.1%	3.63 [1.54, 8.55]
Matsumoto 2006	20	30	28	30	2.6%	7.00 [1.38, 35.48]
Matziolis 2007	21	28	31	32	1.7%	10.33 [1.18, 90.26]
Mombert 2007	17	21	21	21	1.0%	11.06 [0.56, 219.68]
Oberst 2008	28	35	32	34	2.5%	4.00 [0.77, 20.85]
Skowronski 2005	56	100	76	100	6.4%	2.49 [1.36, 4.56]
Sparmann 2003	104	120	120	120	1.1%	38.05 [2.26, 642.03]
Stulberg 2006	33	54	43	62	5.5%	1.44 [0.67, 3.11]
Tingart 2008	372	500	474	500	7.1%	6.27 [4.03, 9.77]
Zumstein 2006	21	30	24	30	3.8%	1.71 [0.52, 5.62]
Total (95% CI)		**2128**		**2187**	**100.0%**	**4.14 [3.03, 5.66]**
Total events	1452		1937			

Heterogeneity: Tau² = 0.30; Chi² = 57.18, df = 24 (P = 0.0002); I² = 58%
Test for overall effect: Z = 8.94 (P < 0.00001)



NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Additional radiological outcomes

The Advisory panel considered other radiological outcomes, including:

- tibiofemoral angle
- femoral component angle in reference to the mechanical axis of the leg
- tibial component angle in reference to the mechanical axis of the leg
- femoral component angle in reference to the mechanical axis of the femur, and
- tibial component angle in reference to the mechanical axis of the tibia.

The experts felt that these were of less substantial clinical relevance, the most accurate assessment of alignment being mechanical axis alignment. These outcomes are presented in full at Appendix O. In summary, all the above outcomes were similar between the standard and computer-aided approaches, or favoured computer-navigation.

Clinical and peri-hospital outcomes

Range of motion

Eight studies reported range of motion of the limb postoperatively (Table 16). In general there were only small differences between navigated and conventional knees, where reported.

Table 16 Clinical and peri-hospital outcomes: range of motion

Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)
Level II studies			
Decking 2005	3 months	Conventional (n = 25)	...
		Navigated (n = 27)	...
		P value	0.369
Matziolis 2007	…	Conventional (n = 28)	109° ± 7° (100 to 120°)
		Navigated (n = 32)	108° ± 15° (70 to 140°)
		P value	NS
Level III-1 studies			
Kim 2007	…	Conventional (n = 100)	126° (-1° to +127°)
		Navigated (n = 100)	127° (0 to +127°)
		P value	0.939
Martin 2007	3 months	Conventional (n = 100)	MBK prostheses: 100° ± 15° (70 to 140°) LPS Flex Mobile prostheses: 108° ± 14° (75 to 135°) *p* = 0.014
		Navigated (n = 100)	MBK prostheses: 102° ± 13° (80 to 130°) LPS Flex Mobile prostheses: 109° ± 15° (70 to 150°) *p* = 0.04
		P value	…
Song 2007	…	Conventional (n = 44)	127.3° ± 10.0°
		Navigated (n = 42)	128.1° ± 10.4°
		P value	0.640
Level III-2 studies			
Matsumoto 2006	…	Conventional (n = 30)	105.5° (50 to 125°)
		Navigated (n = 30)	113.0° (85 to 130°)
		P value	0.011
Molfetta 2008	…	Conventional (n = 30)	95.5°± 5.7° (88 to 105°)
		Navigated (n = 30)	97° ± 7.4° (85 to 110°)
		P value	> 0.05 (NS)
Stulberg 2006	Pain/function scores at 1 and 6 months.	Conventional (n = 40)	103.2° ± 13.5° (65 to 135°)
		Navigated (n = 38)	105.1° ± 10.2° (80 to 125°)
		P value	...

NOTES: SD = standard deviation; … = not reported; NS = non significant

Knee Society Score

The Knee Society rating system (KSS) is the standard clinical evaluation system for reporting results for patients undergoing total knee arthroplasty. The system is subdivided into a knee score, which rates the knee joint only and a functional score which measures the patient's ability to walk and climb stairs (Insall et al 1989). Both the knee and functional subscores of the Knee Society rating system have a maximum point scale of 100. For each scale, a grading score of 80-100 indicates an excellent result, 70-79 a good result, 60-69 a fair result, and below 60 poor (Asif and Choon 2005).

Table 17 demonstrates the eight studies (three randomised controlled studies, two pseudo-randomised controlled studies and three nonrandomised comparative studies) identified that reported Knee Society Scores following total knee arthroplasty (Decking et al 2007; Kim et al 2007; Martin et al 2007; Matsumoto et al 2006; Matziolis et al 2007; Molfetta et al 2008; Spencer et al 2007; Stulberg et al 2006).

Four studies reported the Knee Society Score as a cumulative score of the knee and functional subscores (Decking et al 2005/2007; Martin et al 2007; Matziolis et al 2007 and Spencer et al 2007). In these studies, the Knee Society score was reported at various time points including three, six, 12 and 24 months. Each of the studies reported similar values for the Knee Society scores at the various time points with no study reaching statistical significance.

Four studies reported the Knee Society Score as the individual knee[2] and functional subscores (Kim et al 2007; Matsumoto et al 2006; Molfetta et al 2008; Stulberg et al 2006). Similarly to the combined score, both the knee and functional subscores between the conventional and navigated total knee arthroplasty groups were comparable. No statistical significance was detected in three studies, while in the fourth study no statistical analysis was reported.

[2] Assumption. Studies report a total and functional score. It has been assumed that the total score refers to the knee sub score of the Knee Society score.

Table 17 Clinical and peri-hospital outcomes: knee society score

Study	Outcome time point	Treatment group	Knee society score Mean ± SD (range)
Level II studies			
Decking 2005 & Decking 2007*	3 months; 12 months	Conventional (n = 25)	3 months: 160.6 ± 22.2 12 months: 168.4 ± 24.9
		Navigated (n = 27)	3 months: 167.7 ± 24.8 12 months: 176.2 ± 17.2
		P value	3 months: 0.18 12 months: 0.46
Matziolis 2007	6 months	Conventional (n = 28)	144 ± 29 (101 to 200)
		Navigated (n = 32)	149 ± 34 (89 to 200)
		P value	NS
Spencer 2007	3 months; 6 months; 12 months; 24 months	Conventional (n = 30)	3 months: 125.9 ± 32.1 6 months: 151.8 ± 29.8 12 months: 152.2 ± 36.0 24 months: 158.9 ± 29.0
		Navigated (n = 30)	3 months: 125.2 ± 30.5 6 months: 149.1 ± 24.5 12 months: 153.5 ± 26.9 24 months: 156.4 ± 33.1
		P value	3 months: 0.934 6 months: 0.691 12 months: 0.870 24 months: 0.757
Level III-1 studies			
Kim 2007	…	Conventional (n = 100)	Total: 94 (91 to 100) Functional: 84 (79 to 100)
		Navigated (n = 100)	Total: 93 (89 to 100) Functional: 85 (78 to 100)
		P value	0.456
Martin 2007	3 months	Conventional (n = 100)	160 ± 22 (92 to 200)
		Navigated (n = 100)	160 ± 24 (73 to 200)
		P value	NS
Level III-2 studies			
Matsumoto 2006	…	Conventional (n = 30)	Total: 89.5 (73 to 97) Functional: 95.5 (80 to 100)
		Navigated (n = 30)	Total: 84.5 (53 to 100) Functional: 94.3 (80 to 100)
		P value	Total: 0.16 Functional: 0.58
Molfetta 2008	…	Conventional (n = 30)	Total: 85 ± 5.9 (70 to 91) Functional: 87 ± 4.9 (78 to 90)
		Navigated (n = 30)	Total: 84 ± 5.4 (73 to 91) Functional: 90 ± 5.3 (78 to 92)
		P value	Total: >0.05 Functional: >0.05
Stulberg 2006	Pain/function scores at 1 and 6 months. Radiologic at 4 weeks	Conventional (n = 40)	*6 month:* Total: 84.6 ± 18.3 (23 to 100) Functional: 62 ± 15.7 (45 to 90)
		Navigated (n = 38)	*6 month:* Total: 83.4 ± 18.5 (32 to 100) Functional: 64 ± 19.4 (30 to 100)
		P value	...

NOTES: SD = standard deviation; * Same patient cohort. Knee Society scores at 3 months follow-up reported in Decking et al 2005, Knee Society scores at 12 months follow-up reported in Decking et al 2007; NS = non significant; … = not reported

Other clinical outcomes

A variety of other clinical outcomes were reported by ten studies (Böhling et al 2005; Chang et al 2006; Church et al 2007; Decking et al 2005/2007; Ensini et al 2006; Kalairajah et al 2006; Kim et al 2007; Martin et al 2007; Song et al 2007; Spencer et al 2007). These included scores such as the WOMAC score, the Oxford score, the Hospital for Special Surgery score as well as a range of measures of clinically significant parameters (eg pain, blood pressure, temperature etc.; see Appendix P).

In the majority of studies there was no statistical difference in outcome between the navigated and conventional method. Only one study, Church et al (2007), reported a statistically significant difference between conventional and navigated total knee arthroplasty among all the clinical outcomes reported. Church reported a significantly better outcome in terms of the Modified Mayo Clinic Embolic score in the navigated total knee arthroplasty group compared to the conventional total knee arthroplasty group ($P = 0.004$). However, it is unclear whether this improvement in number of emboli was of any clinical relevance.

Surgical time

Twenty-two studies (eight randomised controlled studies, four pseudo-randomised controlled trials and ten nonrandomised controlled trials) were identified that compared surgical time between computer-navigated TKA and the conventional technique (Bäthis et al 2004a; Bäthis et al 2004b; Böhling et al 2005; Chang et al 2006; Chauhan et al 2004; Chin et al 2005; Church et al 2007; Confalonieri et al 2005; Decking et al 2005; Haaker et al 2005; Jenny et al 2001; Jenny et al 2005; Kim et al 2008; Macule-Beneyto et al 2006; Martin et al 2007; Matsumoto et al 2006; Matziolis et al 2007; Molfetta et al 2008; Oberst et al 2008; Tingart et al 2008; Weinrauch et al 2006; Zumstein et al 2006) . Ten studies (two randomised controlled studies, two pseudo-randomised controlled studies and six nonrandomised comparative studies) were considered suitable for meta analysis (Bäthis et al 2004a; Bäthis et al 2004b; Chang et al 2006; Decking et al 2005; Haaker et al 2005; Jenny et al 2005; Martin et al 2007; Matziolis et al 2007; Tingart et al 2008; Zumstein et al 2006). Twelve studies that did not report standard deviation along with the mean surgical time were excluded from the meta-analysis.

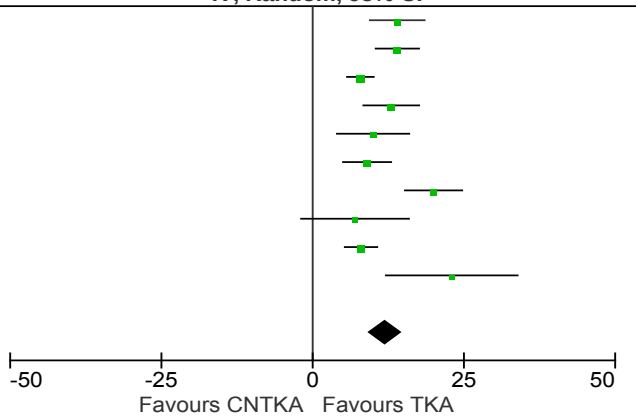
Meta-analysis under a random effects model revealed an overall mean difference of 11.99 minutes (95% CI: 9.27 to 14.74) in favour of the conventional technique (Figure 7). This result was statistically significant ($P < 0.00001$). One study (Matziolis et al 2007) crossed the line of no effect, and the spread of confidence intervals indicates a relatively precise result.

Figure 7 Surgical time (all studies)

Study or Subgroup	CNTKA Mean	CNTKA SD	CNTKA Total	Conventional TKA Mean	Conventional TKA SD	Conventional TKA Total	Weight	Mean Difference IV, Random, 95% CI
Bathis 2004a	78	12	50	64	11	50	10.6%	14.00 [9.49, 18.51]
Bathis 2004b	78	12	80	64	11	80	11.9%	14.00 [10.43, 17.57]
Chang 2006	100.6	4.33	50	92.7	5.09	29	13.5%	7.90 [5.69, 10.11]
Decking 2005	92	9	27	79	8	25	10.4%	13.00 [8.38, 17.62]
Haaker 2005	111	22	100	101	21	100	8.7%	10.00 [4.04, 15.96]
Jenny 2005	108	22	235	99	22	235	11.3%	9.00 [5.02, 12.98]
Martin 2007	88	16	100	68	18	100	10.3%	20.00 [15.28, 24.72]
Matziolis 2007	101	17	32	94	18	28	5.8%	7.00 [-1.90, 15.90]
Tingart 2008	86	20	500	78	23	500	13.0%	8.00 [5.33, 10.67]
Zumstein 2006	114	22	30	91	21	30	4.5%	23.00 [12.12, 33.88]
Total (95% CI)			**1204**			**1177**	**100.0%**	**11.99 [9.24, 14.74]**

Heterogeneity: Tau² = 13.30; Chi² = 37.60, df = 9 (P < 0.0001); I² = 76%

Test for overall effect: Z = 8.54 (P < 0.00001)



NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Twelve studies (six randomised controlled studies, two pseudo-randomised controlled trials, and four nonrandomised controlled trials) were not considered suitable for meta-analysis (Böhling et al 2005; Chauhan et al 2004; Chin et al 2005; Church et al 2007; Confalonieri et al 2005; Jenny et al 2001; Kim et al 2008; Macule-Beneyto et al 2006; Matsumoto et al 2006; Molfetta et al 2008; Oberst et al 2008; Weinrauch et al 2006). This was due to the fact that the data was not presented fully, as the standard deviation was not reported (Table 18). All twelve studies reported an increase in the surgical time with the use of computer navigation. In cases where statistical analysis was reported, the difference between the computer-navigated and conventional total knee arthroplasty groups was statistically significant.

Table 18 Surgical time: studies not included in the meta-analysis

Study	Treatment group	Surgical time (minutes) Mean ± SD (range)
Level II studies		
Chauhan 2004	Conventional (n = 36)	67 (55 to 90)
	Navigated (n = 35)	80 (60 to 120)
	P value	0.001
Chin 2005	Conventional (IM: n = 30) (EM: n = 30)	IM: 83.5 (60.0 to 125.0) EM: 90.3 (55.0 to 145.0)
	Navigated (n = 30)	118.2 (80.0 to 180.0)
	P value	0.000
Church 2007	Conventional (n = 12)	56.8 (49 to 63)
	Navigated (n = 14)	74.1 (60 to 98)
	P value	0.0003
Kim 2008	Conventional (210 knees)	*
	Navigated (210 knees)	
	P value	
Macule-Beneyto 2006	Conventional (n = 84)	76.9
	Navigated (n = 102)	93.6
	P value	< 0.001
Weinrauch 2006	Conventional (n = 31)	77.4
	Navigated (n = 39)	113.1
	P value	< 0.001
Level III-1 studies		
Böhling 2005	Conventional (n = 50)	80 (40 to 135)
	Navigated (n = 50)	93 (55 to 145)
	P value	...
Oberst 2008	Conventional (34 knees)	...

Table 18 continued Surgical time: studies not included in the meta-analysis

Study	Treatment group	Surgical time (minutes) Mean ± SD (range)
Level III-1 studies		
	Navigated (32 knees)	(additional 41 mins)
	P value	<0.05
Level III-2 studies		
Confalonieri 2005	Conventional IM: 40 knees EM: 37 knees	IM: 92 (67 to 112) EM: 81 (57 to 106)
	Navigated (38 knees)	109 (82 to 133)
	P value	IM: 0.0001 EM: 0.0002
Matsumoto 2006	Conventional (n = 30)	104
	Navigated (n = 30)	124
	P value	...
Molfetta 2008	Conventional (n = 30)	82 (54 to 110)
	Navigated (n = 30)	98 (75 to 115)
	P value	...
Level III-2/3 studies		
Jenny 2001	Conventional (n = 30)	90
	Navigated (n = 30)	110
	P value	...

NOTES: SD = standard deviation; IM = intramedullary alignment; EM = extramedullary alignment; * Surgical time and tourniquet presented in inappropriate groups unable to be analysed. However, surgical time and tourniquet was increased using computer navigation; …= not reported.

Tourniquet time

Ten studies (five randomised controlled studies, one pseudo-randomised controlled study and four nonrandomised controlled studies) were identified that compared tourniquet time between conventional TKA and the conventional technique (Anderson et al 2005; Bolognesi et al 2005; Decking et al 2005; Ensini et al 2006; Kalairajah et al 2005; Kalairajah et al 2006; Kim et al 2007; Kim et al 2008; Rosenburger et al 2008; Stulberg et al 2006). Five studies (three randomised controlled studies and two nonrandomised comparative studies) were considered suitable for meta-analysis (Decking et al 2005; Ensini et al 2006; Kalairajah et al 2006; Rosenburger et al 2008; Stulberg et al 2006). The remaining studies were excluded as they did not report mean and standard deviation for tourniquet time.

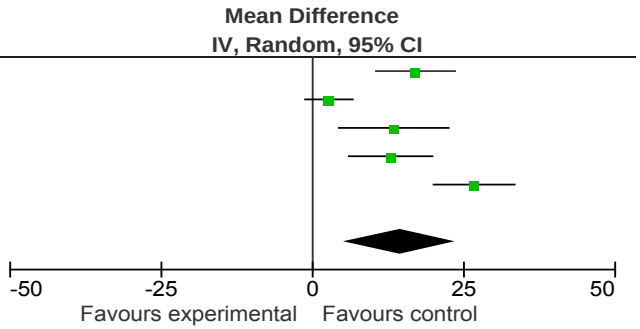
Meta-analysis under a random effects model revealed an overall mean difference of 14.38 minutes (95% CI: 5.28 to 23.48) in favour of the conventional technique (Figure 8). This result was statistically significant ($P < 0.00001$).

Figure 8 Tourniquet time (all studies)

Study or Subgroup	CNTKA Mean	CNTKA SD	CNTKA Total	Conventional TKA Mean	Conventional TKA SD	Conventional TKA Total	Weight	Mean Difference IV, Random, 95% CI
Decking 2005	88	12	27	71	12	25	20.1%	17.00 [10.47, 23.53]
Ensini 2006	98.4	13.3	60	95.7	8.1	60	21.6%	2.70 [-1.24, 6.64]
Kalairajah 2006	86.8	10.2	14	73.4	11.8	10	18.4%	13.40 [4.34, 22.46]
Rosenburger 2008	104	16.9	50	91.1	18.3	50	19.9%	12.90 [6.00, 19.80]
Stulberg 2006	99.6	16.3	38	72.9	13.7	40	20.0%	26.70 [20.00, 33.40]
Total (95% CI)			**189**			**185**	**100.0%**	**14.38 [5.28, 23.48]**

Heterogeneity: Tau² = 95.90; Chi² = 41.93, df = 4 (P < 0.00001); I² = 90%

Test for overall effect: Z = 3.10 (P = 0.002)



NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Five studies (two randomised controlled studies, one pseudo-randomised controlled study and two nonrandomised controlled studies) were not considered suitable for meta-analysis (Anderson et al 2005; Bolognesi et al 2005; Kalairajah et al 2005; Kim et al 2007; Kim et al 2008). All five studies reported an increase in the tourniquet time with the use of computer navigation (Table 19). In all cases the difference between the computer-navigated and the conventional total knee arthroplasty groups was statistically significant.

Table 19 Tourniquet time: studies not included in the meta-analysis

Study	Treatment group	Surgical time (minutes) Mean ± SD (range)
Level II studies		
Kalairajah 2005	Conventional (n = 30)	74 (40 to 132)
	Navigated (n = 30)	89 (55 to 125)
	P value	0.002
Kim 2008	Conventional (210 knees)	*
	Navigated (210 knees)	
	P value	
Level III-1 studies		
Kim 2007	Conventional (n = 100)	44 (32 to 58)
	Navigated (n = 100)	59 (53 to 81)
	P value	< 0.001
Level III-2/3 studies		
Bolognesi 2005	Conventional (n = 50)	57
	Navigated (n = 50)	68
	P value	0.004
Level III-3 studies		
Anderson 2005	Conventional (n = 51)	75
	Navigated (n = 116)	90
	P value	< 0.001

NOTE: SD = standard deviation; * Surgical time and tourniquet presented in inappropriate groups unable to be analysed. However, surgical time and tourniquet was increased using computer navigation.

Length of hospital stay

Three studies (two randomised controlled trials and one nonrandomised comparative study) compared the length of hospital stay between computer-navigated TKA and the conventional technique (Anderson et al 2005; Chin et al 2005; Weinrauch et al 2006; see Table 20). In two studies (Chin et al 2005; Weinrauch et al 2006) the length of hospital stay between the groups was comparable. In the third study (Anderson et al 2005), no numerical values were provided; however, the authors state that there was no statistically significant difference between the two groups in terms of length of hospital stay.

Table 20 Clinical and peri-hospital outcomes: length of hospital stay

Study	Treatment group	Length of hospital stay (days) Mean ± SD (range)
Level II studies		
Chin 2005	Conventional (IM: n = 30) (EM: n = 30)	IM: 6.8 (4.0 to 20.0) EM: 7.6 (3.0 to 19.0)
	Navigated (n = 30)	7.4 (4.0 to 17.0)
	P value	0.582
Weinrauch 2006	Conventional (n = 31)	6.94
	Navigated (n = 39)	7.23
	P value	...

NOTES: SD = standard deviation; IM = intramedullary alignment; EM = extramedullary alignment; … = not reported.

Long-term linking data

A total of 11 case-series were included; study information regarding patient population, patient characteristics and outcomes are presented in Table 21 and Table 22. The alignment outcomes and occurrence of revision surgery and treatment failures reported by each study can be seen in Table 23.

Table 21 Study information

Study	Study period	Prosthesis	Component	Attachment method	Follow-up (mean years [range])
Aglietti 1988	1979–1983	Total Condylar Posterior Stabilised Prosthesis (Insall-Burstein)	Metal-backed tibial component	…	5 (3–8)
Berend 2004	1983–2000	Anatomic Graduated Component (AGC) Prothesis Total Knee System (Biomet Inc.; United States)	Metal-backed tibial component	Cemented	5 (2–14.2)
Feng 1994	1983–1987	Microloc Tricompartmental Prothesis (Johnson & Johnson; New Jersey)	Metal-backed patellar component	Cemented, cementless, central stem with cement	6.1 (4–9)
Hamilton 1982	1972–1977	University of California at Irvine (UCI) Total Knee Prosthesis (Waugh et al; United States)	…	…	4.5 (3–8)
Harvey 1995	1982–1985	Accord (DePuy Int.; United States)	Cemented tibial component	Cemented	5
Jeffery 1991	1976–1981	Denham Prosthesis (Biomet; United States)	'using earliest design components'	…	8 [median] (0–12)
Morgan 2007	1990–1993	Kinemax Posterior Cruciate Retaining (PCR) (Howmedica; United States)	…	…	9
Ritter 1994	1975–1983	…	Posterior Cruciate Condylar	…	… (0.2–13)
Rodriguez 2001	1976–1979	Total Condylar Prosthesis (Johnson & Johnson; United States)	All polyethylene with central stem	Cemented	19 (18–24)
Tew 1985	1972–1983	Early Freeman/ICLH prosthesis, modified Freeman/ICLH prosthesis, Sheehan prosthesis, Manchester prosthesis, Oxford prosthesis or Kinematic prosthesis	…	…	… (0.5–9)
Windsor 1989	1974–1986	1) Total Condylar prosthesis (see component type) 2) Posterior-stabilised prosthesis (see component type) 3) Posterior-stabilised prosthesis (see component type)	1) Polyethylene tibial component 2) All-polyethylene tibial component 3) Metal backed tibial component	…	…

NOTES: … = not reported

Table 22 Patient population

Study	Total treated		Mean age (years)	Age[range] (years)	Male (*n*)/ Female (*n*)	Diagnosis (knees [*n*])				Exclusions		
	Patients (*n*)	Knees (*n*)				OA	RA	Other	NR	Patients (*n*)	Knees (*n*)	Reason
Aglietti 1988	80	95	66.5	27–79	9/62	61	24	0	…	9	10	Death (7 patients), severe RA (2 patients)
Berend 2004	2125	3152	70	33–93	844/1281	3152	0	0	…	…	…	…
Feng 1994	136	186	62.9	30–86	57/129	130	50	6	…	44	58	Death (10 patients), illness/relocation (19 patients), lost to follow-up (15 patients)
Hamilton 1982	97	121	…	…	29/51	63	35	2	…	17	21	Death (4 patients), lost to follow-up (7 patients), letter/phone response only (6 patients)
Harvey 1995	101	122	64.5	38–83	12/69	46	55	…	…	20	21	Death (6 knees), infection (2 knees), lost to follow-up (3 knees)
Jeffery 1991	…	139	66 [median]	21–85	17/85	50 patients	52 patients	…	…	…	24	Emigration (2 knees), lost radiograph (2 knees), long-leg radiographs not taken before and/or after operation (20 knees)
Morgan 2007	153	197	64.9	35–84	44/109	128	69	…	…	0	0	…
Ritter 1994	…	421	…	…	…/257	253 patients	60 patients	10 patients	…	…	…	…
Rodriguez 2001	164	220	65	31–83	…	109	111	…	…	12	18	Lost to follow-up
Tew 1985	…	428	…	…	…	…	…	…	…	…	…	Infection (if influenced results)
Windsor 1989	…	1430	67	20–87	445/985	1117	193	120	…	…	…	…
Studies (*n*)	7	11	7	8	9	10	10	6	0	5	6	
Average/range/total	2856 (total)	6511 (total)	65.83 (average)	20–93 (range)	1457/3028 (total)	4806 (total)	537 (total)	128 (total)	0 (total)	102 (total)	152 (total)	

NOTES: OA = osteoarthritis, RA = rheumatoid arthritis; … = not reported;

Table 23 Main findings regarding limb alignment and long-term treatment success

Study	Observations		Finding
	Patients (*n*)	Knees (*n*)	
Aglietti 1988	71	85	Valgus limb alignment up to 15° not linked with an increase in lucent lines; however varus alignment was ($P < 0.0001$) Varus alignment of tibial component >2° associated with lucent lines; valgus alignment 2–7° was not ($P < 0.0001$)
Berend 2004	2125	3152	Regression tree analysis found varus tibial component alignment >3° resulted in increased odds of failure (Hazard ratio: 17.2; $P < 0.0001$) BMI >33.7kg/m^2 combined with overall varus limb alignment increased failure rates ($P < 0.0001$) Mean overall postoperative anatomical tibiofemoral alignment was +1.6° valgus (in patients with failure due to medical bone collapse, which was the most common failure cause [20 knees/41 failed knees]) compared with +3.9° valgus for overall patient population
Feng 1994	92	128	Postoperative lower extremity malalignment (femoral-tibial angle <4° or >8°) significant predictor of clinical and radiographic failure ($P <0.01$) Varus malposition of tibial component (tilt >5°) also significant predictor of clinical and radiographic failure ($P < 0.01$) Femoral subluxation leads to failure/revision ($P < 0.01$); those patients with varus (<4°) and valgus (>8°) alignment had higher revision rate than those with neutral alignment (4–8°)
Hamilton 1982	80	100	Fifteen knees with failed result and a preoperative varus alignment reverted to a varus deformity postoperatively, 10 knees with a failed result and preoperative valgus alignment all returned to valgus angulations postoperatively. (*P* values not reported)
Harvey 1995	81	101	No significant relationship was found between alignment and incidence of radiolucencies ($P > 0.05$)
Jeffery 1991	102	115	Subsequent loosening had a strong association with poor postoperative alignment ($P = 0.001$). Knees with preoperative varus deformity were more likely to loosen than knees with preoperative valgus deformity; however, there was no link between preoperative alignment when examining postoperative alignment and prosthesis loosening.
Morgan 2007	153	197	No association between immediate postoperative coronal alignment and revision surgery ($P = 0.8$)
Ritter 1994	…	421	Kaplan-Meier survival curves showed no significant difference between survival in patients with normal (5–8° valgus) alignment and patients with valgus (>9°) alignment (Log rank $P < 0.2838$, Wilcoxon $P < 0.4313$) but a significant difference between survival in patients with valgus and varus (>0° varus) alignment (Log rank $P < 0.0385$, Wilcoxon $P < 0.0425$) and patients with normal and varus alignment (Log rank $P < 0.0297$, Wilcoxon $P < 0.0193$).
Rodriguez 2001	…	…	Survivorship analysis, using revision as an endpoint found the likelihood of TKA survival at 21 years to be 77%, and using mechanical failures as an endpoint, found the likelihood of total knee arthroplasty survival at 21 years to be 85%. There was no significance seen in the link between postoperative alignment and the need for revision surgery. (*P* values not reported)
Tew 1985	…	428	In relation to both first and latest radiographic results patients with extreme varus/valgus malalignment had very significantly higher failure rates ($P < 0.001$) than patients with intermediate malalignment. Knees with normal alignment were least likely to drift into deformity, and those that did were associated with a lower failure rate (not significant due to small numbers)
Windsor 1989	…	1430	There was no significant link between postoperative alignment and treatment failure. Mechanical errors and infection was seen as the major causes of failure. (*P* values not reported)
Total	2704	6157	

NOTE: BMI = body mass index

Table 24 Alignment definition and outcomes

Study	Angle/alignment measured	Definition of angle/measurement used	Revisions (Knees (*n*)[%])	Failures (*n* [%])	Time to failure (years)	Cause
Aglietti 1998	Tibial component position, femoral component position	Ideal tibial component position: 90°±2° to long axis of tibia in the frontal plane; up to 5° posterior tilt; no anterior tilt in the sagittal plane. Ideal femoral component position: 6–10° of valgus with anterior flange flush with anterior cortex.	2 (2.4%)	…	…	Loosening
Berend 2004	Anatomical tibiofemoral alignment, tibial component alignment, overall limb alignment	…	Same as failures	41 knees (1.3%)	4.2	Medical bone collapse, ligamentous imbalance, progressive radiolucencies, pain
Feng 1994	Femorotibial angles, limb alignment, component orientation, femoral-tibial component subluxation	Femoral-tibial component subluxation classifications: absent (0–5mm), moderate (5–10mm), severe (>10mm)	Same as failures	40 knees (21.5%)	3.5 (patellar revision only)	Polyethylene wear, loosening, tibial tray fracture, sepsis, dislocation/ligament laxity
Hamilton 1982	…	Normal alignment considered 5–8° valgus alignment	19 (19%)	27 knees (27%)	…	Loosening, component fracture, instability, patellofemoral pain, dislocation
Harvey 1995	Mechanical axis – reference point	Diagram given defining mechanical axis, angle of error and formula to calculate total error (ie degree of valgus/varus alignment). 'In a perfectly aligned knee this angle should be 0°'	2 (2%)	…	…	Infection
Jeffery 1991	Tibiofemoral angle in reference to Maquet's line	Diagram defining tibiofemoral angle and Maquet's line. Ideal alignment measurements not specified	…	…	…	Loosening, infection, translocation
Morgan 2007	Coronal tibiofemoral angle	'Tibiofemoral angle found by intersecting the femoral anatomical axis with the tibial anatomical axis'.	6 (3%)	…	…	…
Ritter 1994	Anatomical tibiofemoral alignment	Normal alignment: 5–8° valgus Varus alignment: >0° varus Valgus alignment: >9° valgus	Same as failures	8 knees (1.9%)	…	Malalignment

Table 24 continued Alignment definition and outcomes

Study	Angle/alignment measured	Definition of angle/measurement used	Revisions (Knees (*n*)[%])	Failures (*n* [%])	Time to failure (years)	Cause
Rodriguez 2001	Tibiofemoral alignment	…	13 (5.9%)	Tibial: 9 cases; Femoral: 6 cases; Combined: 15 (6.8%)	…	Component loosening, sepsis, instability, dislocation, ligament rupture, fractures
Tew 1985	Coronal tibiofemoral angles	Defined reasonably, ideal ranges not specified	…	122 knees (28.5%)	…	Pain, radiologic evidence of technical failure, loosening, bony destruction
Winsor 1989	Tibiofemoral alignment	…	…	25 knees (1.7%)	Time to tibial loosening: 4.7 Time to femoral loosening: 2 Combined: 5.6	Infection, mechanical failure including: loosening, instability and fracture

Summary of findings

Some authors believe prosthesis and limb alignment are the most important determinants of long-term implant survival (Benjamin 2006). Others believe the contrary, that is, whilst alignment is important, it may not be the most important predictor of long-term clinical health outcomes (Stulberg et al 2006; Pagnano et al 2008). Eleven studies were identified as being relevant to limb alignment with medium to long-term outcomes.

Seven studies reported the occurrence of failures following total knee arthroplasty, in 1.3 per cent to 28.5 per cent of knees, with one study reporting failure in 1.9 per cent of patients. The main causes of failure were loosening of the tibial or femoral component, dislocation, varus or valgus malalignment, fracture, instability, pain and infection. Some studies found a connection between postoperative varus alignment and increased likelihood of failure. Aglietti et al (1998) found that up to 15° postoperative valgus limb alignment did not increase radiographic failures, whereas any varus limb alignment did ($P < 0.0001$). In the same study, varus deviation of the tibial component ≥2° proved to be detrimental to the mid-term (five-year) survival of the implant. Valgus deviation of 2–8° from the mechanical axis did not interfere with the integrity of the implant; therefore, the authors suggest some degree of valgus alignment may be ideal for long-term success. Berend et al (2000) conducted regression tree analysis to determine that a tibial component with >3° of postoperative varus alignment had significantly increased odds of failure (Hazard Ratio 17.2; $P < 0.0001$). Similarly, Feng et al (1994) concluded postoperative limb alignment was a significant predictor of clinical and radiographic failures when the femoral-tibial angle was <4° or >8° ($P < 0.01$). Windsor et al (1989) did not provide statistical significance for its findings; however, the authors suggest postoperative varus tibiofemoral alignment, varus component positioning and excessive tibial bone resection may have predisposed knees to tibial loosening which lead to failure.

Tew et al (1985) found failure rate to be significantly higher in knees with extreme (>2° varus; >12° valgus) postoperative limb malalignment ($P < 0.001$). The study also found knees aligned between 3° and 7° valgus were less likely to drift into deformity resulting in failure ($P < 0.001$). However, it was noted that success was not limited to optimally aligned limbs, for example 53 per cent (28/53) of knees with postoperative limb alignment outside of the desired range remained successful at long-term (eight-year) follow-up. Therefore, Tew et al (1985) concluded that successful total knee arthroplasty outcomes might not simply be determined by intraoperative alignment or the development of postoperative malalignment. Similarly, several other studies suggested other factors may contribute to treatment failure rather than limb alignment alone. These compounding factors included increased Body Mass Index, manufactured errors within the prosthesis, time since the operation, the type of prosthesis used, flexion spacing, tilting of the tibia, medial-lateral instability and heterotopic ossification (Tew et al 1985; Windsor et al 1989; Morgan et al 2007). Rodriguez et al (2001) conducted survivorship analysis, using mechanical failure as an end point, from this the likelihood of the knee replacement surviving until long-term (21-year) follow-up was found to be 85 per cent. Rodriguez et al (2001) also reported that limb alignment was not directly related to outcomes of failure.

Studies have suggested preoperative valgus alignment was useful in obtaining optimal postoperative limb alignment. Berend et al (2000) found patients with slight varus alignment prior to surgery were only slightly valgus when compared to all of the patients undergoing treatment. Jeffery et al (1991) found knees with preoperative varus deformity were more likely to experience prosthesis loosening than knees with preoperative valgus

alignment ($P = 0.05$); however, the authors found no relationship between preoperative varus or valgus deformity when examining postoperative alignment and prosthesis loosening. Similarly, Ritter et al (1994) reported Kaplan-Meier survival curves which indicated no significant difference between patients with 'normal' limb alignment and valgus limb alignment ($P < 0.2838$), but a significant difference between patients with 'normal' alignment and varus alignment ($P < 0.0193$) and patients with varus alignment and valgus alignment ($P < 0.0425$). This led the authors to conclude that for best long-term implant survival following total knee arthroplasty, surgeons should consider locating the prosthesis in a neutral or slightly valgus position.

Five studies reported the occurrence of revision surgery in their patient population following total knee arthroplasty as a separate outcome to treatment failure. This ranged from 2 per cent to 19 per cent of knees, with three additional studies reporting the same number of revisions as failures. The main indications for revision surgery were similar to the causes of treatment failure; these included dislocation, loosening, infection and instability. Morgan et al (2007) reported six cases (3%) of knees requiring revision surgery due to aseptic loosening or instability. There was no significant difference seen in implant survival rates between patients with ideal alignment and varus or valgus alignment ($P = 0.78$). When Rodriguez et al (2001) used revision as an endpoint in its survivorship analysis, the likelihood of retention of the prosthesis at long-term (21-year) follow-up was 77 per cent.

Each study had a sufficient number of patients recruited; therefore, it is unlikely that significant differences were overlooked due to inadequate power to detect small changes. However, some studies separated their patients into subgroups on the basis of limb alignment, which reduced patient numbers and may have influenced the ability to detect significant differences between these subgroups. For example, in the study by Tew et al (1985) knees with 'normal' alignment were associated with a reduced failure rate compared with knees with extreme malalignment; however, the significance of this could not be determined, which may have been due to insufficient subgroup sample size. Not all studies reported explicit inclusion and exclusion criteria, and some studies had losses to follow-up where intention to treat analysis was not specified. These factors contribute to confounding the findings obtained from the studies which, by the general nature of case-series, are already highly biased. Therefore, it is difficult to draw reliable conclusions from this evidence.

In conclusion, there is little evidence available linking postoperative limb alignment with long-term success, particularly in regards to ideal alignment. The findings from the 11 included case-series either favoured perioperative valgus alignment or found no connection between perioperative alignment and failure. Although some studies reported a significant advantage when postoperative limb alignment remained within several degrees (usually ±3°) of the mechanical axis, not all of the evidence supports this, which makes it difficult to assume this is ideal alignment. Higher level evidence to sustain this is required.

Summary of effectiveness outcomes

The effectiveness of computer-navigated total knee arthroplasty was reported in two sections: radiological outcomes and clinical and peri-hospital outcomes. Table 25 summarises the effectiveness results of computer-navigated total knee arthroplasty.

Whilst various radiological outcomes were reported in the literature, for the purposes of this report, only outcomes related to the postoperative mechanical axis were included, as these were deemed the most clinically relevant.

Sixteen studies compared computer-navigated total knee arthroplasty with the conventional technique in terms of postoperative deformity. Three separate analyses based on the level of evidence of the included studies were performed. The mean of the mean postoperative deformities slightly favoured computer navigation in two of the three analyses, while the pooled standard deviation favoured computer navigation in all three analyses, indicating that the use of computer navigation for total knee arthroplasty promotes greater overall technical accuracy.

Deviation of the mechanical axis from the target angle of 180º in either direction was reported in eight studies. A meta-analysis of all eight studies suggests that the use of computer navigation significantly ($P < 0.00001$) reduces the amount of deviation in the postoperative knee by a mean of 0.74º when compared to the deviation resulting from conventional navigation.

Satisfactory alignment (postoperative deviation of three degrees or less from 180º in either direction) was reported in 25 studies and meta-analysed in three separate analyses based on the level of evidence. Each of the three analyses demonstrated that computer-navigated total knee arthroplasty provides a significantly greater chance (ranging from 2.88 to 4.14 times) of achieving a postoperative knee within three degrees of the target angle than conventional arthroplasty.

Clinical outcomes were rarely and inconsistently reported in the studies included. The two most commonly reported clinical outcomes, range of motion and Knee Society score, were both reported by eight studies each. Computer navigation did not lead to any clear benefit over the conventional technique in either range of motion or the Knee Society score. Only one study reported a significantly improved clinical outcome (Modified Mayo Clinic Embolic Score) using computer navigation. However, the clinical significance of this difference is unclear.

Surgical duration was reported in twenty-five studies. A meta-analysis of ten studies demonstrated that computer navigation significantly ($P < 0.00001$) increased surgical time by a mean of 11.99 minutes when compared to the conventional technique. Similarly, a meta-analysis of five studies demonstrated tourniquet time was significantly ($P < 0.00001$) increased by a mean of 14.38 minutes through the use of computer navigation. There was no difference between the navigated and conventional techniques with regard to the length of hospital stay.

Overall, radiological results favour computer navigation. These outcomes are statistically significant and robust over a range of measurements. These radiological results may support improved long-term revision rates using computer navigation. However, at the present time, the clinical effectiveness of the technique is poorly reported. No comparative studies were identified which investigated the long-term clinical effectiveness of computer navigation compared to standard total knee arthroplasty. In addition, the evidence-base which investigated postoperative mechanical alignment of total knee arthroplasty with long-term clinical effectiveness was poor and did not unequivocally prove a link between malalignment and revision surgery. Therefore, 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.

Table 25 Summary of results – computer-navigated total knee arthroplasty

Result	Outcome	Overall result
Radiological results	Postoperative deformity	No difference
	Deviation	Favours navigation
	Satisfactory alignment	Favours navigation
Clinical and peri-hospital outcomes	Range of motion	No difference
	Knee Society score	No difference
	Other clinical outcomes	No difference
	Surgical time	Favours conventional
	Tourniquet time	Favours conventional
	Length of hospital stay	No difference

Expert opinion

Two subgroups of particular interest within the scope of this review were the complex knee and the deformed knee, ie:

- valgus knee
- post-osteotomy knee
- grossly anatomically deformed knee
- previously operated knees with metal hardware in situ.

No study separated outcomes for these patient subgroups. Expert clinical opinion of the Advisory panel suggests that computer navigation may be extremely valuable for gaining correct alignment in these instances.

What are the economic considerations?

Economic evaluation of new healthcare technologies is important when determining whether the new initiative offers additional benefits and at what cost. Economic evaluations are able to determine whether the new initiative is dominated by (or dominates) the existing technology, such that the costs are higher (lower) and the effectiveness is less (greater). Economic evaluation is particularly important if the new initiative offers health benefits at additional costs. Within a constrained healthcare budget, determining the additional cost that would be paid for a given health gain is important when ascertaining whether such incremental costs represent value for money.

The usual process for an economic evaluation is first to determine the incremental effectiveness, which is the additional benefits associated with the new technology relative to current practice. The second step is to determine the incremental cost, which is the difference in cost between the new initiative and current practice. Finally the incremental cost-effectiveness ratio (ICER) can be calculated using the following ratio:

$$ICER = \frac{Cost_{New} - Cost_{Comparator}}{Effectiveness_{New} - Effectiveness_{Comparator}}$$

Search strategies

As described in the 'approach to assessment', a search strategy was developed to systematically identify studies in which computer-navigated total knee arthroplasty was used.

Databases of peer-reviewed literature including Medline, PubMed, CINAHL and Cochrane have been searched. The bibliographies of all retrieved publications were hand-searched for any relevant references missing in the database search. Web-based searches included the Internet engines 'Google' and 'Google scholar'.

In addition to the search terms described in the 'approach to assessment' section, Cost$ or Econ$ were added. This was to identify any published cost-effectiveness analysis. The inclusion and exclusion criteria remained the same.

Background – Evidence of cost-effectiveness

Three recent studies comparing computer-navigated total knee arthroplasty with conventional manual methods have included a cost-effectiveness component to the analysis (Dong et al 2006; Novak et al 2007; Slover et al 2008). The lack of long-term clinical research linking prosthesis alignment with improved clinical outcomes has meant that these economic evaluations have utilised modelling techniques to extrapolate future events. Therefore only the **potential** cost-effectiveness of computer-navigated total knee arthroplasty has been reported to date.

Dong *et al* (2006) reported on an early assessment of the likely cost-effectiveness of total knee replacement using computer-navigation compared with the conventional manual method. In the absence of formal clinical trial evidence, this study drew upon existing clinical evidence relating to the clinical outcome, cost and effectiveness of total knee

replacement. The objective of the study was to apply a Markov model to the findings. Nine Markov states were identified based on the progress of the disease after total knee replacement. Effectiveness was expressed by quality-adjusted life years (QALYs). The simulation was carried out initially for 120 cycles of a month each, starting with 1000 total knee replacements.

The results of the analysis found that computer-assisted total knee replacement was a long-term cost-effective technology. However, the QALYs gained were small. After the first two years, the incremental cost per QALY of computer-assisted total knee replacement was dominant because of cheaper and more QALYs. Sensitivity analysis identified that the incremental cost-effectiveness ratio (ICER) was sensitive to the effect and extra cost of computed-assisted surgery, and to the utility of the health state 'normal health after primary total knee replacement'. The results were robust to the utilities of the other Markov states.

The study concluded that 'compared to conventional total knee replacement, computer-assisted total knee replacement is a cost-saving technology in the long term and may offer small additional QALYs'. The study found that despite costing more initially, computer-assisted total knee replacement resulted in a reduced revision rate and complication rate through more accurate and precise alignment. However, this study was an early assessment of total knee replacement and therefore lacked real long-term evidence for the rate of revision of computer-navigated surgery. Another issue is that the costs were based on the UK National Health Service; therefore, they may not be applicable to the Australian setting.

Novak *et al* (2007) undertook a decision-analysis model to estimate the cost-effectiveness of computer-assisted TKA. Model inputs and parameters were obtained by a review of the published literature. Sensitivity analyses were performed to evaluate the impact of alignment, total knee failure rates secondary to misalignment, and costs of computer-assisted surgery systems.

The authors concluded that the additional cost of the computer-navigated procedure is US$1500 per procedure; this is associated with a 14 per cent improvement in coronal alignment precision. The incremental cost-effectiveness ratio of using computer-navigated surgery is US$45 554 per QALY. The authors calculated that computer-navigated surgery would be cost saving if the incremental cost was $629 or less per procedure. These values were sensitive to the cost of the computer navigation system, the accuracy of alignment and the probability of revision with misalignment.

Slover *et al* (2008) employed a Markov decision model to evaluate the impact of hospital volume on the cost-effectiveness of computer-navigated total knee arthroplasty in a theoretical cohort of sixty-five-year-old patients with end-stage arthritis of the knee in the United States. The authors concluded that computer-navigated surgery becomes less cost-effective as the annual hospital volume decreases, the cost of navigation increases and the impact on revision rates decreases. For example, based on centres that perform 250, 150 and 25 computer-assisted TKA per annum, a reduction in annual revision rate of 2 per cent, 2.5 per cent and 13 per cent respectively would be required for computer-navigated surgery to be cost-effective. Therefore computer-navigated surgery is less likely to be a cost-effective investment in healthcare centres with a low volume of joint replacements.

Rationale for the cost-effectiveness analysis

The rationale for the cost-effectiveness analysis is that computer navigation leads to improved prosthetic alignment, which leads to a reduction in the incidence of early revision, since better alignment may improve prosthetic longevity.

The results of the studies demonstrate that, in general, computer-navigated total knee arthroplasty appears to provide a limited benefit over the conventional technique. In terms of satisfactory alignment, computer navigation led to a greater number of patients achieving satisfactory alignment for the mechanical axis, femoral component angle (in reference to the mechanical axis of the leg) and femoral component angle (in reference to the femoral mechanical axis).

Definitive assessment of the cost-effectiveness of computer-navigated TKA may require long-term evidence from randomised trials. In the absence of such data, it may be important to estimate the likely cost-effectiveness of new health technologies early in the life cycle. This is particularly true for health technologies in which potential health benefits are measurable years after the procedure.

Intuitively it is compelling to assert that improved alignment leads to a reduction in revision rate; however, in the absence of data to support this hypothesis an alternative approach is required for the economic modelling. The approach taken in this section is to answer the following questions:

- What improvement in revision rate would be required to make computer navigation cost-effective?
- Is this improvement in revision plausible given the improvement in alignment?'

To answer these questions of the following assumptions will be made:

- The cost-effectiveness is restricted to primary unilateral knee replacement surgery. Bilateral knee replacement surgery has been excluded.
- Only incremental costs are calculated; therefore, costs constant between treatment groups, such as medication, have been excluded.
- The rates of minor and major complications after TKA are the same for computer-navigated and conventional surgery; therefore, they have been excluded.
- Only one revision procedure was allowed
- The rates of infection after TKA are the same in both groups; therefore, they have been excluded.
- The perspective of the cost analysis is limited to the costs faced by the healthcare system.
- A discount rate of 5 per cent per annum was applied to all costs and benefits.

Estimates of costs

Average capital costs per procedure

Average capital costs per procedure are based on estimates of the purchase price of equipment, life of equipment, maintenance and number of procedures performed per annum. These estimates were provided by the applicant or determined from expert opinion (see Table 26). The opportunity cost of capital was included with the forgone capital return calculated using a 5 per cent discount rate. The values are sensitive to the number of procedures per annum.

For the basis of the cost-effectiveness analysis, average capital costs for the navigation equipment are estimated based upon the average number of procedures (70 per annum) over the estimated lifetime of the machine ($797 per procedure). The average number of procedures was calculated from actual usage data within Australia[3]. For the sensitivity analysis, the lower estimate is $189 per procedure based upon 250 procedures per annum over 7 years and the upper estimate is $1486 per procedure based upon 50 procedures per annum over 3 years. The rationale of estimating the capital cost of performing 250 procedures per annum is to see the effect on the cost of performing computer-navigated TKA in a high throughput centre.

Table 26 Calculation of average capital costs per procedure for computer-navigated TKA

Item	Cost $AU (range)	Life (range)	Annual cost $AU /machine (range)
Purchase price of Navigation Equipment*	$155 000	5** (3-7 years)	$31 500 (22 143 – 51 667)
Foregone capital return	5% of $155 000	Annual	$7750
Maintenance	1 years warranty, thereafter $2000 per month service agreement***		$17 021 (14 875 – 17 402)
Total opportunity cost of capital			$55 771 (47 295 – 74 292)
Average cost based on estimated procedures/machine/year****		50 (low) 70 (average) 250 (high)	$1115 (946 – 1486) $797 (676 – 1061) $223 (189 – 297)

NOTES: * Cost of major capital equipment provided by Stryker. These are based on average list prices and include; hardware, re-usable instruments (x2) and software. ** Provided by Styker. *** Maintenance cost provided by Stryker. This is based upon 1-year warranty and monthly service agreement thereafter (discounted at 5%). **** Based on actual usage data provided by Stryker and BrainLab.

Cost per procedure

The costs of conventional TKA, revisions and other treatments were taken from the AR-DRG (I04Z version 5.1 round 11 Private hospital 2006-7), Medicare Benefits Schedule item codes and the median charged Medicare fee (Table 27).

The incremental cost of performing computer-navigated total knee arthroplasty as opposed to current practice is approximately $1029 per procedure. The bulk of this

[3] Usage rates were provided by Stryker and Brainlab, and are based on the total number of computer-navigated procedures per year divided by the number of machines. Number of procedures per machine was not available.

additional cost is associated with the additional capital cost of buying the computer navigation equipment ($797.72), the higher estimated procedural fee ($1487.69 versus $1190.15), and the additional disposables required ($105). These costs are offset somewhat by a reduction in the number of trays required during the procedure.

The fee for computer-navigated surgery includes a premium (25%) on the fees allocated for comparative services, reflecting the additional surgical time required to perform the TKA (see effectiveness section of this report)[4].

Table 27 Average incremental costs per procedure

Item	TKA		Computer-navigated TKA		Incremental Cost
	Units	Cost ($)	Units	Cost ($)	
Capital cost	0	0	1	$797	$797.72
Consumables					
Disposables (computer-navigated TKA)	0	0	1	$105	$105.00
Trays	10	$23.80	4	$12.50	-$188.00
Tray			1	$17.50	$17.50
Procedure					
MBS 49518	1	$1190.15			
MBS (new) [a]			1	$1487.69	$297.54
Other costs					
DRG I04Z [b]	1	$15 382	1	$15 382	0
Out of pocket [c]	1	$705.85	1	$705.85	0
Incremental cost TKA per patient					$1028.76

[a] New MBS fee is based on the fact that computer navigation takes 25% longer. [b] AR DRG I04Z version 5.1 Round 11 Private hospital (2006-7). [c] Out of pocket equals the median charged Medicare fee 2007-8 minus the MBS fee.

Financial implications

In 2006/2007 the number of primary total knee arthroplasty procedures performed in Australia was as follows: MBS 49518 = 12,935; MBS 49519 = 920; MBS 49521 = 1,013; and MBS 49524 = 301. (Total procedures = 15 169). Based on these data, the additional cost to the Australian healthcare system of performing all TKA with computer navigation would be $15.605 million ($4.68 million if 30%[5]) per year. It is worth noting that the number of primary TKA performed has been increasing by between 500 and

[4] It is worth noting that computer-navigation is not used to reduce the level of surgical skill required to perform the procedure but to assist with prothesis alignment. Therefore it would be inappropriate to reduce the MBS fee based on different skill-mix.

[5] The Advisory Panel estimated that the maximum proportion of computer–navigated TKA procedures would be 30%.

1000 procedures per year; therefore, this figure is likely to be conservative in the long run.

The case for cost escalation is minimised because the new procedure will not influence the number of primary total knee replacement arthroplasties; however, it may reduce the number of revision procedures required.

Markov model and cost-effectiveness analysis

A 15-year cohort simulation with 1-month cycle length and a starting number of 1000 primary TKAs was performed. A 15-year-period was chosen to reflect the expected life of a modern prosthesis; beyond this period prosthesis failure would be a significant reason for revision surgery. A cycle length of one month was chosen. This was to capture the actual periods spent in each state more accurately. The age of the simulated cohort was 69 to reflect the average of TKA patients.

Effectiveness was expressed in terms of QALYs. Costs and QALYs were discounted at 5 per cent in line with current MSAC guidelines. The difference between computer navigation and the conventional manual technique were expressed by the incremental cost-effectiveness ratio. Figure 9 represents the Markov state transition model for total knee arthroplasty.

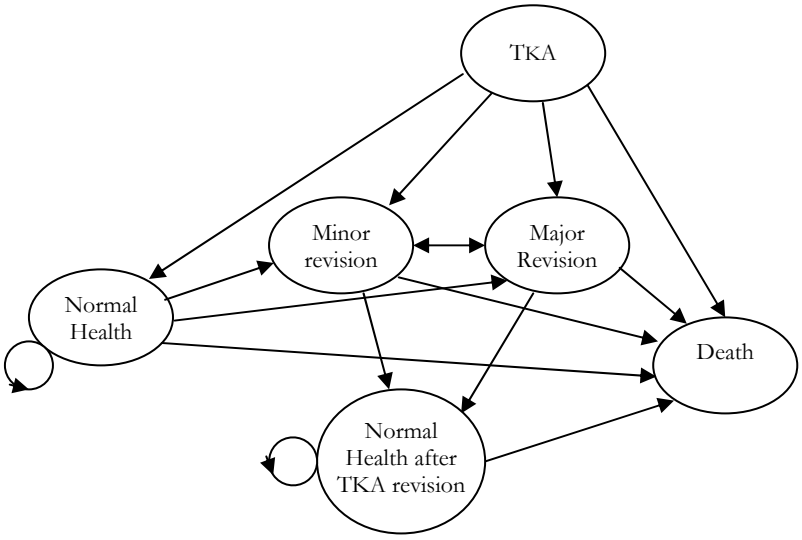


Figure 9 Markov state transition model for total knee arthroplasty

Transition probabilities

The transition probabilities for manual TKA were estimated from a variety of sources as indicated in Table 28. The principal hypothesis of the economic evaluation was that computer-navigated TKA leads to better alignment of the prosthesis and consequently results in a decreased revision rate. The revision rate of manual TKA was estimated from the 'National Joint Replacement Registry' Australian Orthopaedic Association 2008 report. The economic evaluation therefore tested the costs and benefits associated with a potential reduction in revision rate, through superior alignment of computer navigation, of 1, 2 and 3 percentage points.

The transition probabilities between states were expressed as 1-month probabilities. Since the transition probabilities are obtained from various resources with different follow-up periods, a two-step calculation was used to determine the 1-month probabilities. Firstly, the 1-month rate (r) was calculated using: $r = -\ln (1 - P)/t$, where P is the probability at the original follow-up period and t is the time in months of the follow-up. Secondly, the 1-month probability ($P_{1\text{-month}}$) was calculated from the 1-month rate (r) using the formula: $P_{1\text{-month}} = 1 - \exp(-r)$.

It is worth noting that not all revisions are due to misalignment. Dong and Buxton (2006) estimated that 70.4 per cent of complications following TKA are due to misalignment. The AOA-NJRR data suggests that 21.2% of all revisions are due to infection. However, this data is only on short term follow up and the data relating to wear would not be expected to be reported under seven to ten years and this is currently outside the scope of the AOA-NJRR.

The probability of peri-operative death for patients undergoing a total knee arthroplasty and a revision knee arthroplasty were taken from Mahomed et al (2005). This study presented data from 124,986 primary TKA and 11,726 revision procedures found in the 2000 US Medicare database. The perioperative mortality rates were 0.7 per cent and 1.1 per cent for patients treated with primary TKA and revision knee replacement, respectively.

Table 28 Weighted transition probabilities for the Markov states for conventional TKA (1-Month)

Transition	Value of probability[a]	Source
TKA to normal health after primary TKA	0.998917	Assumed
TKA to minor revision	0.000332	1
TKA to major revision	0.000166	1
Normal health after primary TKA to major revision	0.000332	1
Normal health after primary TKA to minor revision	0.000166	1
Minor revision to normal health after TKA revision	0.996394	Assumed
Minor revision to major revision	0.000397	1
Major revision to normal health after TKA revision	0.995122	Assumed
Major revision to minor revision	0.001668	1
Death related to primary TKA	0.000585	2
Death related to revision to TKA	0.000921	2
Death (all reasons)	0.002288	3

NOTES: [a] probabilities were calculated from rate using the formula: Pt = 1 – exp (-r);
1) National Joint Replacement Registry' Australian Orthopaedic Association 2008
2) Mahomed et al (2005)
3) Converted from ABS death rates of the age group 69-70 years

Costs and utility values for minor and major TKA revision

Unfortunately the AR-DRG codes combine costs for both major and minor revisions. Therefore the estimated cost of TKA revision was based a study performed by Smith using Australian data. This study demonstrated that the average cost for all revision surgery is $25 000 (minor revisions cost approximately $12 000 and major revisions, which include complete component change over, cost approximately $45 000).

No ideal set of utility values were available; estimates were derived from several sources following the guidance of Dong and Buxton (2006). Jacobson (1991) estimated the utility value of minor prosthesis revision in 70 patients using the University of California, Los Angeles (ULCA) Pain-Walking-Function-Activity rating. This instrument measured the following domains: pain, walking, function and activity. Data from Rorabeck (1997) and Kane (2003) were used to estimate utility values for major revision and normal health following primary (revision) TKA, respectively. Both studies used the Knee Society rating score pre- and postoperatively.

Table 29 Costs and estimated utility values of Markov States for TKA

Markov State	Cost	Utility	
		Value	Source
Total Knee Arthroplasty (TKA)	$17 516.00 (Conventional) 18 544.76 (Comp Navigated)	-	-
Normal health after primary TKA	0	0.78	1 & 4
Minor revision	$12 000	0.66	2
Major revision	$45 000	0.51	3
Normal health after TKA revision	0	0.68	4
Death	0	0	-

1) Kind P, Hardman G, Macran S. UK population norms for EQ-5D (1999)
2) Jacobson JJ, Schweitzer SO, Kowalski CJ (1991)
3) Kane RL, Saleh KJ, Wilt TJ et al (2003)
4) Rorabeck CH, Murray P (1997)

Results of the Markov Model

Incremental cost-effectiveness ratios were calculated for four different effectiveness scenarios. The scenarios compared the long-term, 10-year revision rate of computer-navigated TKA with conventional surgery. The four scenarios were:

- Scenario 1: No improvement in the long-term revision rate. This is the most conservative scenario which implies that computer-navigated surgery is no more effective than current practice.

- Scenario 2: A 1 percentage point reduction, or 17 per cent improvement, in the 10-year revision rate

- Scenario 3: A 2 percentage point reduction, or 33 per cent improvement, in the 10-year revision rate, and

- Scenario 4: A 3 percentage point reduction, or 50 per cent improvement, in the 10-year revision rate.

The final scenario, in which a 3 percentage point reduction in the 10-year revision rate of primary TKA leads to a halving of the number of individuals requiring revision surgery, is the most optimistic.

Revision rates

The analysis shows that approximately 4.71 per cent of patients with primary TKA would require a major revision and 2.36 per cent would require a minor revision 15 years

after conventional surgery. For computer-navigated TKA the corresponding figures for scenario 2 are 3.95 per cent major and 1.98 per cent minor revisions; for scenario 3 are 3.18 per cent major and 1.60 per cent minor revisions; and for scenario 4 are 2.40 per cent major revisions and 1.20 per cent minor revisions.

The reduction in TKA revision rates lead to a corresponding increase in the cumulative quality adjusted life years at 15 years. For the 1000 patient cohort simulation, the cumulative discounted QALYs for conventional TKA was 6771.5. The cumulative discounted QALYs for scenario 2 was 6776.7, for scenario 3 was 6782.0 and for scenario 4 was 6787.3. This gave a QALY gain of 5.2, 10.5 and 15.8 for scenarios 2, 3 and 4 respectively.

Table 30 Summary of Markov simulation and cost-effectiveness analysis (The ICER is presented in the last column)

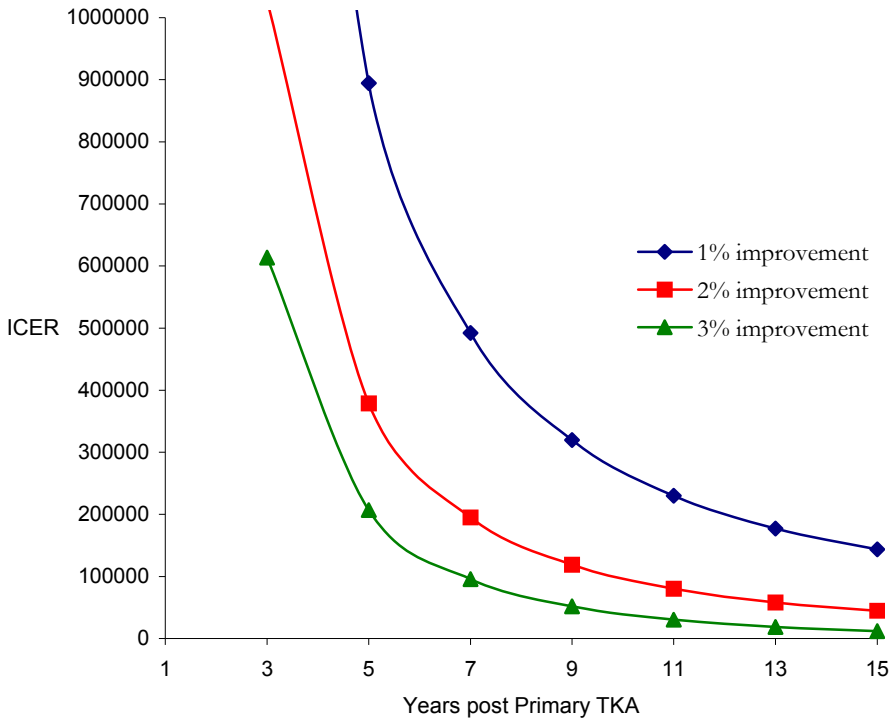
Year[a]	Cumulative major revision (%)	Cumulative minor revision (%)	Cumulative death (%)	Discounted cost ($)	Discounted QALYs[b]	Incremental cost/ QALY ($)[c]
		Conventional surgery				
1	0.39	0.20	2.54	$17 707 007	732.8	
3	1.14	0.57	7.76	$18 045 022	2039.4	
5	1.84	0.92	12.69	$18 331 755	3159.4	
7	2.49	1.25	17.36	$18 574 987	4119.5	
9	3.11	1.56	21.78	$18 781 316	4942.6	
11	3.68	1.85	25.96	$18 956 342	5648.1	
13	4.21	2.11	29.92	$19 104 814	6252.9	
15	4.71	2.36	33.66	$19 230 761	6771.5	
	Computer-navigated surgery - 1% revision improvement					
1	0.33	0.16	2.54	$18 703 895	732.9	
3	0.95	0.48	7.76	$18 985 923	2039.8	$2 269 938
5	1.54	0.77	12.69	$19 225 642	3160.4	$894 393
7	2.08	1.05	17.36	$19 429 401	4121.3	$491 782
9	2.60	1.30	21.78	$19 602 593	4945.1	$319 704
11	3.08	1.54	25.96	$19 749 804	5651.6	$230 064
13	3.53	1.77	29.92	$19 874 932	6257.3	$177 290
15	3.95	1.98	33.67	$19 981 289	6776.7	$143 526
	Computer-navigated surgery - 2% revision improvement					
1	0.26	0.13	2.54	$18 671 990	732.9	
3	0.76	0.38	7.76	$18 897 808	2040.2	$1 027 645
5	1.23	0.62	12.69	$19 090 136	3161.4	$378 784
7	1.67	0.84	17.36	$19 253 940	4123.0	$194 956
9	2.09	1.05	21.78	$19 393 450	4947.7	$118 807
11	2.47	1.24	25.96	$19 512 271	5655.0	$80 321
13	2.84	1.42	29.92	$19 613 469	6261.7	$58 317
15	3.18	1.60	33.67	$19 699 659	6782.0	$44 633
	Computer-navigated surgery - 3% revision improvement					
1	0.20	0.10	2.54	$18 640 055	733.0	
3	0.57	0.29	7.76	$18 809 441	2040.6	$613 488
5	0.92	0.46	12.69	$18 953 995	3162.4	$206 851
7	1.26	0.63	17.36	$19 077 358	4124.8	$95 952
9	1.57	0.79	21.78	$19 182 637	4950.3	$51 779
11	1.86	0.93	25.96	$19 272 481	5658.5	$30 347
13	2.14	1.07	29.92	$19 349 155	6266.1	$18 602
15	2.40	1.20	33.67	$19 414 589	6787.3	$11 613

[a] Only odd years shown.
[b] 5% discount rate used
[c] ICER (incremental cost-effectiveness ratio) calculated from year 1 to year 15, respectively. The start total knee replacement number of simulations is 1000

These results are also presented in Figure 10. The figure shows the incremental cost-effectiveness ratio of computer-navigated TKA versus conventional TKA over the 15-year period. The high ICERs for all scenarios in the first 5 years are indicative of the higher cost of the primary TKA; however, in the long term some of the higher costs are recouped by a cost saving in the reduced revision rate. This fact and the small number of QALYs gained in association with fewer revision procedures, leads to a diminishing ICER in subsequent years.

Scenario 2 (moderate improvement in revision rate) is unlikely to be cost-effective. Based on these findings computer-navigated arthroplasty is unlikely to be a dominant strategy, in that it reduces cost and increases QALYs.

Figure 10 Incremental cost-effectiveness ratio of computer-navigated TKA versus conventional TKA over a 15 year period



Sensitivity analysis

In the base case analysis, scenarios 3 and 4 appeared marginally cost-effective in the long term compared to conventional TKA. In the base case we calculated the capital cost of the navigation equipment based on 70 procedures per year. For the sensitivity analysis we assumed that the navigation equipment is used for 250 procedures per year. The obvious impact of doing this is to reduce the incremental cost of the computer-navigation TKA from $1029 to $421 per procedure. This means that the initial cost of performing computer-navigated TKA is now similar to the cost of conventional surgery, and the cost saving which occurred through reduced revisions is more influential. The results of this analysis are presented in Table 31 and Figure 11.

Table 31 Sensitivity analysis results - Markov simulation and cost-effectiveness analysis

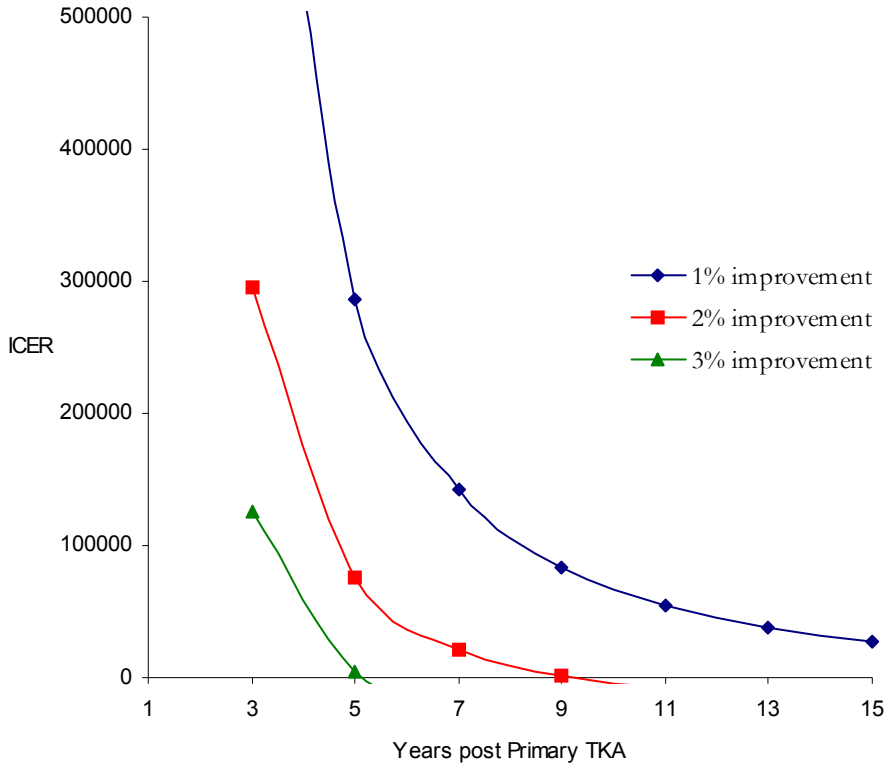
Year[a]	Cumulative major revision (%)	Cumulative minor revision (%)	Cumulative death (%)	Discounted cost ($)	Discounted QALYs[b]	Incremental cost/ QALY ($)[c]
		Conventional surgery				
1	0.39	0.20	2.54	$17 707 007	732.8	
3	1.14	0.57	7.76	$18 045 022	2039.4	
5	1.84	0.92	12.69	$18 331 755	3159.4	
7	2.49	1.25	17.36	$18 574 987	4119.5	
9	3.11	1.56	21.78	$18 781 316	4942.6	
11	3.68	1.85	25.96	$18 956 342	5648.1	
13	4.21	2.11	29.92	$19 104 814	6252.9	
15	4.71	2.36	33.66	$19 230 761	6771.5	
	Computer-navigated surgery – 1% revision improvement					
1	0.33	0.16	2.54	$18 096 354	732.9	
3	0.95	0.48	7.76	$18 378 381	2039.8	$804 234
5	1.54	0.77	12.69	$18 618 101	3160.4	$286 508
7	2.08	1.05	17.36	$18 821 859	4121.3	$142 095
9	2.60	1.30	21.78	$18 995 052	4945.1	$83 202
11	3.08	1.54	25.96	$19 142 263	5651.6	$53 908
13	3.53	1.77	29.92	$19 267 390	6257.3	$37 427
15	3.95	1.98	33.67	$19 373 747	6776.7	$27 344
	Computer-navigated surgery – 2% revision improvement					
1	0.26	0.13	2.54	$18 064 449	732.9	
3	0.76	0.38	7.76	$18 290 267	2040.2	$295 531
5	1.23	0.62	12.69	$18 482 594	3161.4	$75 339
7	1.67	0.84	17.36	$18 646 398	4123.0	$20 505
9	2.09	1.05	21.78	$18 785 909	4947.7	$891
11	2.47	1.24	25.96	$18 904 729	5655.0	Dominant
13	2.84	1.42	29.92	$19 005 928	6261.7	Dominant
15	3.18	1.60	33.67	$19 092 118	6782.0	Dominant
	Computer-navigated surgery – 3% revision improvement					
1	0.20	0.10	2.54	$18 032 513	733.0	
3	0.57	0.29	7.76	$18 201 899	2040.6	$125 902
5	0.92	0.46	12.69	$18 346 454	3162.4	$4886
7	1.26	0.63	17.36	$18 469 817	4124.8	Dominant
9	1.57	0.79	21.78	$18 575 095	4950.3	Dominant
11	1.86	0.93	25.96	$18 664 940	5658.5	Dominant
13	2.14	1.07	29.92	$18 741 614	6266.1	Dominant
15	2.40	1.20	33.67	$18 807 047	6787.3	Dominant

a) Only odd years shown.

b) 5% discount rate used

c) ICER (incremental cost-effectiveness ratio) calculated from year 1 to year 15, respectively. The start total knee replacement number of simulations is 1000.

Figure 11 Sensitivity analysis - Incremental cost-effectiveness ratio of computer-navigated TKA versus conventional TKA over a 15 year period



Another potential driver of the analysis is the utility values given to each Markov state. Changing the utility values (±20%) of the 'normal health after a revision', 'major revision' and 'minor revision' states favour computer navigation. For example, in the worst-case scenario (all utilities reduced by 20%), for the 1000 patient cohort simulation, the cumulative discounted QALYs for conventional TKA was 6729.1 at 15 years. The cumulative discounted QALYs for scenario 2 was 6741.2, for scenario 3 was 6753.5 and for scenario 4 was 6765.9. This gave a QALY gain of 12.2, 24.4 and 36.8 for scenarios 2, 3 and 4 respectively. The incremental cost-effectiveness ratio at 15 years is $61 702, $19 188 and $4993 for scenarios 2, 3 and 4 respectively.

The model is sensitive to the state 'normal health after TKA revision. In our model we assumed that this health state was 0.1 lower than the normal health state for this cohort of patients. These data were based on utility values from Rorabeck and Murray (1997) and Dong and Buxton (2006). The assumption being that a person who has required a second TKA is unlikely to enjoy the same quality of life as somebody needing only one TKA. If we make the utility value of this health state the same as 'normal health after primary TKA' the QALYs gained by reducing the revision rates are reduced and hence the ICER of computer-navigated TKA increases. In the 1000 patient cohort simulation, the QALY gain is now 0.2, 0.4 and 0.6 for scenarios 2, 3 and 4 respectively, with an incremental cost-effectiveness ratio at 15 years of $4 025 131, $1 250 141 and $324 856 for scenarios 2, 3 and 4 respectively.

In summary, the results of the sensitivity analysis demonstrate that the incremental cost-effectiveness ratios are driven by the capital cost of the computer-navigated equipment, the predicted reduction in revision rate and the utility weight 'normal health after TKA revision'.

What are the other considerations?

Consumer considerations

The following statement was provided by the Consumers Health Forum of Australia nominee to represent the consumers' perspective on computer-navigated total knee arthroplasty:

> Through consultation with the Joint Replacement Support Group of Arthritis WA and with other consumer representatives of the Consumers Health Forum, one comment appears more important than any other, the need for a successful replacement that will last for as long as possible.
>
> Total knee arthroplasty is major surgery and most patients will put it off for as long as possible as they understand that there is a limited lifespan on the prosthesis. Thus when they have the procedure, they want it to be successful. This is more important than the length of surgery, length of time as an inpatient or the size of the scar.
>
> It appears from the literature that Computer-Assisted Total Knee Arthroplasty improves the lifespan of the prosthesis due to a more accurate alignment of the implant. For consumers this would be the favourable method over manual procedures.

Only 10 studies reported results of clinical outcomes which may be of particular concern to the consumer. These included scores such as the WOMAC score, Oxford score and the Hospital for Special Surgery score, as well as other clinically significant parameters. In the majority of studies there was no statistical difference in outcome between navigated and conventional method.

Discussion

Limitations of the evidence

This review examining the safety and effectiveness of computer-navigated total knee arthroplasty was limited by the available evidence.

Whilst the evidence base was not limited in quantity of studies, the evidence was limited in regards to the number of studies reporting certain important outcomes. The majority of studies reported radiological outcomes as a measure of effectiveness of computer navigation. However, few studies reported any clinical or safety outcome, thus limiting the assessment of these aspects of computer navigation. Furthermore, in cases where radiological, clinical or safety outcomes were reported, follow-up was generally short-term only.

The evidence base was dominated by studies utilising a wide variety of effectiveness outcomes, particularly radiological outcomes, which in many cases were reported using inconsistent nomenclature. The variety of outcomes observed suggests that for radiological outcomes, there is no standard outcome which can be used as a measure of effectiveness. Interpretation of radiological outcomes in particular was made difficult by the poor explanation given in the studies of the alignments reported. For example, in many cases only the magnitude and not the direction of the postoperative deformity were stated. Therefore, while in many cases the direction was able to be calculated from the information provided in the studies, in a substantial number of cases the direction could not be determined.

Safety

Safety data was reported in only a small proportion of the studies included in the report. In cases where safety was reported, often the data was reported poorly. This may represent study bias where the primary concern of the authors was to present data on effectiveness, rather than safety. No data were presented in the identified literature for the conventional technique in regards to technical adverse events. This resulted in an inability to compare the technical safety of the computer-navigated device with conventional total knee arthroplasty. Given the technical difference in performing total knee arthroplasty with computer navigation versus the manual alternative, there may be a learning curve associated with the computer-navigated technique.

Effectiveness

The reporting of effective outcomes was compromised by the variety and inconsistencies in reporting of the outcome measurements, particularly radiological measurements. Many studies did not report the number of patients included in the outcome analysis. Therefore, it was assumed that all patients were considered. Similarly, not all studies reported the time at which radiological measurements were taken. In these cases it was assumed that the radiological measurements were performed using weight-bearing radiographs at a minimum of 6 weeks postoperatively.

Meta-analyses were able to be performed for the radiological outcomes as well as the duration of operation and tourniquet time. In some cases, separate meta-analyses were

able to be performed based on the level of evidence of the included studies. This approach allowed for comment to be made regarding the validity of the results.

The evidence did not allow for a sub-group analysis of valgus, post-osteotomy, grossly anatomically deformed knees or previously operated knees with metal hardware in situ. This was due to the inconsistent descriptions of the study populations of each study.

Conclusions

Safety

Adverse events were reported inconsistently across the included studies in this review. However, in cases where comparative data was available, the incidence of complications was comparable between total knee arthroplasty performed using computer navigation and the conventional technique.

The total knee arthroplasty procedure using computer navigation was not associated with any mortality. In the majority of cases the clinical adverse events experienced were relatively minor in nature and, where comparative data was available, comparable to the conventional technique. Infection and deep vein thrombosis were reported as the most common clinical adverse events with rates of 1.1 per cent and 1.7 per cent respectively using computer navigation and 0.8 per cent and 1.6 per cent respectively using the conventional technique.

The most common technical adverse event for computer-navigated total knee arthroplasty was difficulty with tracker fixation or loosening of the tracker (2.3%). The rate of conversion to the conventional manual technique due to technical failure of the navigation system was 12/955 knees (1.3%).

Blood loss between the two different techniques was reported to be significantly less using computer navigation in two out of eight studies reporting this safety outcome.

Overall the safety of computer-navigated total knee arthroplasty appears to be comparable to the conventional technique.

Effectiveness

Radiological effectiveness

Various radiological outcomes were reported as measures of effectiveness for computer-navigated total knee arthroplasty. Outcomes related to the postoperative mechanical axis achieved were selected as those most relevant to assess the true effectiveness of the technique.

For each of the radiological outcomes reported in this review (postoperative deformity, deviation of the mechanical axis from the target angle of 180º and satisfactory alignment of the postoperative alignment of the mechanical axis) computer navigation resulted in the greatest accuracy of implantation. Analyses using the best available evidence demonstrated that both techniques had similar mean postoperative deformities (1.20º for the conventional technique and 1.25º for computer-navigated technique) with similar deviations (pooled standard deviation 2.99º for conventional technique and 2.27° for computer-navigated technique).

The odds of achieving satisfactory postoperative alignment (defined as being within 3º of the target angle of 180º) are 2.88 times greater using computer navigation.

Clinical outcomes

The two most reported clinical outcomes, range of motion and Knee Society score, were comparable between both conventional and computer-navigated total knee arthroplasty techniques. Similarly the remainder of clinical outcomes reported were also comparable between the two techniques. The Modified Mayo Clinic Embolic score was significantly ($P = 0.004$) better in the computer-navigated group. The clinical relevance of this outcome is unclear.

The included studies (both comparative and case series) did not report on long-term clinical outcomes. In an effort to comment on how short-term radiological outcomes may relate to long-term clinical outcomes, separate searches were undertaken to identify literature which linked postoperative knee alignment with long-term outcomes. Relatively few low-level studies were identified and there was variability in the outcomes reported; therefore, meta-analysis was not possible. Overall, the data did not provide a specific link between postoperative alignment and long-term clinical outcomes such as revision.

Surgical time was significantly ($P < 0.00001$) longer by 12 minutes using computer navigation. Tourniquet time was prolonged by 14.5 minutes ($P < 0.00001$) when computer navigation was used; however, due to the technical differences between the techniques, this increase is not a surprise.

The evidence on the effectiveness of computer-navigated total knee arthroplasty suggests that the technique is at least as effective as the conventional approach, despite the shortcomings of the literature assessed. At the moment it is unclear whether the significant improvements in radiological outcomes translate to measurable clinical benefits for the patient, such as a reduction in revision rates. Further long-term trials are required to address this specific issue.

Cost-effectiveness

The objective of the economic evaluation was to compare the cost-effectiveness of computer-navigated total knee arthroplasty (TKA) with the conventional manual technique. The absence of long-term data supporting improved clinical effectiveness of computer-navigation meant that a Markov model was applied with the rationale being that improved alignment may lead to a reduction in TKA revision rate.

Model inputs, including costs, effectiveness and transition probabilities, were obtained from a review of the literature. Four scenarios were tested: 1) No improvement in the 10-year revision rate (approximately 6%), 2) a 1 percentage point improvement in the 10-year revision rate, 3) a 2 percentage point improvement and 4) a 3 percentage point improvement (i.e. a 50% reduction).

Based on a number of estimates and assumptions:

- The incremental cost of receiving computer-navigated TKA rather than conventional manual TKA was $1029 per procedure. The additional cost is associated with the capital cost of buying the computer navigation equipment, the higher estimated procedural fee, and the disposables required. These costs

are offset somewhat by a reduction in the number of trays required during the procedure.

- If computer-navigation TKA is no more effective or only modestly effective at reducing the probability of a revision TKA (scenarios 1 & 2), then this technique is unlikely to be cost-effective.

Computer-navigation surgery is potentially a cost-effective treatment for total knee arthroplasty in the long-term provided the corresponding improvement in the 10-year revision rate of TKA improves by 2 per cent or more (scenarios 3 & 4).

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise or Affiliation
Professor Robyn Ward (Chair)	medical oncology
Dr William Glasson (Deputy Chair)	ophthalmology
Associate Professor Frederick Khafagi (Deputy Chair)	nuclear medicine
Associate Professor John Atherton	cardiology
Professor Justin Beilby	health research
Professor Jim Butler	health economics
Professor Peter Cameron	trauma and emergency medicine
Associate Professor Kirsty Douglas	health research
Dr Kwun Fong	thoracic medicine
Professor Richard Fox	medical oncology
Professor Jim Bishop AO	Chief Medical Officer, Department of Health and Ageing
Professor Helen Lapsley	health economics
Mr Russell McGowan	consumer health issues
Dr Ian Prosser	haematology
Dr Judith Soper	radiology
Dr Graeme Suthers	genetics/medical oncology
Dr Shiong Tan	general practice
Professor Ken Thomson	radiology
Professor Andrew Wilson	public health physician
Dr Caroline Wright	colorectal surgery

Appendix B Advisory panel and evaluators

Advisory panel for MSAC Application 1123: Computer-navigated total knee arthroplasty

Dr David Wood	Chair
Dr Judy Soper *(Deputy Chair)*	Member of MSAC
Dr Graham Mercer	Australian Orthopaedic Association nominee
Dr Richard de Steiger	Australian Orthopaedic Association nominee
Mr Ben Horgan (until September 2008)	Consumers' Health Forum of Australia nominee
Dr Janet Wale (from September 2008)	Consumers' Health Forum of Australia nominee

Evaluators

Mr Luis Zamora	ASERNIP-S
Ms Amber Watt	ASERNIP-S
Dr Alun Cameron	ASERNIP-S
Ms Deanne Leopardi	ASERNIP-S
Dr Stephen Goodall	CHERE

Appendix C Approach to assessment

Search strategy

Table 32 Bibliographic databases searched

Electronic Database	Time period & search limits
AustHealth – including: Australian Medical Index, APAIS Health	1996 - April 2008 Limits: humans
CINAHL	1996 - April 2008 Limits: humans
Cochrane Library – including: Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, Health Technology Assessment Database, NHS Economic Evaluation Database	1996 - April 2008
EMBASE	1996 - April 2008 Limits: humans
PubMed	1996 - April 2008 Limits: humans
Web of Science – Science Citation Index Expanded	1996 - April 2008 Limits: humans

NOTES: APAIS – Australian Public Affairs Information Service; NHS – National Health Service

Table 33 Electronic internet databases searched

Electronic Database	Internet address
Centre for Reviews and Dissemination (CRD) / International Network of Agencies for Health Technology Assessment (INAHTA) databases – including: NHS Economic Evaluation Database (NHS EED) / Database of Abstracts of Reviews of Effect (DARE) / Heath Technology Assessment (HTA) Database	http://www.york.ac.uk/inst/crd/
National Health and Medical Research Council (NHMRC) (Australia)	http://www.health.gov.au/nhmrc/
Australian Department of Health and Ageing	http://www.health.gov.au/
Scirus – for Scientific Information Only	http://www.scirus.com
Trip database	http://www.tripdatabase.com
Current Controlled Trials metaRegister	http://controlled-trials.com/
National Library of Medicine Health Services / Technology Assessment Text	http://text.nlm.nih.gov/
National Library of Medicine Locator Plus database	http://locatorplus.gov
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/pages/grey_literature_report
US Department of Health and Human Services (reports and publications)	http://www.os.dhhs.gov/

Table 34 Health technology assessment internet sites

Argentina
• Institute for Clinical Effectiveness and Health Policy (IECS) http://www.iecs.org.ar/iecs-visor-publicaciones-ing.php
Australia
• Adelaide Health Technology Assessment (AHTA) http://www.health.adelaide.edu.au/publichealth/consult/health_techn_assess.html
• Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/asernip-s.htm
• Centre for Clinical Effectiveness, Monash University http://www.mihsr.monash.org/cce/
• Health Economics Unit, Monash University http://chpe.buseco.monash.edu.au
• Medical Services Advisory Committee (MSAC) http://www.msac.gov.au
Austria
• Institute of Technology Assessment (ITA) http://www.oeaw.ac.at/ita/e1-3.htm
Brazil
• Departamento de Ciência e Tecnologia (DECIT) http://portal.saude.gov.br/portal/saude/area.cfm?id_area=1088
Canada
• Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/site/index.php?home
• Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/publications/
• Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/index.php/en/home
• Canadian Association for Health Services and Policy Research (CAHSPR) http://www.cahspr.ca
• Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org
• Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca
• Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm
• Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca
• Institute of Health Economics (IHE) http://www.ihe.ca/
• Ministry of Health and Long-Term Care – Medical Advisory Secretariat http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html
Denmark
• Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) http://www.dacehta.dk
• Danish Institute for Health Services Research (DSI) http://www.dsi.dk/engelsk.html
Finland
• Finnish Office for Health Technology Assessment (FinOHTA) http://finohta.stakes.fi/EN/index.htm
France
• Committee for Evaluation and Diffusion of Innovative Techniques (CEDIT) http://cedit.aphp.fr/english/index_present.html
• French National Authority for Health (HAS) http://www.has-sante.fr
Germany
• German Agency for Health Technology Assessment (DAHTA) http://www.dimdi.de/dynamic/en/hta/db/index.htm
Hungary
• Unit of Health Economics and Technology Research Assessment (HunHTA) http://hecon.uni-corvinus.hu/corvinus.php?lng=en
The Netherlands
• Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/adviezen.php?phpLang=en
• Netherlands Organisation for Health Research and Development (ZonMw) http://www.zonmw.nl/en/home.html
New Zealand

Table 34 continued Health technology assessment internet sites

• New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/
Norway
• Norwegian Knowledge Centre for the Health Services http://www.kunnskapssenteret.no
Spain
• Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud Carlos III / Health Technology Assessment Agency (AETS) http://www.isciii.es/htdocs/en/investigacion/Agencia_quees.jsp
• Andalusian Agency for Health Technology Assessment (AETSA) http://www.juntadeandalucia.es/index.html
• Catalan Agency for Health Technology Assessment (CAHTA) http://www.gencat.cat/salut/depsan/units/aatrm/html/en/dir394/index.htm
Sweden
• Swedish Council on Technology Assessment in Healthcare (SBU) http://www.sbu.se/en/
• Center for Medical Health Technology Assessment http://www.cmt.liu.se/?l=en
Switzerland
• Swiss Network on Health Technology Assessment (SNHTA) http://www.snhta.ch/
United Kingdom
• NHS Quality Improvement Scotland http://www.nhshealthquality.org/nhqis/CCC_FirstPage.jsp
• National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.ncchta.org/
• University of York NHS Centre for Reviews and Dissemination (NHS CRD) http://www.york.ac.uk/inst/crd/
• National Institute for Clinical Excellence (NICE) http://www.nice.org.uk
United States
• Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/clinic/techix.htm
• Harvard School of Public Health – Cost-Utility Analysis Registry http://www.tufts-nemc.org/cearegistry/
• U.S. Blue Cross/ Blue Shield Association Technology Evaluation Centre (TEC) http://www.bcbs.com/betterknowledge/tec/
• Veterans' Affairs Technology Assessment Program (VATAP) http://www.va.gov/vatap/publications.htm

Inclusion criteria

Table 35 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	*Effectiveness:* systematic reviews and clinical studies (including randomised and nonrandomised comparative studies) will be included. Non-systematic reviews, case series, case reports, letters, editorials, animal, in-vitro and laboratory studies will be excluded. *Safety:* systematic reviews and clinical studies (including randomised and nonrandomised comparative studies) will be included. Non-systematic reviews, case series, case reports, letters, editorials, animal, in-vitro and laboratory studies will be excluded.
Patient	Male or female patients >18 years diagnosed with osteoarthritis, rheumatoid arthritis, systemic lupus erythematosus or miscellaneous diseases and disorders including acute trauma. Cadaveric studies will not be included unless there is a paucity of evidence on living patients.
Intervention	Image-free, computer-navigated total knee arthroplasty. Image-based systems and robotic systems shall be excluded. Unicompartmental data will be included if available.
Comparator	Standard (or minimally-invasive) total knee arthroplasty
Outcome	*Effectiveness:* Postoperative limb alignment, rate of revision surgery, patient satisfaction, functional scores (eg WOMAC), quality of life *Safety:* Infection/complication rates, blood loss, thromboembolic events *Economics:* Duration of surgery
Language	Non-English language articles will be excluded unless they appear to provide a higher level of evidence than English language articles. It is anticipated that translation of foreign-language studies will not be required.

Search terms

The following search is based on PubMed platform.

#1 [MeSH] Surgery, Computer-Assisted [MeSH] AND Arthroplasty, Replacement, Knee

#2 Text: knee replacement

#3 Text: knee arthroplast*

#4 #2 OR #3

#5 Text: computer assist*

#6 Text: computer aid*

#7 Text: computer navigat*

#8 Text: computer guid*

#9 #5 OR #6 OR #7 OR #8

#10 #4 AND #9

#11 #3 OR #10

#12 #1 OR #11

Appendix D Critical appraisal of randomised controlled studies

Table 36 Critical appraisal summary of randomised controlled trials: study design details

Study NHMRC level	Sample size	Participants	Randomisation details	Blinding	Interventions and outcomes
Level II RCTs					
Bejek et al 2007 Level II	Total: 138 knees Intervention: 69 knees Comparator: 69 knees	No inclusion or exclusion criteria provided. Groups well matched at baseline for age and gender.	No details of randomisation, concealment or implementation.	Blinding not reported.	Interventions detailed. Primary outcomes reported.
Chauhan et al 2004 Level II	Total: 70 Intervention: not reported Comparator: not reported	Eligibility criteria not described. Groups well matched at baseline.	Randomisation through randomisation schedule (blocking size of 4). Staff & patients blinded to randomisation process. No details of implementation.	Radiologist analysing all radiographs blinded to original intervention and outcome variables. Data analysed by blinded statistician.	Interventions detailed. Primary outcomes defined.
Chin et al 2005 Level II	Total: 90 patients Intervention: 30 patients Comparator: 60 patients*	Inclusion criteria not described. No exclusion criteria used. Groups well matched at baseline.	Randomisation, concealment & implementation through sealed envelopes.	Radiographic measurements validated by blinded assessor.	Interventions detailed. Primary outcomes defined.
Church et al 2007 Level II	Total: 26 patients Intervention: 14 patients Comparator: 12 patients	Eligibility criteria described. Groups well matched at baseline.	Randomisation through computerised random number generator. No details of concealment or implementation.	Anaesthetists analysing ECG images blinded to original surgical intervention.	Interventions detailed. Primary outcomes defined.
Decking et al 2005 & 2007 Level II	Total: 52 patients Intervention: 27 patients Comparator: 25 patients	Eligibility criteria not described. Groups well matched at baseline.	Randomisation, concealment & implementation through sealed, numbered envelopes.	Blinding not reported.	Interventions detailed. Primary and secondary outcomes not well defined.
Ensini et al 2006 Level II	Total: 107 patients/120 knees Intervention: 60 knees Comparator: 60 knees	Eligibility criteria described. Groups well matched at baseline.	No details of randomisation, implementation or concealment.	Surgeon analysing postoperative radiographs blinded to original intervention.	Interventions detailed. Primary and secondary outcomes defined.
Kalairajah et al 2006 Level II	Total: 24 patients Intervention: 14 patients Comparator: 10 patients	Eligibility criteria not described. Groups well matched at baseline.	Randomisations through coin toss without the knowledge of the patient, anaesthetist (before the onset of the procedure) and ward staff.	Ward staff performing mental test scores blinded to surgical intervention.	Interventions detailed. Primary outcomes defined. Secondary outcomes not defined.
Kalairajah et al 2005 Level II	Total: 60 patients Intervention: 30 patients Comparator: 30 patients	Eligibility criteria described. Groups well matched at baseline.	Randomisation & concealment through sealed envelopes. No details of implementation.	Patient, anaesthetist (before onset of procedure) and ward staff not aware of which procedure had been undertaken.	Interventions detailed. Primary and secondary outcomes defined.

Table 36 continued Critical appraisal summary of randomised controlled trials: study design details

Study NHMRC level	Sample size	Participants	Randomisation details	Blinding	Interventions and outcomes
Level II RCTs					
Kim et al 2008 Level II	Total: 260 patients (420 knees) Intervention: 210 knees Comparator: 210 knees	Eligibility criteria not described in detail. Groups well matched at baseline.	Randomisation through sequential pool based on a table of randomised numbers. Concealment and implementation not reported.	Blinding not reported.	Interventions were given in little detail. Primary and secondary outcomes defined.
Macule-Beneyto et al 2006 Level II	Total: 202 patients Intervention: 109 patients Comparator: 93 patients	Eligibility criteria not described. Groups well matched at baseline.	Randomisation achieved through use of random number tables. Concealment & implementation not reported.	Blinding not reported.	Interventions detailed. Primary and secondary outcomes defined.
Matziolis 2007 Level II	Total: 60 patients/knees Intervention: 32 patients/knees Comparator: 28 patients/knees	Eligibility criteria described. Groups well matched for age and weight at baseline.	Randomisation by random number generator. Concealment & implementation not reported.	Blinding not reported.	Interventions detailed. Primary and secondary outcomes defined.
Mombert et al 2007 Level II	Total: 42 patients Intervention 21 patients Comparator: 21 patients	Eligibility criteria not described. Groups well matched at baseline.	Randomisation through computer randomisation. Concealment & implementation not reported.	Blinding not reported.	Interventions detailed. Primary outcomes defined.
Spencer et al 2007 Level II	Total: 60 patients Intervention: 30 patients Comparator: 30 patients	Eligibility criteria not described. Comparability of baseline characteristics of groups not reported	No details of randomisation, concealment or implementation.	Physiotherapists blinded to original intervention.	Interventions reasonably detailed. Primary outcomes defined.
Stockl et al 2004 Level II	Total: 64 patients Intervention: 32 patients Comparator: 32 patients	Eligibility criteria described. Groups well matched at baseline.	Randomisation through random permuted blocks of predefined size. Concealment & implementation through sealed sequentially numbered envelopes.	Blinding not reported.	Interventions detailed. Primary outcomes defined.
Weinrauch et al 2006 Level II	Total: 70 patients Intervention: 39 Comparator standard: 31	Eligibility criteria not described. Groups well matched at baseline	No details of randomisation, concealment or implementation.	Assessing physiotherapists blinded to surgical intervention.	Interventions detailed. Primary outcomes defined.

Table 36 continued Critical appraisal summary of randomised controlled trials: study design details

Study NHMRC level	Sample size	Participants	Randomisation details	Blinding	Interventions and outcomes
Level III-1 pseudo-RCTs					
Bäthis et al 2004b Level III-1	Total: 160 patients Intervention: 80 patients Comparator: 80 patients	Eligibility criteria described. Groups comparable at baseline.	'Randomisation' by day of operation. Concealed & implemented by independent study administrator.	Blinding not reported.	Interventions detailed. Primary outcomes defined.
Böhling et al 2005 Level III-1	Total: 100 Intervention: 50 Comparator: 50	Eligibility criteria not described. Groups well matched for age and gender.	'Randomisation' through alternate allocation. No detailed of concealment or implementation.	Blinding not reported.	Interventions detailed. Primary outcomes not well defined.
Kim et al 2007 Level III-1	Total: 100 patients/200 knees Intervention: 100 knees Comparator: 100 knees	Eligibility criteria not well described. Patients acted as their own control.	'Randomisation' through alternate allocation. No details of concealment or implementation.	Clinical & radiological data recorded & complied by blinded observers.	Interventions detailed. Primary outcomes defined.
Martin et al 2007 Level III-1	Total: 200 patients Intervention: 100 knees Comparator: 100 knees	Eligibility criteria described. Patients well matched for all characteristics except BMI.	'Randomisation' based on patient codes. No details of concealment or implementation.	Blinding not reported.	Interventions detailed. Primary outcomes defined.
Oberst et al 2008 Level III-1	Total: 71 knees/64 patients Intervention: 34 knees Comparator: 35 knees	Eligibility criteria described. Patients well matched for age, gender & weight.	'Randomisation' through alternate allocation. No details of concealment or implementation.	Blinding not undertaken.	Interventions detailed. Primary outcomes defined.
Song et al 2007 Level III-1	Total: 86 patients Intervention: 42 knees Comparator: 44 knees	Eligibility criteria briefly described. Groups well matched at baseline	'Randomisation' through alternate allocation. No details of concealment or implementation/	Tests undertaken and reported on by blinded observer.	Interventions details. Primary outcomes defined.
Sparmann et al 2003 Level III-1	Total: 240 patients/knees Intervention: 120 knees Comparator: 120 knees	Eligibility criteria briefly described. Groups comparable at baseline.	'Randomisation', implementation & concealment through alternate allocation.	Blinding not reported.	Intervention detailed. Primary outcomes not well defined.

Notes: NHMRC = National Health and Medical Research Council; RCT = randomised controlled trial; ECG = electrocardiogram; BMI = body mass index.

Table 37 Critical appraisal summary of randomised controlled trials: results details

Study	Numbers analysed	Statistical methods	Outcomes and estimation	Ancillary analyses	Adverse events	Follow-up
Level II RCTs						
Bejek et al 2007 Level II	Power calculations not reported. Intention-to-treat or per-protocol analysis not defined.	Tests not detailed. Significance levels not defined.	Results for each outcome detailed. Standard deviations as measure of variability.	No subgroup analyses performed.	Described for both groups.	Follow-up not reported. Losses to follow-up were not reported.
Chauhan et al 2004 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance levels not defined.	Results for each outcome detailed. Means with range as measure of variability for secondary outcomes.	No subgroup analyses performed.	Described for both groups.	Radiography at 6 weeks. Losses to follow-up not reported.
Chin 2005 Level II	Power calculations not reported. Intention-to-treat and per-protocol analysis not defined.	Tests detailed. Significance levels not defined.	Results for each outcome detailed. Means with ranges as measure of variability.	No subgroup analyses performed.	Described briefly for both groups.	Radiographic scans for evaluation taken as soon as patient able to weight-bear fully. Losses to follow-up: Intervention: n = 0 Comparator: n = 0
Church et al 2007 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance levels not defined.	Results for each outcome detailed. Mean and range as measure of variability.	No subgroup analyses performed.	Described briefly for both groups.	Peri-operative observations only. Losses to follow-up not reported.
Decking et al 2005 & 2007 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Means with standard deviations as measure of variability.	No subgroup analyses performed.	Adverse events for reported for both groups.	3-month radiological follow-up. Losses to follow-up not reported. 12-month functional follow-up. No losses to follow-up
Ensini et al 2006 Level II	Power calculations made before patient recruitment and met. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Mean and standard deviation as measure of variability.	Subgroup analyses performed on 'outlier' patients with alignment deviation > 3°.	Described briefly for both groups.	Mean follow-up 28 months for clinical/functional assessment Losses to follow-up not reported.

Table 37 continued Critical appraisal summary of randomised controlled trials: results details

Study	Numbers analysed	Statistical methods	Outcomes and estimation	Ancillary analyses	Adverse events	Follow-up
Level II RCTs						
Kalairajah et al 2006 Level II	Power calculations made and met. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Median, mean, interquartile range and standard error of mean reported as measure of variability.	No subgroup analyses performed.	Adverse events were not detailed.	Primary and secondary outcomes measured at one and three days postoperatively. Losses to follow-up not reported.
Kalairajah et al 2005 Level II	Power calculations made before patient recruitment & met. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance levels defined.	Results for each outcome detailed. Means with range and 95% confidence interval as measure of variability.	No subgroup analyses performed.	Adverse events were not detailed.	Total blood loss, haemoglobin loss assessed on the second postoperative day. Losses to follow-up not reported.
Kim et al 2008 Level II	Power calculations were not made before patient recruitment. There were no losses to follow-up due to the short observation periods; therefore intention to treat was precluded.	Tests detailed. Significance level defined.	Results for key outcomes detailed. Means with ranges as measure of variability.	Subgroup analysis performed in patients with fat emboli or bone-marrow-cell emboli present postoperatively, in connection to their preoperative characteristics.	Thromboembolic events described for both treatment groups.	48 hours. Losses to follow-up not reported; however, from results appears no patients dropped out.
Macule-Beneyto et al 2006 Level II	Power calculations made before patient recruitment and met. Intention-to-treat analysis defined.	Tests detailed. Significance level defined.	Not all results for each outcome detailed. Means and standard deviation as measure of variability.	No subgroup analyses performed.	Adverse events not detailed.	Immediate post-surgery (first few days). Losses to follow-up: Intervention=7; Comparator=9 (post-op radiographs not possible)
Matziolis 2007 Level II	Power calculations not reported. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Mean, standard deviation and distribution of values determined for each measure.	No sub-group analysis performed.	Blood loss was the only adverse event reported.	Immediate radiological follow-up. 6-month functional follow-up. Losses to follow-up not reported.

Table 37 continued Critical appraisal summary of randomised controlled trials: results details

Study	Numbers analysed	Statistical methods	Outcomes and estimation	Ancillary analyses	Adverse events	Follow-up
Level II RCTs						
Mombert et al 2007 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests not detailed. Significance levels not defined.	Results for each outcome detailed. Missing results table. Mean and 95% confidence interval as measure of variability.	No subgroup analyses performed.	Adverse events not detailed.	Radiography at three months postoperatively. Losses to follow-up not reported.
Spencer et al 2007 Level II	Power calculation made in the original study, not in these variables assessed at follow-up. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined	Results for each outcome detailed. Means with 95% confidence interval as measure of variability.	No subgroup analyses performed.	Knee pain was the only adverse event detailed.	Functional outcomes at 3, 6, 12 & 24 months post-op. Losses to follow-up: Intervention = 5 (2 deaths, 1 loss, 2 unable to attend) Comparator = 6 (4 deaths, 2 losses)
Stockl et al 2004 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Mean with standard deviation and range as measures of variability. External validity of the measurement technique assessed. Inter- and intra-observer reliabilities assessed.	No subgroup analyses performed.	Adverse events not detailed.	Follow-up and losses to follow-up not reported.
Weinrauch et al 2006 Level II	Power calculations not reported. Intention-to-treat and per-protocol analyses not defined.	Tests detailed. Significance level defined	Parametric / nonparametric test and frequencies used ie *P* values, mean	No sub-group analyses performed.	Adverse events briefly described, some data missing for different approaches, haemoglobin etc	No losses to follow-up
Level III-1 pseudo RCTs						
Bäthis et al 2004b Level III-1	Power calculations not reported. Intention-to-treat and per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Means with interquartile range and 95% confidence interval as measure of variability. Intra- & inter- observer reliabilities assessed.	No sub-group analysis performed.	Adverse events not detailed.	Postoperative radiological follow-up. Losses to follow-up not reported.

Table 37 continued Critical appraisal summary of randomised controlled trials: results details

Study	Numbers analysed	Statistical methods	Outcomes and estimation	Ancillary analyses	Adverse events	Follow-up
Level III-1 pseudo RCTs						
Böhling et al 2005 Level III-1	Power calculations not reported. Intention-to-treat and per-protocol analysis not defined.	Tests detailed. Significance level not defined.	Results for multiple outcomes detailed. Standard deviations as measure of variability.	No sub-group analysis performed.	Adverse events not detailed.	Radiological evaluation 14 days post-op. Clinical outcomes at 7 months (mean). Losses to follow-up not reported.
Kim et al 2007 Level III-1	Power calculations reported and met. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Ranges as measure of variability. Intra- and inter-observer reliabilities assessed.	No sub-group analysis performed.	Adverse events briefly described for both groups.	Radiological & functional follow-up to 3 years. No patient lost to radiological follow-up.
Martin et al 2007 Level III-1	Power calculations not reported. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Means with ranges, 95% confidence interval and standard deviations as measure of variability. Intra- & inter-observer reliabilities assessed.	Sub-group analysis performed to examine differences in outcome for different prostheses.	Adverse events briefly described for both groups.	3-month radiological follow-up. Losses to follow-up not reported.
Oberst et al 2008 Level III-1	Power calculations relevant to Knee Society score reported & met. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for radiological outcomes detailed. Knee Society score not reported. Means with standard deviation as measure of variability.	No sub-group analysis performed.	Adverse events not detailed.	Postoperative radiological follow-up. Losses to follow-up not reported.
Song et al 2007 Level III-1	Power calculations not reported. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level defined.	Results for each outcome detailed. Means with standard deviation as measure of variability.	No sub-group analysis performed.	Adverse events not detailed.	1-year follow-up. 4/86 losses to follow-up (reasons not reported)
Sparmann et al 2003 Level III-1	Power calculations not reported. Intention-to-treat or per-protocol analysis not defined.	Tests detailed. Significance level not defined.	Results for radiological outcomes detailed. Ranges as measure of variability.	No sub-group analysis performed.	Adverse events reported for both groups.	Postoperative to 3-month radiological follow-up. Losses to follow-up not reported.

Appendix E Studies included in the review

Studies included for safety

Comparative studies

Anderson KC, Buehler KC & Markel DC, 2005. Computer assisted navigation in total knee arthroplasty: comparison with conventional methods. *Journal of Arthroplasty* 20(7 Suppl 3): 132-138.

Bäthis H, Perlick L, Tingart M, Luring C, Zurakowski D & Grifka J, 2004. Alignment in total knee arthroplasty. A comparison of computer-assisted surgery with the conventional technique. *Journal of Bone and Joint Surgery - Series B* 86(5): 682-687.

Bäthis H, Perlick L, Tingart M, Luring C & Grifka J, 2004. CT-free computer-assisted total knee arthroplasty versus the conventional technique: Radiographic results of 100 cases. *Orthopedics* 27(5): 476-480.

Bejek Z, Solyom L & Szendroi M, 2007. Experiences with computer-navigated total knee arthroplasty. *International Orthopaedics* 31(5): 617-622.

Bolognesi M & Hofmann A. 2005. Computer navigation versus standard instrumentation for TKA: A single-surgeon experience. *Clinical Orthopaedics and Related Research* (440): 162-169.

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Chauhan SK, Scott RG, Breidahl W & Beaver RJ, 2004. Computer-assisted knee arthroplasty versus a conventional jig-based technique. A randomised, prospective trial. *Journal of Bone and Joint Surgery - Series B.* 86(3): 372-377.

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Yau WP, Chiu KY, Zuo JL & Tang WM, 2008. Computer navigation did not improve alignment in a lower-volume total knee practice. *Clinical Orthopaedics and Related Research* 466(4): 935-945.

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Appendix F Clinical trials and health technology assessments

Clinical trials

The United States National Institute of Health (clinicaltrials.gov), the National Research Register (UK) and the Australian New Zealand Clinical Trials Registry were searched on 1 October 2008. A number of randomised and nonrandomised controlled trials were identified. The most significant trials are listed below. None of the identified trials is expected to be published within the timelines of this review.

Ongoing

1) ClinicalTrials.gov identifier NCT00279838
"Computer Assisted Navigation in Total Knee Arthroplasty"
Total enrolment: 200, expected completion NR (Received January 18, 2006)
Treatment, Randomized, Open Label, Active Control, Factorial Assignment, Efficacy Study

2) ClinicalTrials.gov identifier NCT00375856
"An Investigation of Computer-Assisted Total Knee Replacement Kinematics on Patient Performance: An Examination of the DePuy P.F.C.® SigmaTM Posterior Cruciate Substituting Knee and the DePuy P.F.C.® Sigma RP Rotating Platform Knee Systems"
Total enrolment: 140, expected completion October 2009
Treatment, Randomized, Single Blind, Historical Control, Factorial Assignment, Efficacy Study

3) ClinicalTrials.gov identifier NCT00431509
"A Randomized Trial Comparing Navigated and Conventional Implantation Techniques in Knee Replacement Surgery. Influence on Operative Result, Health-Related Quality of Life, and Coordinative Abilities."
Total enrolment: 477, expected completion June 2009
Treatment, Randomized, Single Blind, Active Control, Parallel Assignment, Safety/Efficacy Study

4) ClinicalTrials.gov identifier NCT00512421
"Phase 2 Study of Computer Assisted Surgery vs Conservative Surgery- Accuracy Study."
Total enrolment: 200, expected completion NR (Received August 5, 2007)
Screening, Longitudinal, Random Sample, Retrospective/Prospective Study

5) ClinicalTrials.gov identifier NCT00300326
"An Investigation of Total Knee Arthroplasty Kinematics on Patient Performance – The Zimmer Legacy® LPS Flex Knee System"
Total enrolment: 60, expected completion January 2010
Treatment, Randomized, Open Label, Historical Control, Parallel Assignment

6) ClinicalTrials.gov identifier NCT00409266
"CT Assessment of Minimally Invasive Surgery and Computer Assisted Navigation in Total Knee Arthroplasty"
Total enrolment: NR, expected completion NR (Received December 6, 2006)

Treatment, Non-Randomized, Open Label, Uncontrolled, Single Group Assignment

Recruiting

1) ClinicalTrials.gov identifier NCT00733330
"Computer Assisted Navigation in Minimally Invasive Total Knee Arthroplasty: Comparing the Alignment Achieved Using the DePuy Ci Minimally Invasive (Mi) Versus the DePuy Non Navigated Conventional Total Knee Arthroplasty"
Total enrolment: 154, expected completion December 2009
Treatment, Non-Randomized, Open Label, Uncontrolled, Parallel Assignment, Safety/Efficacy Study

Health technology assessments

HTA reports identified by the search, which may be relevant to this review are:

Bathis H., Shafizadeh S et al, 2006. Are computer assisted total knee replacements more accurately placed? A meta-analysis of comparative studies. *Der Orthopade*, 35(10): 1056-1065 [German].

Bauwens K, Matthes G et al, 2007. Navigated total knee replacement. A meta-analysis. *The Journal of Bone and Joint Surgery. American Volume,* 89 (2): 261-269.

Brophy J, 2007. The use of image-free computer-assisted systems in total knee replacement surgeries. *McGill University Health Centre (MUHC)* 11-05-7 A.D. http://www.mcgill.ca/tau/publications

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Medical Advisory Secretariat. Computer-assisted hip and knee arthroplasty: navigation and active robotic systems. *Ontario Health Technology Advisory Committee Website* , 2004. 11-05-2007.
http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_arthro_020104.pdf

Appendix G Long-term linking data: included and excluded studies

Included studies

Case-series:

Aglietti P, Buzzi R., 1988. 'Posteriorly stabilised total-condylar knee replacement. Three to eight years' follow-up of 85 knees.', *Journal of Bone and Joint Surgery British* 70(2): 211–216.

Berend ME, Ritter MA et al, 2004. 'Tibial component failure mechanisms in total knee arthroplasty', *Clinical Orthopaedics and Related Research* 428: 26–34.

Feng EL, Stulberg SD et al, 1994. 'Progressive subluxation and polyethylene wear in total knee replacements with flat articular surfaces', *Clinical Orthopaedics and Related Research* 299: 60–71.

Hamilton LR, 1982. 'UCI total knee replacement. A follow-up study', *Journal of Bone and Joint Surgery American* 64(5): 740–744.

Harvey IA, Manning MP et al, 1995. 'Alignment of total knee arthroplasty: the relationship to radiolucency around the tibial component', *Medical Engineering and Physics* 17(3): 182–187.

Jeffery RS, Morris RW et al, 1991. 'Coronal alignment after total knee replacement', *Journal of Bone and Joint Surgery British*, 73(5): 709–714.

Morgan SS, Bonshahi A. et al, 2007. 'The influence of postoperative coronal alignment on revision surgery in total knee arthroplasty', *International Orthopedics* [Epub ahead of print].

Ritter MA, Faris PM et al, 1994. 'Postoperative alignment of total knee replacement. Its effect on survival', *Clinical Orthopaedics and Related Research* 299: 153–156.

Rodriguez JA, Bhende H et al, 2001. 'Total condylar knee replacement: a 20-year follow-up study', *Clinical Orthopaedics and Related Research* 388: 10–17.

Tew M, Waugh W, 1985. 'Tibiofemoral alignment and the results of knee replacement.', *Journal of Bone and Joint Surgery British* 67(4): 551–556.

Windsor RE, Scuderi GR et al, 1989. 'Mechanisms of failure of the femoral and tibial components in total knee arthroplasty', *Clinical Orthopaedics and Related Research* 248: 15–19.

Excluded studies

Randomised controlled trials:

Insufficient follow-up

Martin A, Wohlgenannt O et al, 2007. 'Imageless navigation for TKA increases implantation accuracy', *Clinical Orthopaedics and Related Research* 460: 178–184.

Matsuda Y, Ishii Y et al, 2005. 'Varus-valgus balance and range of movement after total knee arthroplasty', *The Journal of Bone and Joint Surgery (Br)* 87(6): 804–808.

Mullaji A, Kanna R et al, 2007. 'Comparison of limb and component alignment using computer-assisted navigation versus image intensifier-guided conventional total knee arthroplasty', *The Journal of Arthroplasty* 22(7): 953–959.

Park SE, & Lee CT, 2007. 'Comparison of robotic-assisted and conventional manual implantation of primary total knee arthroplasty', *The Journal of Arthroplasty* 22(7): 1054–1059.

Uvehammer J, 2001. 'Knee joint kinematics, fixation and function related to joint area design in total knee arthroplasty', *Acta Orthopaedica Scandinavica Supplementum* 299(72): 1–52.

Invalid outcome(s)

Baker PN, Khaw FM et al, 2007. 'A randomised controlled trial of cemented versus cementless press-fit condylar total knee replacement. 15 year survival analysis', *The Journal of Bone and Joint Surgery (Br)* 89(12): 1608–1614.

Bertin K, 2005. 'Cruciate-retaining total knee arthroplasty at 5 to 7 years follow-up', *Clinical Orthopaedics and Related Research* 436: 177–183.

Rees JL, Beard DJ et al, 2005. 'Real in vivo kinematic differences between mobile-bearing and fixed-bearing total knee arthroplasties', *Clinical Orthopaedics and Related Research* 432: 204–209.

Case-series:

Cadaveric

Bargren JH, Blaha JD et al, 1983. 'Alignment in total knee arthroplasty. Correlated biomedical and clinical observations', *Clinical Orthopaedics and Related Research* 173: 178–183.

Insufficient follow-up

Benjamin J, 2006. 'Component alignment in total knee arthroplasty', *Instructional Course Lectures* 55: 405–412.

Cooke NJ, & Burnett R, 2008. 'An aid to tibial alignment in total knee replacement', *Annals of the Royal College of Surgeons of England* 90(1): 73–74.

Hernandez-Vaquero D, & Fernandez-Carreira JM, 2004. 'Correct limb alignment after a knee arthroplasty', *The Journal of Arthroplasty* 19(5): 668.

Hungerford DS, 1995. 'Alignment in total knee replacement', *Instructional Course Lectures*, 44: 455–468.

Kashyap SN, & van Ommeren JW, 2008. 'Clinical experience with less invasive surgery techniques in total knee arthroplasty: a comparative study', *Knee Surgery, Sports Traumatology, Arthroscopy: Official Journal of the ESSKA* 16(6): 544–548.

Lam LO, & Shakespeare D, 2003. 'Varus/valgus alignment of the femoral component in total knee arthroplasty', *Knee* 10(3): 237–241.

Ozcelik A, Seber S et al, 2004. 'Bone anatomy and rotational alignment in total knee arthoplasty', *Clinical Orthopaedics and Related Research* 422: 270.

Sah AP, Scott R. et al, 2008. 'Custom-made angled inserts for tibial coronal malalignment in total knee arthroplasty', *The Journal of Arthroplasty* [article in press].

Invalid outcome(s)

Fisher DA, Dierckman B et al, 2007. 'Looks good but feels bad: factors that contribute to poor results after knee arthroplasty', *The Journal of Arthroplasty* 22(6 Suppl 2): 39–42.

Hernigou P, Deschamps G, 2004. 'Alignment influences wear in the knee after medial unicompartmental arthorplasty', *Clinical Orthopaedics and Related Research* 423: 161–165.

Kubiak P, Archibeck MJ et al, 2008. 'Cruciate- retaining total knee arthroplasty in patients with at least fifteen degrees or coronal plane deformity', *The Journal of Arthroplasty* 23(3): 366–370.

Michaela G, Florian P et al, 2008. 'Long-term outcome after high tibial osteotomy', *Archives of Orthopaedic and Trauma Surgery* 128(1): 111–115.

Appendix H Results of assessment: critical appraisal

Table 38 Critical appraisal of nonrandomised comparative studies

Study	Study design	Sample size	Outcomes			Statistical methods	Duration of follow-up
			Safety	Effect.	Description		Losses to follow-up
Level III-2							
Bäthis et al 2004a	Concurrent cohorts Blinding not reported	Total: 100 patients Intervention: 50 patients Comparator: 50 patients		●	Radiological	Tests described Significance level stated	Radiological: … Losses: …
Confalonieri et al 2005 Manzotti et al 2008	Concurrent cohorts Blinding not undertaken	Total: 115 knees Intervention: 38 knees Comparator 77 knees*	●	●	Radiological Brief safety	Tests described Significance level stated	Radiological: 12 months Losses: none at 6 months/ not reported at 12 months
Chang & Yang 2006	Concurrent cohorts Evaluating radiologist blinded	Total: 71 patients/79 knees Intervention: 50 knees Comparator: 29 knees	●	●	Radiological Functional (OKS) Brief safety	Tests described Significance level stated	Radiological: 3 months Functional: 6 months Losses: …
Haaker et al 2005	Concurrent matched-pair Blinding not reported	Total: 200 patients Intervention: 100 patients Comparator: 100 patients		●	Radiological	Tests described Significance level stated	Radiological: 3 weeks Losses: …
Hart et al 2003	Concurrent cohorts Blinding not reported	Total 120 patients/120 knees Intervention: 60 knees Comparator: 60 knees	●	●	Radiological Brief safety	Tests described Significance level not stated	Radiological: Post-op Losses: Nil
Malik et al 2007	Concurrent, consecutive cohorts Blinding not reported	Total: 28 Intervention: 14 Comparator: 14		●	Radiological	Tests described Significance level not stated	Radiological: Post-op Losses: …
Matsumoto et al 2006†	Concurrent matched-pair Evaluating radiologist blinded	Total: 60 patients Intervention: 30 patients Comparator: 30 patients	●	●	Radiological Functional (KSS/KSFS/ROM) Brief safety	Tests described Significance level stated	Radiological: Post-op Functional: 2 years Losses: Nil
Molfetta & Caldo 2008	Concurrent matched-pair case control Evaluating surgeon blinded	Total: 60 patients/60 knees Intervention: 30 patients Comparator: 30 patients	●	●	Radiological Functional (KSS/ROM) Brief safety	Tests described Significance level not stated	All outcomes: 5.4 years (mean) Losses: …
Stulberg et al 2006	Consecutive, concurrent cohorts Evaluator blinded	Total: 78 knees Intervention: 38 knees Comparator: 40 knees	●	●	Radiological Functional (KSS/KSFS/ROM) Brief safety	Tests not described Significance levels not stated	Radiological: 1 & 6 months Functional: 1 & 6 months Losses:…

Table 38 continued Critical appraisal of nonrandomised comparative studies

Study	Study design	Sample size	Outcomes			Statistical methods	Duration of follow-up
			Safety	Effect.	Description		Losses to follow-up
Level III-2							
Tingart et al 2008	Concurrent cohorts Blinding not reported	Total: 1000 patients Intervention: 500 patients Comparator: 500 patients	●	●	Radiological Brief safety	Tests described Significance level stated	Radiological: … Losses: …
Zumstein et al 2006	Concurrent cohorts Evaluating radiologists blinded	Total‡: 88 patients/90 knees Intervention: 30 knees Comparator: 30 knees	●	●	Radiological Safety	Tests described Significance level stated	Radiological: … Losses: 2 patients (1 from each study group)
Level III-2/3							
Bolognesi et al 2005	Consecutive cohorts (historical/concurrent NR) Blinding not reported	Total: 98 patients/100 knees Intervention: 50/50 Comparator: 50/48	●	●	Radiological Brief safety	Tests described Significance level stated	Radiological: 6 weeks Losses: …
Jenny & Boeri 2001	Matched cohort study (historical/concurrent NR) Blinding not reported	Total: 60 patients Intervention: 30 patients Comparator: 30 patients		●	Radiological	Tests described Significance level stated	Radiological: Post-op Losses: …
Kim et al 2005	Cohort study (historical/concurrent NR) Blinding not reported	Total: 147 knees Intervention: 69 knees Comparator: 78 knees		●	Radiological	Tests described Significance level stated	Radiological: 4-12 months Losses: …
Skowronski et al 2005	Cohort study (historical/concurrent NR) Blinding not reported	Total: 200 knees Intervention: 100 knees Comparator: 100 knees		●	Radiological	Tests described Significance level stated	Radiological: Post-op Losses: …
Level III-3							
Anderson et al 2005	Matched, consecutive historical cohort Blinding not reported	Total: 167 patients Intervention: 116 Comparator: 51	●	●	Radiological Functional (ROM) Brief safety	Tests described Significance level stated	Radiological: Post-op Functional: 6 months Losses: …
Daubresse et al 2005	Cohort study with historical control Blinding not reported	Total: 100 patients/100 knees Intervention: 50 knees Comparator: 50 knees	●	●	Radiological Brief safety	Tests described Significance level stated	Radiological: 3 months Losses: …
Jenny et al 2005	Matched cohorts (historical control) Blinding not reported	Total: 470 Intervention: 235 Comparator: 235	●	●	Radiological Safety	Tests described Significance level stated	Radiological: 3 months Losses: …

Table 38 continued Critical appraisal of nonrandomised comparative studies

Study	Study design	Sample size	Outcomes			Statistical methods	Duration of follow-up
			Safety	Effect.	Description		Losses to follow-up
Level III-3							
Rosenberger et al 2008	Cohort study with historical control Blinding not reported	Total:100 patients Interventional: 50 patients Comparator: 50 patients	●	●	Radiological Brief safety	Tests described Significance level stated	Radiological: Post-op Losses: Nil
Yau et al 2008	Cohort study with historical control Blinding of evaluators	Total: 66 patients/104 knees Intervention: 33/52 Comparator: 33/52		●	Radiological	Tests described Significance level stated	Radiological: 6 weeks Losses: Nil
Zorman et al 2005	Cohort study with historical control Blinding not reported	Total: 134 knees Intervention: 72 knees Comparator: 62 knees	●	●	Radiological Brief safety	Tests described Significance level not reported	Radiological: … Losses: …

NOTES: ROM range of motion; KSS Knee Society Score; OKS Oxford Knee Score; KSFS Knee Society Functional Score; *two different approaches were used: 40 knees treated with an intramedullary approach and 37 with an extramedullary approach; † incorporating data from duplicate publication Matsumoto et al (2004); ‡ total number of patients includes 30 patients operated on using CT-navigation (excluded from analysis); … = not reported.

Appendix I Radiological, clinical and peri-hospital outcomes

Table 39 demonstrates the radiological, clinical and peri-hospital outcomes reported by the included studies. The table presents each reported outcome as it has been reported and highlights inconsistencies in the nomenclature of these outcomes.

Only radiological outcomes relevant to this report have been reported.

Table 39 Radiological, clinical and peri-hospital outcomes reported by included studies

Study	Radiological outcomes	Clinical outcomes	Peri-hospital outcomes
Level II studies			
Bejek 2007	Limb axis Positioning of femoral component Positioning of tibial component	…	…
Chauhan 2004	Standing femorotibial angle Varus/valgus alignment of femoral component Varus/valgus alignment of tibial component	…	Surgical time
Chin 2005	Mechanical axis femur versus mechanical axis tibia Mechanical axis of tibia versus tibia implant placement Mechanical axis of femur versus femur implant placement Mechanical axis versus femur component Mechanical axis versus tibia component	…	Surgical time Length of hospital stay
Church 2007	…	Embolic score (Modified Mayo Clinic grading system for echogenic emboli).	Surgical time
Decking 2005 & Decking 2007*	Mechanical axis of the leg Femoral plateau angle Tibial plateau angle	Knee Society Score WOMAC subscores (pain, stiffness, physical function)	Surgical time Tourniquet time
Ensini 2006	Mechanical axis angle Femoral component alignment Tibial component alignment	Oxford score Patellofemoral joint score Satisfaction score	Tourniquet time
Kalairajah 2006	…	Mental test score Respiratory rate Oxygen saturation Pulse rate Systolic blood pressure Diastolic blood pressure Temperature	Tourniquet time
Kalairajah 2005	…	Total blood loss Haemoglobin loss Blood loss reduction	Tourniquet time
Kim 2008	…	…	Surgical time
Macule-Beneyto 2006	Postoperative axis	…	Surgical time
Matziolis 2007	Position of entire limb Position of femoral component Position of tibial component	Knee Society Score	Surgical time
Mombert 2007	Hip-knee-ankle angle	…	…

Table 39 continued Radiological, clinical and peri-hospital outcomes reported by included studies

Study	Radiological outcomes	Clinical outcomes	Peri-hospital outcomes
Level II studies			
Spencer 2007	…	Knee Society Score WOMAC score Oxford knee score Bartlett patellar score SF-36 score (anterior knee pain, clinically significant pain, all pain, satisfaction rate)	…
Stökl 2004	Mechanical axis	Insall-Salvati index	…
Weinrauch 2006	…	…	Surgical time Length of hospital stay
Level III-1 studies			
Bäthis 2004b	Hip-knee-ankle angle Frontal femoral component angle Frontal tibial component angle	…	Surgical time
Böhling 2005	Leg axis	Hospital for Special Surgery Score	Surgical time
Kim 2007	Limb alignment (tibiofemoral angle) Mechanical axis Femoral angle Tibial angle	Knee Society Score Hospital for Special Surgery score Pain Range of movement Stairs Walking support	Surgical time Tourniquet time
Martin 2007	Varus/valgus angle (mechanical axis) Lateral distal femoral angle Medial proximal tibial angle inaccuracy	Insall knee score Range of motion Ligament balancing Anterior drawer test Feeling of instability Step test Instability during step test Anterior knee pain	Surgical time
Oberst 2008	Mechanical axis (hip-knee-ankle angle)	…	Surgical time
Song 2007	Mechanical axis angle	Modified Hospital for Special Surgery score Range of motion	…
Sparmann (2003)	Mechanical axis Femoral component Tibial component	…	…
Level III-2 studies			
Bäthis 2004a	Neutral leg axis Femoral component deviation from neutral position Tibial component deviation from neutral position	…	Surgical time
Confalonieri 2005†	Hip-knee-ankle angle Frontal femoral component angle Frontal tibial component angle	…	Surgical time
Chang 2006	Mechanical axis deviation of the leg Femoral component angle Tibial component angle	Oxford Knee Score	Surgical time
Haaker 2005	Mechanical axis deviation Femoral component angle Tibial component angle	…	Surgical time
Hart 2003	Anatomic lateral tibiofemoral angle Anatomic lateral distal femoral angle Anatomic medial proximal tibial angle	…	…

Table 39 continued Radiological, clinical and peri-hospital outcomes reported by included studies

Study	Radiological outcomes	Clinical outcomes	Peri-hospital outcomes
Level III-2 studies			
Malik 2007	Difference between femoral mechanical axis and tibial mechanical axis Difference between femoral component axis and femoral mechanical axis Difference between tibial component axis and tibial mechanical axis	…	…
Matsumoto 2006‡	Reported in Matsumoto 2004.	Knee Society Score Knee Society Functional Score Range of motion	Surgical time
Matsumoto 2004	Mechanical axis angle Femoral component angle Tibial component angle	…	…
Molfetta 2008	Lower limb alignment	Range of motion Knee Score Function Score	Surgical time
Stulberg 2006	Mechanical axis	Knee Society Score (knee score, function score) Range of motion Pain score	Tourniquet time
Tingart 2008	Mechanical axis of the leg/Hip-knee-ankle angle Frontal femoral component angle Frontal tibial component angle	…	Surgical time
Zumstein 2006	Mechanical axis of the leg Femoral component position Tibial component position	…	Surgical time
Level III-2/3 studies			
Bolognesi 2005	Femoral component alignment Tibial component alignment	…	Tourniquet time
Jenny & Boeri 2001	Mechanical femorotibial angle Coronal orientation of femoral component Coronal orientation of tibial component.	…	Surgical time
Kim 2005	Overall alignment Femoral cut Tibial cut	…	…
Skowronski 2005	Mechanical axis	…	…
Level III-3 studies			
Anderson 2005	Mechanical alignment of lower extremity Alignment of femoral component; Alignment of tibial component	…	Length of hospital stay
Daubresse 2005	Mechanical femorotibial (HKA) angle; Alignment of femoral component; Alignment of tibial component	…	…
Jenny 2005	Mechanical femorotibial angle Orientation of the femoral component Orientation of tibial component	…	Surgical time
Rosenburger 2008	Mechanical alignment Orientation of femoral component Orientation of tibial component	…	Tourniquet time
Yau 2008	Mechanical alignment of lower limb Distal lateral femoral angle Proximal medial tibial angle	…	…
Zorman 2005	Mechanical axis alignment of the limb Position of femoral implant Position of tibial implant	…	Surgical time

NOTES: * Same patient cohort. Radiological results at 3 months follow-up reported in Decking et al 2005, functional results at 12 months follow-up reported in Decking et al 2007. †Incorporates duplicate publication of Manzotti et al (2008); ‡ Incorporates duplication publication of Matsumoto et al 2004. … = not reported; WOMAC = Western Ontario and McMaster Universities Osteoarthritis index; SF-36 = short form-36; HKA = hip-knee-ankle angle

Appendix J Radiological outcomes: summary measures

Table 40 demonstrates the summary measures of central tendency and measures of variability reported by the included studies for radiological outcomes. The radiological outcomes have been categorised as follows:

- mechanical axis alignment (angle created between femoral and tibial mechanical axes)
- tibiofemoral angle (angle created between shaft of the tibia and shaft of the femur)
- femoral component alignment (reference: mechanical axis of the limb)
- femoral component alignment (reference: femoral mechanical axis)
- tibial component alignment (reference: mechanical axis of the limb), and
- tibial component alignment (reference: tibial mechanical axis).

The angles and deviations presented assume that the goal alignment angles were 0° neutral (180º) for the mechanical axis, 5° to 7° for the tibiofemoral angle, 90º for femoral component alignment and 90º for tibial component alignment. The most common measures reported included the mean deviation ± SD, satisfactory alignment (± 3° from goal alignment), mean alignment angle (angle achieved), mean angle (angle achieved presented in format of 180° ± angle achieved for mechanical and tibiofemoral angle, or 90° ± angle achieved for femoral/tibial component alignment). In cases where the goal alignment angle was different, this is stated in the table.

Table 40 Radiological outcomes

			Femoral component		Tibial component	
Study	Mechanical axis	Tibiofemoral angle	Reference: mechanical axis of leg	Reference: femoral mechanical axis	Reference: mechanical axis of leg	Reference: tibial mechanical axis
Level II studies						
Bejek 2007¶	…	Mean alignment angle ± SD (range) Satisfactory alignment (%)	Mean angle ± SD (range)§ Mean deviation§ Distribution of deviations§		Mean angle ± SD (range) § Mean deviation§ Distribution of deviations§	
Chauhan 2004	Distribution of deviations	…	Distribution of deviations	…	Distribution of deviations	…
Chin 2005	Mean alignment angle (range)	…	Mean angle (range)‖	Mean angle (range)‖	Mean angle (range)‖	Mean angle (range)‖
Decking 2005 & Decking 2007*	Distribution of deviations	…	…	Distribution of deviations	…	Distribution of deviations
Ensini 2006	Mean alignment angle ± SD Outliers outside ± 3º (%)	…	Mean alignment angle ± SD Outliers outside ± 3º (%)	…	Mean alignment angle ± SD Outliers outside ± 3º (%)	…

Table 40 continued Radiological outcomes

Study	Mechanical axis	Tibiofemoral angle	Reference: mechanical axis of leg	Reference: femoral mechanical axis	Reference: mechanical axis of leg	Reference: tibial mechanical axis
Level II studies						
Macule-Beneyto 2006	Satisfactory alignment (%) Varus/Valgus deviation (%)	…	…	…	…	…
Matziolis 2007	Mean deviation ± SD (range) Outliers outside ± 3º (n)	…	…	Mean deviation ± SD; Outliers outside ± 3º (n)	…	Mean deviation ± SD Outliers outside ±3º(n)
Mombert 2007	Mean alignment angle (95% CI) Outliers outside ± 3° (n)	…	…	…	…	…
Stökl 2004	Mean alignment angle ± SD (range)	…	…	…	…	…
Level III-1						
Bäthis 2004b	Median deviation (IQR); Satisfactory alignment (n, %); Outliers outside ± 3º (n)	…	Mean deviation (95% CI); Satisfactory alignment (n, %)	…	Mean deviation (95%CI); Satisfactory alignment (n, %)	…
Böhling 2005	Satisfactory alignment (IQR; n, %)	…	…	…	…	…
Kim 2007	Outliers outside ± 3º (n, %)	Outliers outside ± 3º (n, %)	Outliers outside ± 3º (n, %)	…	Outliers outside ± 3º (n, %)	…
Martin 2007	Mean alignment angle ± SD (range; 95% CI) Satisfactory alignment (n, %)	…	Mean deviation SD (range, 95% CI) Satisfactory alignment (n)**		Mean deviation SD (range, 95% CI) Satisfactory alignment (n)**	
Oberst 2008	Mean deviation ± SD; Mean alignment angle ± SD Satisfactory alignment (n, %)	…	…	…	…	…
Song 2007	Mean alignment angle ± SD	…	…	…	…	…
Sparmann (2003)	Distribution of deviations	…	Patient's who achieved 0° deviation§ Outliers outside ± 3° (n) §		Patient's who achieved 0° deviation§ Outliers outside ± 3° (n) §	
Level III-2 studies						
Bäthis 2004a	Mean deviation ± SD (range) Satisfactory alignment (n, %) Outliers outside ± 3º (n)	…	…	Satisfactory alignment (n, %) Mean deviation ± SD	…	Satisfactory alignment (n, %) Mean deviation ± SD

Table 40 continued Radiological outcomes

Study	Mechanical axis	Tibiofemoral angle	Reference: mechanical axis of leg	Reference: femoral mechanical axis	Reference: mechanical axis of leg	Reference: tibial mechanical axis
Level III-2 studies						
Confaloni eri 2005†	Mean angle ± SD (range)‖ Satisfactory alignment (n, %) Outliers outside ± 3º (n, %)	…	…	Mean angle ± SD (range)‖ Alignment within ± 2º (n, %)	…	Mean angle ± SD (range)‖ Alignment within ± 2º (n, %)
Chang 2006	Mean deviation ± NR (SD) Satisfactory alignment (n, %)	…	Mean angle ± NR (range; SD)‖ Satisfactory alignment (n, %)	…	Mean angle ± NR (range; SD)‖ Satisfactory alignment (n, %)	…
Haaker 2005	Mean deviation ± SD (95%CI; range) Satisfactory alignment (%)	…	…	Mean angle ± SD (95% CI; range)	…	Mean angle ± SD (95% CI; range)
Hart 2003	…	Distribution of deviations; Mean angle (range)‖	…	Mean angle (range)‖	…	Mean angle (range)‖
Malik 2007	Mean alignment angle ± SD	…	…	Mean alignment angle ± SD	…	Mean alignment angle ± SD
Matsumo to 2006‡	…	…	…	Alignment within ± 2º (n, %)	…	Alignment within ± 2º (n, %)
Matsumo to 2004	Mean angle ± SD‖ Satisfactory alignment (n)	…	…	Mean angle ± SD‖	…	Mean angle ± SD‖
Molfetta 2008	Mean deviation ± SD (range)	…	…	…	…	…
Stulberg 2006	Mean alignment angle ± SD (range) Satisfactory alignment ± 3º (n, %) Outliers outside ± 3º	…	…	…	…	…
Tingart 2008	Mean deviation ± SD (range) Median deviation (IQR) Satisfactory alignment (n, %) Outliers outside ± 3º (n)	…	Mean deviation ± SD (range) Satisfactory alignment (n, %)	…	Mean deviation ± SD (range) Satisfactory alignment (n, %)	…
Zumstein 2006	Mean alignment angle ± SD (range; variance) Satisfactory alignment (n, %)	…	Mean alignment angle ± SD (range; variance) Satisfactory alignment (n, %)	…	Mean alignment angle ± SD (range; variance) Satisfactory alignment (n, %)	…

Table 40 continued Radiological outcomes

Study	Mechanical axis	Tibiofemoral angle	Reference: mechanical axis of leg	Reference: femoral mechanical axis	Reference: mechanical axis of leg	Reference: tibial mechanical axis
Level III-2/3 studies						
Bolognesi 2005†	…	…	…	Mean angle ± SD‖ Satisfactory alignment (n, %)	…	Mean angle ± SD‖ Satisfactory alignment (n, %)
Jenny & Boeri 2001	Satisfactory alignment (n, %)	…	…	Alignment within ± 2º (n, %)	…	Alignment within ± 2º (n, %)
Kim 2005	Mean alignment angle ± SD (range) Distribution of deviation	…	…	Mean alignment angle ± SD (range)	…	Mean alignment angle ± SD (range)
Skowronski 2005	Distribution of deviation.	…	…	…	…	…
Level III-3 studies						
Anderson 2005	Mean alignment angle Satisfactory alignment (%) Alignment within ± 2º (%)	…	Mean alignment angle Alignment within ± 2º (%)	…	Mean alignment angle Alignment within ± 2º (%)	…
Daubresse 2005	Mean angle ± NR Satisfactory alignment (n, %)	…	…	Mean angle ± NR‖ Outliers within ± 2º (n, %)	…	Mean angle ± NR‖ Outliers within ± 2º (n, %)
Jenny 2005	Mean alignment angle ± SD Satisfactory alignment (n, %) Mean deviation ± SD (range)	…	…	Mean angle ± SD‖ Satisfactory alignment (n, %) Mean deviation ± SD (range)	…	Mean angle ± SD‖ Satisfactory alignment (n, %) Mean deviation ± SD (range)
Rosenburger 2008	Mean alignment angle ± SD (range) Satisfactory alignment (n, %)	…	…	Mean angle ± SD (range) Satisfactory alignment (n, %)	…	Mean angle ± SD (range) Satisfactory alignment (n, %)
Yau 2008	Mean alignment angle ± SD Outliers outside ± 3º Outliers outside ± 5º Outliers outside ± 7°	…	…	Mean angle ± SD Outliers outside ± 3º Outliers outside ± 5º	…	Mean angle ± SD Outliers outside ± 3º Outliers outside ± 5º
Zorman 2005	Mean alignment angle ± SD (range)	…	Mean deviation ± SD (range)§	Mean deviation ± SD (range)§		

NOTES: SD = standard deviation; … = not reported; IQR = interquartile range; CI = confidence interval; * Same patient cohort. Radiological results at 3 months follow-up reported in Decking et al 2005, functional results at 12 months follow-up reported in

Decking et al 2007. ¶ Optimal mean alignment angle of tibiofemoral angle was between 5° and 10° where below 5° was defined as varus and above 10° defined as valgus. ‖ Varus or valgus orientation not reported, excluded. ** Reference axis for femoral and tibial component alignment was the femoral and tibial anatomic axis, respectively, excluded. †Incorporates duplicate publication of Manzotti et al (2008); ‡ Incorporates duplication publication of Matsumoto et al 2004. NR: units not reported. § Reference axis not reported, excluded. †† Goal position of femoral component 90°, goal position of tibial component for varus knees 92°, goal position of tibial component for valgus knees 90°.

Appendix K Mechanical axis and tibiofemoral angle values

Table 41 below demonstrates the reported mechanical axis alignment and tibiofemoral angle outcome values as reported in the included studies. Not all studies included reported values for mechanical axis alignment or the tibiofemoral angle. Only studies which reported such values are presented.

Table 41 Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
Bejek 2007	…	Conventional (n = 69)	…	…	…	…	6.4° ± 3.4° (-3° to 18°)	1.0°*	60.6% (± 2.5°)*	…
		Navigated (n = 69)	…	…	…	…	6.8° ± 1.3° (3° to 10°)	0.1°*	95.4% (± 2.5°)*	…
		P value	…	…	…	…	…	…	…	…
Chauhan 2004	6 weeks	Conventional (n = 36)	…	…	20	> 3°: 10 Valgus 4°: 7 Valgus 3°: 1 Valgus 2°: 11 Valgus 1°: 0 Neutral 0°: 3 Varus 1°: 0 Varus 2°: 5 Varus 3°: 0 Varus 4°: 2 Varus 5°: 0 Varus 6°: 1	…	…	…	…
		Navigated (n = 35)	…	…	29	> 3°: 34 Valgus 4°: 3 Valgus 3°: 5 Valgus 2°: 9 Valgus 1°: 2 Neutral 0°: 11 Varus 1°: 1 Varus 2°: 0 Varus 3°: 1 Varus 4°: 1 Varus 5°: 0 Varus 6°: 1	…	…	…	…
		P value	…	…	…	0.004	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
Chin 2005	Immediate postoperative	Conventional (IM: n = 30) (EM: n = 30)	IM: Valgus 3.1° (0° to valgus 13°) EM: Valgus 2.7° (0° to valgus 6°)	…	…	…	…	…	…	…
		Navigated (n = 30)	Valgus 1.58 ° (0° to valgus 6°)	…	…	…	…	…	…	…
		P value	0.274	…	…	…	…	…	…	…
Decking 2005 & Decking 2007†	3 months	Conventional (n = 25)	Varus 2.3° ± 3.5°	…	…	± 0° to 2°: 9 ± 3° to 4°: 8 ± 5° or more: 8	…	…	…	…
		Navigated (n = 27)	Varus 1.5° ± 2.1°	…	…	± 0° to 2°: 14 ± 3° to 4°: 12 ± 5° or more: 1	…	…	…	…
		P value	…	…	…	0.0265	…	…	…	…
Ensini 2006	…	Conventional (n = 60)	Varus 0.9° ± 2.7°	…	45 (75%)	> 3°: 15 (25%)	…	…	…	…
		Navigated (n = 60)	Varus 0.8° ± 2.0°	…	53 (88.3%)	> 3°: 7 (11.7%)	…	…	…	…
		P value	NS	…	…	NS	…	…	…	…
Macule-Beneyto 2006	Immediate postoperative	Conventional (n = 84)	…	…	30%	Varus: 42.2% Valgus: 27.8%	…	…	…	…
		Navigated (n = 102)	…	…	48.1%	Varus: 26.9% Valgus: 25%	…	…	…	…
		P value	…	…	0.024	…	…	…	…	…
Matziolis 2007	…	Conventional (n = 28)	…	2.6° ± 1.7° (valgus 4.8° to varus 6.6°)	21 (75%)	> 3°: 7 (25%)	…	…	…	…
		Navigated (n = 32)	…	1.4° ± 0.8° (valgus 2.9° to varus 3.1°)	31 (96.9%)	> 3°: 1 (3.1%)	…	…	…	…
		P value	…	0.004	…	…	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
Mombert 2007	3 months	Conventional (n = 21)	Varus 1.6° ± 1.6° (95% CI: varus 7.2° to valgus 4°)	…	17 (81%)	> 3°: 4 (19%)	…	…	…	…
		Navigated (n = 21)	Varus 2.4° ± 2.4° (95% CI: varus 7° to valgus 2.2°)	…	21 (100%)	> 3°: 0 (0%)	…	…	…	…
		P value	NS	…	…	…	…	…	…	…
Stöckl 2004	…	Conventional (n = 32)	0° ± 3.19° (valgus 11° to varus 8°)	…	…	…	…	…	…	…
		Navigated (n = 32)	Varus 0.30° ± 2.35° (valgus 5° to varus 3°)	…	…	…	…	…	…	…
		P value	NS	…	…	…	…	…	…	…
Level III-1 studies										
Bäthis 2004b	…	Conventional (n = 80)	…	Median: 1° (IQR: valgus 2° to varus 2°)	62 (77.5%)	> 3°: 18 (22.5%)	…	…	…	…
		Navigated (n = 80)	…	Median: 0° (IQR: valgus 1° to varus 1°)	77 (96.3%)	> 3°: 3 (3.8%)	…	…	…	…
		P value	…	0.016	…	…	…	…	…	…
Böhling 2005	14 days	Conventional (n = 50)	…	…	23 (46%) (IQR: valgus 2° to valgus 5°)	> 3°: 27 (54%)	…	…	…	…
		Navigated (n = 50)	…	…	47 (94%) (IQR: varus 1° to valgus 2°)	> 3°: 3 (6%)	…	…	…	…
		P value	…	…	0.001	…	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-1 studies										
Kim 2007	…	Conventional (n = 100)	…	…	65 (65%)	> 3°: 35 (35%)	…	…	82 (82%)	> 3º: 18 (18%)
		Navigated (n = 100)	…	…	72 (72%)	> 3°: 28 (28%)	…	…	79 (79%)	> 3º: 21 (21%)
		P value	…	…	…	0.512	…	…	…	0.141
Martin 2007	3 months	Conventional (n = 100)	Varus 2.4° ± 2.1° (varus 9° to valgus 7°; 95% CI: 2.0° to 2.8°)	…	76 (76%)	24 (24%)	…	…	…	…
		Navigated (n = 100)	Varus 1.6° ± 1.5° (varus 6° to valgus 8°; 95% CI: 1.3° to 1.9°)	…	92 (92%)	8 (8%)	…	…	…	…
		P value	…	…	0.002	…	…	…	…	…
Oberst 2008	1 week	Conventional (34 knees)	Varus 1.3° ± 2.7°	2.5° ± 1.6°	28/35 knees (80%)	7/35 knees (20%)	…	…	…	…
		Navigated (32 knees)	Varus 0.4° ± 2.2°	1.8° ± 1.3°	32/34 knees (94.1%)	2/34 knees (5.9%)	…	…	…	…
		P value	…	< 0.05	NS	…	…	…	…	…
Song 2007	…	Conventional (n = 44)	Varus 0.8° ± 2.5°	…	…	…	…	…	…	…
		Navigated (n = 42)	Varus 0.7° ± 1.6°	…	…	…	…	…	…	…
		P value	0.815	…	…	…	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-1 studies										
Sparmann 2003	2 months	Conventional (n = 120)	…	…	104 (86.7%)	16 (13.3%) 0°: 65 1°: 15 2°: 13 3°: 11 3°-7°: 16	…	…	…	…
		Navigated (n = 120)	…	…	121 (100%)	0 (0%) 0°: 69 1°: 31 2°: 17 3°: 4	…	…	…	…
		P value	…	…	…	< 0.0001	…	…	…	…
Level III-2 studies										
Bäthis 2004a	…	Conventional (n = 50)	…	2.2° ± 2.2° (valgus 4° to varus 10°)	38 (76%)	12 (24%)	…	…	…	…
		Navigated (n = 50)	…	1.3° ± 1.1° (valgus 5° to varus 3°)	48 (96%)‡	3 (6%)‡	…	…	…	…
		P value	…	0.0117	…	…	…	…	…	…
Confalonieri 2005	6 months	Conventional IM: 40 knees EM: 37 knees	…	…	IM: 33 (82.5%) EM: 23 (62.1%)	IM > 4°: 35 (89.5%) EM > 4°: 28 (75.7%)	…	…	…	…
		Navigated (38 knees)	…	…	33 (86.8%)	> 4°: 38 (100%)	…	…	…	…
		P value	…	…	0.02	0.002	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2 studies										
Chang 2006	3 months	Conventional (n = 29)	…	3.38° ± 2.93°	17 (58.6%)	12 (41.4%)	…	…	…	…
		Navigated (n = 50)	…	1.89° ± 2.19°	39 (81.3%)	9 (18.8%)	…	…	…	…
		P value	…	0.012	…	…	…	…	…	…
Haaker 2005	3 weeks	Conventional (n = 100)	…	1.80° ± 3.01° (valgus 5° to varus 10°; 95% CI: 1.2° to 2.4°)	28%	72%	…	…	…	…
		Navigated (n = 100)	…	0.77° ± 1.91° (valgus 4° to varus 4°; 95% CI: 0.43° to 1.18°)	79%	21%	…	…	…	…
		P value	…	0.004	0.002	…	…	…	…	…
Hart 2003	…	Conventional (n = 60)	…	…	…	…	…	…	…	0° deviation: 6 (10%) 0.1° to 2.0° deviation: 36 (60%) 2.1° to 4.0° deviation: 14 (23.3%) > 4.1° deviation: 4 (6.7°)
		Navigated (n = 60)	…	…	…	…	…	…	…	0° deviation: 10 (16.7%) 0.1° to 2.0° deviation: 43 (71.7%) 2.1° to 4.0° deviation: 3 (5%) > 4.1° deviation: 4 (6.7°)

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2 studies										
		P value	…	…	…	…	…	…	…	< 0.02
Malik 2007	…	Conventional (n = 14)	Valgus 1.19° ± 2.96°	…	…	…	…	…	…	…
		Navigated (n = 14)	Varus 0.68° ± 3.87°	…	…	…	…	…	…	…
		P value	0.0445	…	…	…	…	…	…	…
Matsumoto 2004	…	Conventional (n = 30)	…	…	20 (66.7%)	10 (33.3%)	…	…	…	…
		Navigated (n = 30)	…	…	28 (93.3%)	2 (6.7%)	…	…	…	…
		P value	…	…	< 0.05	…	…	…	…	…
Molfetta 2008	…	Conventional (n = 30)	…	0.6° ± 0.8° (valgus 2° to varus 2°)	…	…	…	…	…	…
		Navigated (n = 30)	…	0.2° ± 0.6° (valgus 2° to varus 2°)	…	…	…	…	…	…
		P value	…	≤ 0.01 (95%CI: 0.02 to 0.78)	…	…	…	…	…	…
Stulberg 2006	Pain/function scores at 1 and 6 months Radiologic at 4 weeks	Conventional (n = 40)	Valgus 0.24° ± 3.5° (valgus 6° to 8°)	…	33 knees (61.1%)	21 knees (38.9%)	…	…	…	…
		Navigated (n = 38)	Varus 2.1° ± 2.7° (valgus 3° to varus 7°)	…	43 knees (69.4%)	19 knees (30.6%)	…	…	…	…
		P value	…	…	…	…	…	…	…	…
Tingart 2008	…	Conventional (n = 500)	…	2.3° ± 1.9° (valgus 8° to varus 12°) Median: 1° (IQR: valgus 1° to varus 2°)	372 (74.4%)	128 (25.6%)	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2 studies										
		Navigated (n = 500)	…	1.6° ± 1.5° (valgus 8° to varus 8°) Median: 0° (valgus 1° to varus 2°)	474 (94.8%)	26 (5.2%)	…	…	…	…
		P value	…	< 0.001 (mean ± SD)	…	…	…	…	…	…
Zumstein 2006	…	Conventional (n = 30)	Varus 0.8° ± 3.2° (valgus 9° to varus 6°) Variance: 10.6°	…	21 (72.4%)	8 (27.6%)	…	…	…	…
		Navigated (n = 30)	Varus 0.2° ± 2.5° (valgus 5° to varus 6°) Variance: 6.4°	…	24 (82.8%)	5 (17.2%)	…	…	…	…
		P value	0.520 (mean) 0.009 (variance)	…	0.34	…	…	…	…	…
Level III-2/3 studies										
Jenny & Boeri 2001	…	Conventional (n = 30)	…	…	21 (70%)	9 (30%)	…	…	…	…
		Navigated (n = 30)	…	…	25 (83.3%)	5 (16.7%)	…	…	…	…
		P value	…	…	> 0.05	…	…	…	…	…
Kim 2005	Navigated: 4 months or 1 year (if missed) Conventional: at regular yearly follow-ups	Conventional (n = 78)	Varus 0.3° ± 2.3° (8.7°)	…	73%	Deviation within ± 1°: 28% Deviation within ± 2°: 58% Deviation within ± 4°: 91% Deviation within ± 5°: 100%	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2/3 studies										
		Navigated (n = 69)	Varus 0.4° ± 1.5° (8.7°)	…	94%	Deviation within ± 1°: 57% Deviation within ± 2°: 78% Deviation within ± 4°:100% Deviation within ± 5°: 100%	…	…	…	…
		P value	0.776	…	0.001	Deviation within ± 1°: 0.001 Deviation within ± 2°: 0.013 Deviation within ± 4°: 0.015 Deviation within ± 5°: …	…	…	…	…
Skowronski 2005	…	Conventional 100 knee joints	…	…	56 (56%)	44 (44%)				
		Navigated 100 knee joints	…	…	76 (76%)	24 (24%)				
		P value	…	…	…	…				
Level III-3 studies										
Anderson 2005	2 weeks, 2, 3 and 6 months	Conventional (n = 51)	Varus 0.3°	…	84%	Within ± 2°: 71%	…	…	…	…
		Navigated (n = 116)	Varus 0.3°	…	95%	Within ± 2°: 88%	…	…	…	…
		P value	…	…	< 0.02	< 0.015	…	…	…	…
Daubresse 2005	3 months	Conventional (n = 50)	0° ± 3°	…	34 (68%)	16 (32%)	…	…	…	…
		Navigated (n = 50)	0° ± 1°	…	50 (100%)	0 (0%)	…	…	…	…
		P value	0.15	…	< 0.001	…	…	…	…	…

Table 41 continued Mechanical axis alignment and tibiofemoral angle outcome values as reported in included studies

			Mechanical axis				Tibiofemoral angle			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-3 studies										
Jenny 2005	6 and 12 weeks	Conventional (n = 235)	Varus 0.6° ± 3.4°	2.4° ± 2.4° (0° to 15°)	170 (72.3%)	35 (27.7%)	…	…	…	…
		Navigated (n = 235)	0.0° ± 2.0°	1.5° ± 1.6° (0° to 10°)	217 (92.3%)	18 (7.7%)	…	…	…	…
		P value	0.02	< 0.001	< 0.001	…	…	…	…	…
Rosenburger 2008	…	Conventional (n = 50)	Varus 1.88° ± 3.68° (valgus 6.1° to varus 10.1°)	…	…	…	…	…	…	…
		Navigated (n = 50)	Varus 0.28° ± 1.97° (valgus 3.7° to varus 6.0°)	…	…	…	…	…	…	…
		P value	0.001	…	…	…	…	…	…	…
Yau 2008	6 weeks, repeated radiographs ≥ 1 week apart (where necessary)	Conventional (n = 33)	Varus 0.3° ± 3°	…	…	> 3°: 25% > 5°: 12% > 7°: 0%	…	…	…	…
		Navigated (n = 33)	Varus 0.3° ± 3°	…	…	> 3°: 29% > 5°: 10% > 7°: 6%	…	…	…	…
		P value	0.1	…	…	> 3°: 0.356 > 5°: 0.538 > 7°: …	…	…	…	…
Zorman 2005	…	Conventional (n = 62)	Varus 2.7° ± 2.2° (0° to varus 9°) [n = 64]	…	…	…	…	…	…	…
		Navigated (n = 72)	Varus 1° ± 0.6° (0° to varus 2°) [n = 71]	…	…	…	…	…	…	…
		P value	< 0.0001	…	…	…	…	…	…	…

NOTES: SD = standard deviation; * Optimal deviation was 5° to 10°. Deviation reported is deviation from the optimal range; IM = intramedullary alignment; EM = extramedullary alignment; NS = non significant; IQR = interquartile range; CI = confidence interval; †Same patient cohort. Radiological results at 3 months follow-up reported in Decking et al 2005, functional results at 12 months follow-up reported in Decking et al 2007; ‡ Number reported in navigated group, does not add up with number reported in the navigated outliers and navigated satisfactory aligned

Appendix L Femoral and tibial component alignment values in reference to the mechanical axis of the leg

Table 42 Femoral and tibial component outcome values (in reference to the mechanical axis of the leg) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
Chauhan 2004	6 weeks	Conventional (n = 36)	…	…	33 (91.7%)	Varus 4°: 1 (2.8%) Varus 3°: 0 (0%) Varus 2°: 4 (11.1%) Varus 1°: 3 (8.3%) Neutral 0°: 9 (25%) Valgus 1°: 7 (19.4%) Valgus 2°: 6 (16.7%) Valgus 3°: 4 (11.1%) Valgus 4°: 2 (5.6%)	…	…	33 (91.7%)	Varus 4°: 3 (8.3%) Varus 3°: 2 (5.6%) Varus 2°: 11 (30.6%) Varus 1°: 5 (13.9%) Neutral 0°: 9 (25%) Valgus 1°: 5 (13.9%) Valgus 2°: 1 (2.8%)

Table 42 continued Femoral and tibial component outcome values (in reference to the mechanical axis of the leg) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
		Navigated (n = 35)	…	…	35 (100%)	Varus 4°: 0 (0%) Varus 3°: 5 (14.3%) Varus 2°: 2 (5.7%) Varus 1°: 7 (20%) Neutral 0°: 9 (25.7%) Valgus 1°: 8 (22.9%) Valgus 2°: 3 (8.6%) Valgus 3°: 1 (2.9%) Valgus 4°: 0 (0%)	…	…	35 (100%)	Varus 4°: 0 (0%) Varus 3°: 1 (2.9%) Varus 2°: 6 (17.1%) Varus 1°: 6 (17.1%) Neutral 0°: 14 (40%) Valgus 1°: 7 (20%) Valgus 2°: 1 (2.9%)
		P value	…	…	…	0.03	…	…	…	0.047
Ensini 2006	…	Conventional (n = 60)	Varus 0.3° ± 2.5°	…	51 (85%)	9 (15%)	Varus 0.6° ± 1.4°	…	58 (96.7%)	2 (3.3%)
		Navigated (n = 60)	Varus 0.4° ± 1.5°	…	100 (100%)	0 (0%)	Varus 0.4° ± 1.3°	…	59 (98.3%)	1 (1.7%)
		P value	NS	…	…	0.006	NS	…	…	NS
Level III-1 studies										
Bäthis 2004b	…	Conventional (n = 80)	…	2.1° (95% CI: 1.7° to 2.4°)	69 (86.3%)	11 (13.8%)	…	1.5° (95% CI: 1.2° to 1.7°)	75 (93.8%)	5 (6.3%)
		Navigated (n = 80)	…	1.5° (95% CI: 1.2° to 1.7°)	74 (92.5%)	6 (7.5%)	…	1.2° (95% CI: 1.0° to 1.5°)	78 (97.5%)	2 (2.5%)
		P value	…	< 0.01	…	…	…	0.20	…	…
Kim 2007	…	Conventional (n = 100)	…	…	91 (91%)	9 (9%)	…	…	93 (93%)	7 (7%)
		Navigated (n = 100)	…	…	87 (87%)	13 (13%)	…	…	84 (84%)	16 (16%)
		P value	…	…	…	0.502	…	…	…	0.188

Table 42 continued Femoral and tibial component outcome values (in reference to the mechanical axis of the leg) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2 studies										
Chang 2006	3 months	Conventional (n = 29)	…	…	24 (82.8%)	…	…	…	23 (79.3%)	…
		Navigated (n = 43)	…	…	44 (91.8%)	…	…	…	45 (93.75%)	…
		P value	…	…	…	…	…	…	…	…
Tingart 2008	…	Conventional (n = 500)	…	2.4° ± 2.0° (valgus 8° to varus 9°)	341 (68.2%)	159 (31.8%)	…	2.0° ± 1.5° (valgus 4° to varus 6°)	395 (79.0%)	105 (21.0%)
		Navigated (n = 500)	…	1.2° ± 1.1° (valgus 5° to varus 5°)	480 (96.0%)	20 (4.0%)	…	1.1° ± 1.1° (valgus 5° to varus 8°)	477 (95.4%)	23 (4.6%)
		P value	…	< 0.001	…	…	…	< 0.01	…	…
Zumstein 2006	…	Conventional (n = 30)	Varus 0.2° ± 2.7° (valgus 8° to varus 5°) Variance: 7.2°	…	23/29 (79.3%)	6/29 (20.7%)	Varus 1° ± 1.6° (valgus 4° to varus 2°) Variance: 2.6°	…	26/29 (89.7%)	3/29 (10.3%)
		Navigated (n = 30)	Varus 0.2° ± 1.5° (valgus 2° to varus 4°) Variance 2.3°	…	24/26 (92.3%)	2/26 (7.7%)	Varus 0.4° ± 1.9° (valgus 4° to varus 4°) Variance: 3.7°	…	24/26 (7.7%)	2/26 (7.7%)
		P value	0.899 (mean) 0.001(variance)	…	0.045	…	0.434 (mean) 1.0 (variance)	…	1.0	…
Level III-3 studies										
Anderson 2005	2 weeks, 2, 3 and 6 months	Conventional (n = 51)	Valgus 0.8° (valgus 5° to varus 5°)	…	…	Within ± 2°: 80%	Varus 0.5° (valgus 3° to varus 4°)	…	…	Within ± 2°: 84%
		Navigated (n = 116)	Varus 0.5° (valgus 4° to varus 6°)	…	…	Within ± 2°: 85°	Neutral 0° (valgus 4° to varus 3°)	…	…	Within ± 2°: 97%
		P value	< 0.001	…	…	< 0.02	< 0.05	…	…	< 0.005

NOTES: SD = standard deviation; NS = non significant; CI = confidence interval.

Appendix M Femoral and tibial component alignment values in reference to the femoral and tibial mechanical axes

Table 43 Femoral and tibial component outcome values (in reference to the femoral and tibial mechanical axes) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level II studies										
Decking 2005 & Decking 2007*	3 months	Conventional (n = 25)	…	…	…	± 0° to 2°: 20 ± 3° to 4°: 3 ± 5° or more: 2	…	…	…	± 0° to 2°: 20 ± 3° to 4°: 4 ± 5° or more: 1
		Navigated (n = 27)	…	…	…	± 0° to 2°: 22 ± 3° to 4°: 5 ± 5° or more: 0	…	…	…	± 0° to 2°: 26 ± 3° to 4°: 1 ± 5° or more: 0
		P value	…	…	…	0.4740	…	…	…	0.1102
Matziolis 2007	…	Conventional (n = 28)	…	2.2° ± 3.2°	…	3	…	2.0° ± 1.7°	5	…
		Navigated (n = 32)	…	1.0° ± 0.6°	…	0	…	1.4° ± 0.9°	0	…
		P value	…	0.008	…	…	…	0.646	…	…
Level III-2 studies										
Bäthis 2004a	…	Conventional (n = 50)	...	2.0° ± 1.6°	44 (88%)	6 (12%)	…	1.5° ± 1.2°	47 (94%)	3 (6%)
		Navigated (n = 50)	…	1.6°± 1.1°	47 (94%)	3 (6%)	…	1.1° ± 0.9°	49 (98%)	1 (2%)
		P value	…	> 0.05	…	…	…	> 0.05	…	…
Confalonieri 2005	6 months	Conventional IM: 40 knees EM: 37 knees	…	…	…	± 2° IM: 32 (80%) ± 2° EM: 23 (62.1%)	…	…	…	± 2° IM: 34 (85%) ± 2° EM: 26 (70.2%)
		Navigated (38 knees)	…	…	…	33 (86.8%)	…	…	…	34 (89.4%)
		P value	…	…	…	0.03(intervention > comparator (EM))	…	…	…	> 0.05

Table 43 continued Femoral and tibial component outcome values (in reference to the femoral and tibial mechanical axes) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2 studies										
Haaker 2005	3 weeks	Conventional (n = 100)	Valgus 0.49° ± 2.54° (valgus 10° to varus 4°; 95% CI: varus 0.01° to valgus 1°)	…	…	…	Varus 0.67° ± 1.56° (valgus 2° to varus 6°; 95% CI: 89.03° to 89.66°)	…	…	…
		Navigated (n = 100)	Varus 0.57° ± 1.29° (86° to 94°; 95% CI: varus 0.81° to varus 0.3°)	…	…	…	Valgus 0.17° ± 1.14° (valgus 4° to varus 4°; 95% CI: valgus 0.4° to varus 0.06°)	…	…	…
		P value	< 0.001	…	…	…	< 0.001	…	…	…
Malik 2007	…	Conventional (n = 14)	Varus 1.05° ± 1.96°	…	…	…	Valgus 0.65° ± 2.14°	…	…	…
		Navigated (n = 14)	Varus 0.69° ± 1.64°	…	…	…	Valgus 0.84° ± 1.96°	…	…	…
		P value	0.445	…	…	…	0.413	…	…	…
Matsumoto 2006	…	Conventional	…	…	…	Within ± 2°: 21 (70%)	…	…	…	Within ± 2°: 23 (76.7%)
		Navigated	…	…	…	Within ± 2°: 28 (93.3%)	…	…	…	Within ± 2°: 28 (93.3%)
		P value	…	…	…	< 0.05	…	…	…	…
Level III-2/3 studies										
Bolognesi 2005	6 weeks	Conventional (n = 50)	…	…	45 (90%)	5 (10%)	…	…	50 (100%)	0 (0%)
		Navigated (n = 50)	…	…	49 (98%)	1 (2%)	…	…	46 (92%)	4 (8%)
		P value	…	…	…	…	…	…	…	…
Jenny & Boeri 2001	…	Conventional (n = 30)	…	…	…	Within ± 2°: 25 (83%)	…	…	…	Within ± 2°: 24 (80%)
		Navigated (n = 30)	…	…	…	Within ± 2°: 28 (93%)	…	…	…	Within ± 2°: 28 (93%)
		P value	…	…	…	> 0.05	…	…	…	> 0.05

Table 43 continued Femoral and tibial component outcome values (in reference to the femoral and tibial mechanical axes) as reported in included studies

			Femoral component				Tibial component			
Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)	Satisfactory alignment*	Outliers
Level III-2/3 studies										
Kim 2005	Navigated: 4 months or 1 year (if missed); Conventional: at regular yearly follow-ups	Conventional (n = 78)	Valgus 0.8° ± 2.1° (12.4°)	…	…	…	Varus 1.0° ± 1.9° (9.1°)	…	…	…
		Navigated (n = 69)	Valgus 0.1° ± 1.0° (5.5°)	…	…	…	Varus 0.5° ± 1.3° (7.0°)	…	…	…
		P value	0.005	…	…	…	0.04	…	…	…
Level III-3 studies										
Daubresse 2005	3 months	Conventional (n = 50)	…	…	…	Within ± 2°: 37 (74%)	…	…	…	Within ± 2°: 40 (80%)
		Navigated (n = 50)	…	…	…	Within ± 2°: 45 (90%)	…	…	…	Within ± 2°: 50 (100%)
		P value	…	…	…	< 0.05	…	…	…	< 0.001
Jenny 2005	6 and 12 weeks	Conventional (n = 235)	…	1.6° ± 1.6° (0° to 9°)	181 (77%)	54 (23%)	…	1.3° ± 1.4° (0° to 6°)	194 (82.6%)	41 (17.4%)
		Navigated (n = 235)	…	1.1° ± 1.3° (0° to 7°)	209 (88.9%)	26 (11.1%)	…	1.0° ± 1.3° (0° to 6°)	209 (89%)	26 (11%)
		P value	…	< 0.001	< 0.001	…	…	0.03	< 0.05	…
Rosenburger 2008	…	Conventional (n = 50)	Varus 0.44° ± 2.69° (valgus 6.6° to varus 6.5°)	…	36 (72%)	14 (28%)	Varus 1.47° ± 1.94° (valgus 3.4° to varus 6.3°)	…	40 (80%)	10 (20%)
		Navigated (n = 50)	Varus 0.03° ± 1.53° (valgus 2.9° to varus 4.4°)	…	49 (98%)	1 (2%)	Valgus 0.01° ± 1.62° (valgus 4.1° to varus 3.0°)	…	47 (94%)	3 (6%)
		P value	< 0.001	…	…	…	0.037	…	…	…
Yau 2008	6 weeks, repeated ≥ 1 week apart (when necessary)	Conventional (n = 33)	Valgus 0.3° ± 1.7°	…	94.3%	5.7% > ± 5°: 0	0° ± 2°	90.4%	9.6%	…
		Navigated (n = 33)	Valgus 0.3° ± 1.9°	…	94.3%	5.7% > ± 5°: 1 (2%)	Varus 1° ± 2°	86.5%	13.5%	…
		P value	0.999	…	…	…	0.01	…	0.186	…

NOTES: SD = standard deviation; … = not reported; IM = intramedullary alignment; EM = extramedullary alignment; * Same patient cohort. Radiological results at 3 months follow-up reported in Decking et al 2005, functional results at 12 months follow-up reported in Decking et al 2007.

Appendix N Clinical and peri-hospital outcomes

Table 44 Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level II studies							
Chauhan 2004	6 weeks	Conventional (n = 36)	...	...	...	67 (55 to 90)	...
		Navigated (n = 35)	...	...	...	80 (60 to 120)	...
		P value	...	...	...	0.001	...
Chin 2005	Immediate postoperative	Conventional (IM: n = 30) (EM: n = 30)	...	...	...	IM: 83.5 (60.0 to 125.0) EM: 90.3 (55.0 to 145.0)	IM: 6.8 (4.0 to 20.0) EM: 7.6 (3.0 to 19.0)
		Navigated (n = 30)	...	...	...	118.2 (80.0 to 180.0)	7.4 (4.0 to 17.0)
		P value	...	...	...	0.000	0.582
Church 2007	…	Conventional (n = 12)	...	...	Modified Mayo Clinic Embolic score: 6.15 (4 to 8)	56.8 (49 to 63)	...
		Navigated (n = 14)	...	...	Modified Mayo Clinic Embolic score: 4.89 (3 to 7)	74.1 (60 to 98)	...
		P value	...	...	Modified Mayo Clinic Embolic score: 0.004	0.0003	...
Decking 2005 & Decking 2007*	3 months	Conventional (n = 25)	...	160.6 ± 22.2	WOMAC score Pain: 1.9 ± 1.7 Stiffness: 2.8 ± 1.9 Physical function: 2.3 ± 1.5	79 ± 8 Tourniquet time: 71 ± 12	...
		Navigated (n = 27)	...	167.7 ± 24.8	WOMAC score Pain: 1.9 ± 2.0 Stiffness: 2.3 ± 1.8 Physical function: 2.0 ± 1.6	92 ± 9 Tourniquet time: 88 ± 12	...
		P value	0.369	0.18	WOMAC score Pain: 0.53 Stiffness: 0.27 Physical function: 0.37	< 0.001 Tourniquet time: < 0.001	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level II studies							
Ensini 2006	…	Conventional (n = 60)	...	...	Oxford score: 18.8 ± 6.6 Patellofemoral joint score: 22.1 ± 4.5 Satisfaction score: 3.6 ± 0.6	Tourniquet time: 95.7 ± 8.1	...
		Navigated (n = 60)	...	...	Oxford score: 20.0 ± 7.2 Patellofemoral joint score: 22.9 ± 3.9 Satisfaction score: 3.6 ± 0.8	Tourniquet time: 98.4 ± 13.3	...
		P value	...	...	Oxford score: NS Patellofemoral joint score:NS Satisfaction score: NS	...	...
Kalairajah 2006	Microemboli counts recorded from time of application of tourniquet until ten minutes after it had been released. All other at day 1 and day 3.	Conventional (n = 10)	...	...	Mental test score, day 3 (mean ± SEM): 9.3 ± 0.21 Respiratory rate, day 3 (mean ± SEM): 19.0 ± 0.3 Oxygen saturation, day 3 (mean ± SEM): 96.8 ± 0.44 Pulse rate, day 3 (mean ± SEM): 81.1 ± 4.65 Systolic blood pressure, day 3 (mean ± SEM): 130.1 ± 5.76 Diastolic blood pressure day 3 (mean ± SEM): 68.4 ± 3.28 Temperature, day 3 (mean ± SEM): 37.78 ± 0.23	Tourniquet time: 73.4 ± 11.8 (62 to 95)	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level II studies							
		Navigated (n = 14)	...	...	Mental test score, day 3 (mean ± SEM): 9.57 ± 0.2 Respiratory rate, day 3 (mean ± SEM): 19.07 ± 0.2 Oxygen saturation day 3 (mean ± SEM): 97.71 ± 0.16 Pulse rate, day 3 (mean ± SEM): 89.5 ± 3.28 Systolic blood pressure, day 3 (mean ± SEM): 136.29 ± 4.75 Diastolic blood pressure, day 3 (mean ± SEM): 75.86 ± 3.5 Temperature, day 3 (mean ± SEM): 37.69 ± 0.17	Tourniquet time: 86.8 ± 10.2 (72 to 105)	...
		P value	...	...	Mental test score, day 3: 0.24 Respiratory rate, day 3: 0.88 Oxygen saturation, day 3: 0.097 Pulse rate, day 3: 0.13 Systolic blood pressure, day 3: 0.35 Diastolic blood pressure, day 3: 0.24 Temperature, day 3: 0.75	Tourniquet time: 0.001	...
Kalairajah 2005	Day 2	Conventional (n = 30)	...	...	...	Tourniquet time: 74 (40 to 132)	...
		Navigated (n = 30)	...	...	...	Tourniquet time: 89 (55 to 125)	...

Table 44 continued Clinical and peri-hospital outcomes

Study	Outcome time point	Treatment group	Clinical outcomes: Range of motion Mean ± SD (range)	Clinical outcomes: Knee society score Mean ± SD (range)	Clinical outcomes: Other outcomes Mean ± SD (range)	Peri-hospital: Surgical time (minutes) Mean ± SD (range)	Peri-hospital: Length of hospital stay (days) Mean ± SD (range)
Level II studies							
		P value	...	...	...	Tourniquet time: 0.002	...
Kim 2008	…	Conventional (210 knees)	...	...	...	[6]	...
		Navigated (210 knees)	...	...	...		...
		P value	...	...	...		...
Macule-Beneyto 2006	Immediate postoperative	Conventional (n = 84)	...	...	...	76.9	...
		Navigated (n = 102)	...	...	...	93.6	...
		P value	...	...	...	< 0.001	...
Matziolis 2007	…	Conventional (n = 28)	109° ± 7° (100 to 120°)	144 ± 29 (101 to 200)	...	94 ± 18 (60 to 125)	...
		Navigated (n = 32)	108° ± 15° (70 to 140°)	149 ± 34 (89 to 200)	...	101 ± 17 (70 to 163)	...
		P value	NS	NS	...	NS	...
Spencer 2007	6 months, 2 years	Conventional (n = 30)	...	158.9 ± 29.0	WOMAC score: 13.6 ± 13.0 Oxford score: 20.1 ± 15 Bartlett Patellar score: 23.8 ± 4.7 Clinically significant pain: 2 (7%) Anterior knee pain: 14(47%) Satisfaction: 25 (83.3%) SF-36[7]	...	...

[6] Surgical time and tourniquet presented in inappropriate groups unable to be analysed. However, surgical time and tourniquet was increased using computer navigation.
[7] No summary scores reported for the SF-36 Health Survey. However, the SF-36 scores showed no statistical difference between the computer navigation and conventional groups in seven of the eight parameters at each review.

Table 44 continued Clinical and peri-hospital outcomes

Study	Outcome time point	Treatment group	Clinical outcomes: Range of motion Mean ± SD (range)	Clinical outcomes: Knee society score Mean ± SD (range)	Clinical outcomes: Other outcomes Mean ± SD (range)	Peri-hospital: Surgical time (minutes) Mean ± SD (range)	Peri-hospital: Length of hospital stay (days) Mean ± SD (range)
Level II studies							
		Navigated (n = 30)	...	156.4 ± 33.1	WOMAC score: 23.4 ± 21.5 Oxford score: 26.7 ± 21.8 Bartlett Patellar score: 23.0 ± 5.8 Clinically significant pain: 5 (16%) Anterior knee pain: 14(44%) Satisfaction: 26 (86.7%) SF-36[2]	...	...
		P value	...	0.757	WOMAC score: 0.061 Oxford score: 0.607 Bartlett Patellar score:0.161 Clinically significant pain: 0.427 Anterior knee pain: … Satisfaction: …	...	...
Weinrauch 2006	…	Conventional (n = 31)	...	...	...	77.4	6.94
		Navigated (n = 39)	...	...	...	113.1	7.23
		P value	...	...	...	<0.001	...
Level III-1 studies							
Bäthis 2004b	…	Conventional (n = 80)	...	...	...	64 ± 11	...
		Navigated (n = 80)	...	...	...	78 ± 12	...
		P value	...	...	...	< 0.01	...
Böhling 2005	14 days	Conventional (n = 50)	...	...	Hospital for Special Surgery score: median: 83.0 (62 to 97)	80 (40 to 135)	...
		Navigated (n = 50)	...	...	Hospital for Special Surgery score: median: 82.0 (39 to 64)	93 (55 to 145)	...
		P value	...	...	Hospital for Special Surgery score: 0.883	...	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-1 studies							
Kim 2007	…	Conventional (n = 100)	126° (-1° to +127°)	Total: 94 (91 to 100) Functional: 84 (79 to 100) Pain: 46 (35 to 80)	Hospital for Special Surgery score Total: 89 (76 to 100) Functional: 17 (12 to 22) Pain: 25 (21 to 30) Postoperative pain None: 70 (70%) Mild: 30 (30%) Postoperative walking distance < 1 block: 34 (34%) 1 to 5 blocks: 33 (33%) 5 to 10 blocks: 23 (23%) Unlimited: 10 (10%) Postoperative walking support None: 83 (83%) 1 cane: 17 (17%) Stairs Normal: 30 (30%) Without support: 70 (70%)	82 (65 to 94) Tourniquet time: 44 (32 to 58)	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-1 studies							
		Navigated (n = 100)	127° (0 to +127°)	Total: 93 (89 to 100) Functional: 85 (78 to 100) Pain: 44 (35 to 50)	Hospital for Special Surgery score Total: 90 (75 to 100) Functional: 15 (11 to 22) Pain: 25 (20 to 30) Postoperative pain: None: 78 (78%) Mild: 21 (21%) Moderate: 1 (1%) Postoperative walking distance < 1 block: 34 (34%) 1 to 5 blocks: 33 (33%) 5 to 10 blocks: 23 (23%) Unlimited: 10 (10%) Postoperative walking support None: 83 (83%) 1 cane: 17 (17%) Stairs Normal: 30 (30%) Without support: 70 (70%)	97 (50 to 119) Tourniquet time: 59 (53 to 81)	...
		P value	0.939	0.456	Hospital for Special Surgery score: 0.433 Postoperative pain: … Postoperative walking distance: … Postoperative walking support: … Stairs: …	< 0.001 Tourniquet time: < 0.001	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-1 studies							
Martin 2007	3 months	Conventional (n = 100)	MBK prostheses: 100° ± 15° (70 to 140°) LPS Flex Mobile prostheses: 108° ± 14° (75 to 135°) *P* = 0.014	160 ± 22 (92 to 200)	Anterior drawer test Stable: 89 (89%) Unstable: 11 (11%) Feeling of instability No: 98 (98%) Yes: 2 (2%) Step test Positive: 74 (74%) Negative: 26 (26%) Instability during step test No: 86 (86%) Yes: 14 (14%) Anterior knee pain No: 92 (92%) Yes: 8 (8%)	68 ± 18 (37 to 135)	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-1 studies							
		Navigated (n = 100)	MBK prostheses: 102° ± 13° (80 to 130°) LPS Flex Mobile prostheses: 109° ± 15° (70 to 150°) *P* = 0.04	160 ± 24 (73 to 200)	Anterior drawer test Stable: 88 (88%) Unstable: 12 (12%) Feeling of instability No: 93 (93%) Yes: 7 (7%) Step test Positive: 83 (83%) Negative: 17 (17%) Instability during step test No: 88 (88%) Yes: 12 (12%) Anterior knee pain No: 92 (92%) Yes: 8 (8%)	88 ± 16 (51 to 146)	...
		P value	…	NS	Anterior drawer test: NS Feeling of instability: NS Step test: … Instability during step test: … Anterior knee pain: NS	<0.001	...
Oberst 2008	1 week	Conventional (34 knees)	...	...	...	...	...
		Navigated (32 knees)	...	...	...	(additional 41 mins)	...
		P value	...	...	...	<0.05	...
Song 2007	…	Conventional (n = 44)	127.3° ± 10.0°	...	Modified Hospital for Special Surgery score: 65.0 ± 5.9	...	...
		Navigated (n = 42)	128.1° ± 10.4°	...	Modified Hospital for Special Surgery score: 67.2 ± 4.3	...	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-1 studies							
		P value	0.640	...	Modified Hospital for Special Surgery score: 0.732	...	...
Level III-2 studies							
Bäthis 2004a	…	Conventional (n = 50)	...	...	...	64 ± 11	...
		Navigated (n = 50)	...	...	...	78 ± 12	...
		P value	...	...	...	...	...
Chang 2006	3 months	Conventional (n = 29)	...	...	Oxford score: 22.1 ± 2.8	92.7 ± 5.09 (66 to 134)	...
		Navigated (n = 50)	...	...	Oxford score: 20.9 ± 1.1	100.6 ± 4.33 (65 to 145)	...
		P value	...	...	Oxford score: 0.663	0.027	...
Confalonieri 2005	6 months	Conventional IM: 40 knees EM: 37 knees	...	...	...	IM: 92 (67 to 112) EM: 81 (57 to 106)	...
		Navigated (38 knees)	...	...	...	109 (82 to 133)	...
		P value	...	...	...	IM: 0.0001 EM: 0.0002	...
Haaker 2005	3 weeks	Conventional (n = 100)	...	...	...	101 ± 21 (59 to 155)	...
		Navigated (n = 100)	...	...	...	111 ± 22 (80 to 190)	...
		P value	...	...	...	NS	...
Matsumoto 2006	…	Conventional (n = 30)	105.5° (50 to 125°)	Total: 89.5 (73 to 97) Functional: 95.5 (80 to 100)	...	104	...
		Navigated (n = 30)	113.0° (85 to 130°)	Total: 84.5 (53 to 100) Functional: 94.3 (80 to 100)	...	124	...
		P value	0.011	Total: 0.16 Functional: 0.58	...	...	...

Table 44 continued Clinical and peri-hospital outcomes

			Clinical outcomes			Peri-hospital	
Study	Outcome time point	Treatment group	Range of motion Mean ± SD (range)	Knee society score Mean ± SD (range)	Other outcomes Mean ± SD (range)	Surgical time (minutes) Mean ± SD (range)	Length of hospital stay (days) Mean ± SD (range)
Level III-2 studies							
Molfetta 2008	…	Conventional (n = 30)	95.5°± 5.7° (88 to 105°)	Total: 85 ± 5.9 (70 to 91) Functional: 87 ± 4.9 (78 to 90)	...	82 (54 to 110)	...
		Navigated (n = 30)	97° ± 7.4° (85 to 110°)	Total: 84 ± 5.4 (73 to 91) Functional: 90 ± 5.3 (78 to 92)	...	98 (75 to 115)	...
		P value	>0.05	Total: >0.05 Functional: >0.05	...	...	...
Stulberg 2006	Pain/function scores at 1 and 6 months. Radiologic at 4 weeks	Conventional (n = 40)	103.2° ± 13.5° (65 to 135°)	*6 month:* Total: 84.6 ± 18.3 (23 to 100) Functional: 62 ± 15.7 (45 to 90) Pain: 39.5 ± 10.7 (20 to 50)	...	Tourniquet time: 72.9 ± 13.7 (47 to 110)	...
		Navigated (n = 38)	105.1° ± 10.2° (80 to 125°)	*6 month:* Total: 83.4 ± 18.5 (32 to 100) Functional: 64 ± 19.4 (30 to 100) Pain: 39.5 ± 10.7 (20 to 50)	...	Tourniquet time: 99.6 ± 16.3 (60 to 131)	...
		P value	...	...	...	...	...
Tingart 2008	…	Conventional (n = 500)	...	...	...	78 ± 23	...
		Navigated (n = 500)	...	...	...	86 ± 20	...
		P value	...	...	...	...	...
Zumstein 2006	…	Conventional (n = 30)	...	...	...	91 ± 21	...
		Navigated (n = 30)	...	...	...	114 ± 22	...
		P value	...	...	...	0.001	...

Table 44 continued Clinical and peri-hospital outcomes

Study	Outcome time point	Treatment group	Clinical outcomes: Range of motion Mean ± SD (range)	Clinical outcomes: Knee society score Mean ± SD (range)	Clinical outcomes: Other outcomes Mean ± SD (range)	Peri-hospital: Surgical time (minutes) Mean ± SD (range)	Peri-hospital: Length of hospital stay (days) Mean ± SD (range)
Level III-2/3 studies							
Bolognesi 2005	6 weeks	Conventional (n = 50)	...	...	...	Tourniquet time: 57	...
		Navigated (n = 50)	...	...	...	Tourniquet time: 68	...
		P value	...	...	...	0.004	...
Jenny 2001	…	Conventional (n = 30)	...	...	...	90	...
		Navigated (n = 30)	...	...	...	110	...
		P value	...	...	...	...	...
Level III-3 studies							
Anderson 2005	2 weeks, 2, 3 and 6 months	Conventional (n = 51)	...	...	...	Tourniquet time: 75	...
		Navigated (n = 116)	...	...	...	Tourniquet time: 90	...
		P value	...	...	...	< 0.001	NS
Jenny 2005	6 and 12 weeks	Conventional (n = 235)	...	...	...	99 ± 22 (56 to 165)	...
		Navigated (n = 235)	...	...	...	108 ± 22 (70 to 193)	...
		P value	...	...	...	< 0.01	...
Rosenburger 2008	…	Conventional (n = 50)	...	...	...	Tourniquet time: 91.1 ± 18.13 (62 to 126)	...
		Navigated (n = 50)	...	...	...	Tourniquet time: 104 ± 16.9 (67 to 145)	...
		P value	...	...	...	...	...

NOTES: SD = standard deviation; … = not reported; IM = intramedullary alignment; EM = extramedullary alignment; WOMAC = Western Ontario and McMaster Universities Osteoarthritis index functional score; NS = non significant; SEM = standard error of the mean; * Same patient cohort. Radiological results at 3 months follow-up reported in Decking et al 2005, functional results at 12 months follow-up reported in Decking et al 2007.

Appendix O Additional radiological outcomes

Tibiofemoral angle

Three studies were identified that reported tibiofemoral angle outcomes (Bejek 2007; Hart 2003; Kim 2007). One randomised controlled trial reported postoperative deformity, postoperative deviation and percentage of patients who had achieved satisfactory alignment (Bejek 2007). One pseudo-randomised controlled trial reported the proportion of patients who achieved satisfactory alignment and the number of outliers (Kim 2007). One nonrandomised comparative study compared the distribution of deviations between conventional and navigated groups (Hart 2003). Although none of the three studies reported an outcome time point, it is assumed that the outcomes were measured immediately postoperatively.

Postoperative deformity

Bejek (2007) reported the mean postoperative deformity of the tibiofemoral angle in 269 conventional and 269 navigated patients. The optimal postoperative tibiofemoral angle range was defined as being between 5° and 10° where values below 5° indicated varus alignment and values above 10° indicated valgus alignment. Both conventional and navigated groups reported similar mean angles and standard deviations within the target optimal range, although the conventional group reported a wider range of postoperative deformity (Table 45). However, the statistical significance of the comparison was not reported.

Deviation

The mean deviation from the target tibiofemoral angle range of 5° to 10° reported by Bejek (2007) demonstrated a much smaller deviation in favour of computer navigation. The statistical significance of this outcome was not reported.

Satisfactory alignment and outliers

Kim (2007) reported a non-significant ($P = 0.141$) difference between the number of patients who did not achieve satisfactory alignment between 100 conventional and 100 navigated patients. Eighteen percent of patients in the conventional and 21 per cent of navigated patients achieved a tibiofemoral alignment greater than 3° from the target angle.

Although Hart (2003) did not report the proportion of patients who did or did not achieve satisfactory alignment, the number and percentage of patients who achieved no deviation, 0.1° to 2.0° deviation, 2.1° to 4.0° deviation and greater than 4.1° deviation were reported. The study demonstrated a statistically significant ($P < 0.02$) better overall alignment in the navigated group compared to the conventional group. Seventy percent (42/60) and 88.4 per cent (53/60) of patients achieved postoperative deviation within 2.0° of the target angle in the conventional and navigated groups respectively.

Table 45 Radiological outcomes: tibiofemoral angle

Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean	Satisfactory alignment*	Outliers
Level II studies						
Bejek 2007	…	Conventional (n = 69)	6.4° ± 3.4° (-3° to 18°)	1.0°*	60.6% (± 2.5°)*	…
		Navigated (n = 69)	6.8° ± 1.3° (3° to 10°)	0.1°*	95.4% (± 2.5°)*	…
		P value	…	…	…	…
Level III-1 studies						
Kim 2007	…	Conventional (n = 100)	…	…	82 (82%)	> 3º: 18 (18%)
		Navigated (n = 100)	…	…	79 (79%)	> 3º: 21 (21%)
		P value	…	…	…	0.141
Level III-2 studies						
Hart 2003	…	Conventional (n = 60)	…	…	…	0° deviation: 6 (10%) 0.1° to 2.0° deviation: 36 (60%) 2.1° to 4.0° deviation: 14 (23.3%) > 4.1° deviation: 4 (6.7°)
		Navigated (n = 60)	…	…	…	0° deviation: 10 (16.7%) 0.1° to 2.0° deviation: 43 (71.7%) 2.1° to 4.0° deviation: 3 (5%) > 4.1° deviation: 4 (6.7°)
		P value	…	…	…	< 0.02

NOTES: SD = standard deviation; … = not reported; * Optimal deviation was 5° to 10°. Deviation reported is deviation from the optimal range.

Femoral component alignment (reference: mechanical axis of leg)

Five studies (one randomised controlled study, one pseudo-randomised controlled study and three nonrandomised comparative studies) were identified that reported femoral component outcomes in relation to the mechanical axis of the leg (Anderson et al; 2005; Bäthis et al 2004b; Ensini et al 2006; Tingart et al 2008; Zumstein et al 2006).

Three studies (one RCT and two nonrandomised comparative studies) reported postoperative deformity while two studies (one pseudo-randomised controlled study and one nonrandomised comparative study) compared the mean deviation between the conventional and computer-navigated total knee arthroplasty groups (Table 46).

Postoperative deformity

Only one of the three studies, Anderson et al (2005), a nonrandomised comparative study, reported a statistically significant difference in postoperative deformity between the conventional and computer-navigated total knee arthroplasty groups. Anderson et al (2005) reported a statistically significant ($P < 0.001$) improvement in favour of computer navigation. Both of the other studies reported no difference between postoperative deformity between conventional and navigated procedures (Ensini et al 2006; Zumstein et al 2006).

In each of the three studies varus alignment was the predominant deformity observed. Each of the three computer-navigated study arms reported a mean varus deformity. Similarly, two of the three conventional TKA study arms reported a mean varus deformity.

Deviation

Deviation of the femoral component from the mechanical axis of the leg in the frontal plane was defined as the deviation from the target angle of 90°, regardless of whether deviation was in the varus or valgus direction. Both studies reporting the deviation of the femoral component in relation to the mechanical axis of the leg reported a statistically significant difference in favour of computer navigation (Bäthis 2004b; Tingart 2008).

Table 46 Radiological outcomes: femoral component alignment in reference to the mechanical axis of the leg

Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)
Level II studies				
Ensini 2006	…	Conventional (n = 60)	Varus 0.3° ± 2.5°	…
		Navigated (n = 60)	Varus 0.4° ± 1.5°	…
		P value	NS	…
Level III-1 studies				
Bäthis 2004b	…	Conventional (n = 80)	…	2.1° (95% CI: 1.7° to 2.4°)
		Navigated (n = 80)	…	1.5° (95% CI: 1.2° to 1.7°)
		P value	…	< 0.01
Level III-2 studies				
Tingart 2008	…	Conventional (n = 500)	…	2.4° ± 2.0° (valgus 8° to varus 9°)
		Navigated (n = 500)	…	1.2° ± 1.1° (valgus 5° to varus 5°)
		P value	…	< 0.001
Zumstein 2006	…	Conventional (n = 30)	Varus 0.2° ± 2.7° (valgus 8° to varus 5°) Variance: 7.2°	…
		Navigated (n = 30)	Varus 0.2° ± 1.5° (valgus 2° to varus 4°) Variance 2.3°	…
		P value	0.899 (mean) 0.001 (variance)	…
Level III-3 studies				
Anderson 2005	2 weeks, 2, 3 and 6 months	Conventional (n = 51)	Valgus 0.8° (valgus 5° to varus 5°)	…
		Navigated (n = 116)	Varus 0.5° (valgus 4° to varus 6°)	…
		P value	< 0.001	…

NOTES: SD = standard deviation; … = not reported; NS = non significant; CI = confidence interval

Satisfactory alignment and outliers

Satisfactory postoperative alignment was defined as a femoral component within 3° varus or valgus of the target value (90°). Seven studies reporting this outcome were identified and considered suitable for cumulative meta-analysis.

Two randomised controlled trials reporting this outcome were identified (Chauhan et al 2004; Ensini et al 2006). Heterogeneity was low ($I^2 = 0\%$), so meta-analysis under a fixed-effects model was undertaken. This showed a statistically significant total odds ratio (non-event) of 14.56 (95% CI: 1.88 to 112.65) in favour of computer navigation ($P = 0.01$). This indicates that the odds of the femoral component achieving the defined satisfactory postoperative alignment are 14.56 times greater with computer navigation than with conventional total knee arthroplasty (Figure 12).

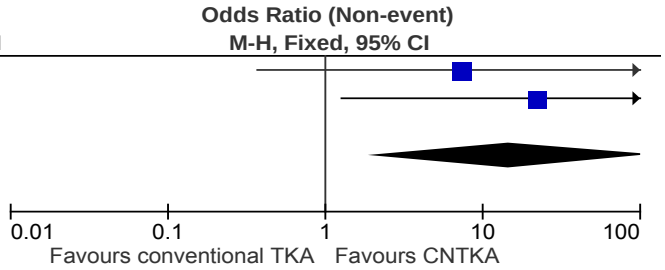
Two pseudo-randomised controlled trials were added to the meta-analysis and given the resultant increase in heterogeneity ($I^2 = 64\%$), a random effects model was employed (Bäthis et al 2004b; Kim et al 2007). This showed a non-significant ($P = 0.23$) odds ratio (non-event) of 2.23 (95% CI: 0.59 to 8.37) for satisfactory postoperative alignment with computer navigation than with conventional total knee arthroplasty (Figure 13).

A further three nonrandomised comparative studies were added to the analysis (Chang et al 2006; Tingart et al 2008; Zumstein et al 2006). Heterogeneity was high ($I^2 = 84\%$), so meta-analysis under a random effects model was undertaken. This showed a statistically significant odds ratio (non-event) of 3.20 (95%CI: 1.02 to 10.05) in favour of computer navigation ($P = 0.05$). This indicates that the odds of the femoral component achieving satisfactory postoperative alignment are 3.20 times greater with computer navigation than with conventional TKA (Figure 14). However, the inconsistency of this finding with the findings of the two other meta-analyses for the satisfactory alignment of the femoral component does not demonstrate a clear and rigorous benefit for computer navigation and may be a result of the limited data available for meta-analysis.

Figure 12 Femoral component satisfactory postoperative alignment in reference to mechanical axis of the leg (RCTs only)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Fixed, 95% CI
Chauhan 2004	33	36	35	35	52.1%	7.42 [0.37, 149.08]
Ensini 2006	51	60	60	60	47.9%	22.32 [1.27, 392.87]
Total (95% CI)		**96**		**95**	**100.0%**	**14.56 [1.88, 112.65]**
Total events	84		95			

Heterogeneity: Chi² = 0.28, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 2.57 (P = 0.01)

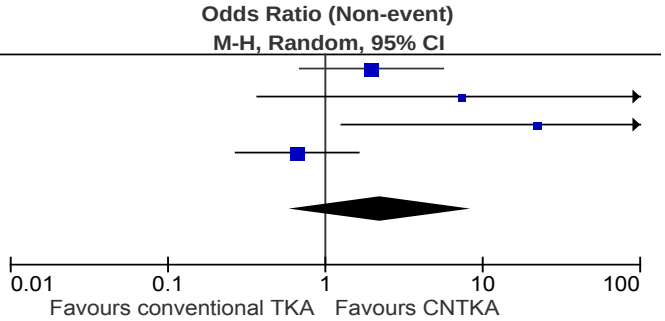


NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 13 Femoral component satisfactory postoperative alignment in reference to mechanical axis of the leg (RCTs & pseudo-RCTs)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004b	69	80	74	80	35.0%	1.97 [0.69, 5.60]
Chauhan 2004	33	36	35	35	13.5%	7.42 [0.37, 149.08]
Ensini 2006	51	60	60	60	14.4%	22.32 [1.27, 392.87]
Kim 2007	91	100	87	100	37.1%	0.66 [0.27, 1.63]
Total (95% CI)		**276**		**275**	**100.0%**	**2.23 [0.59, 8.37]**
Total events	244		256			

Heterogeneity: Tau² = 1.02; Chi² = 8.38, df = 3 (P = 0.04); I² = 64%
Test for overall effect: Z = 1.19 (P = 0.23)

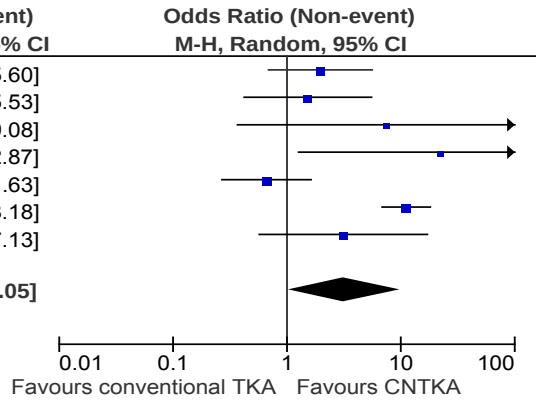


NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 14 Femoral component satisfactory postoperative alignment in reference to mechanical axis of the leg (all studies)

Study or Subgroup	Conventional TKA Events	Total	Computer navigated TKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004b	69	80	74	80	16.9%	1.97 [0.69, 5.60]
Chang 2006	24	29	44	50	15.7%	1.53 [0.42, 5.53]
Chauhan 2004	33	36	35	35	8.4%	7.42 [0.37, 149.08]
Ensini 2006	51	60	60	60	8.8%	22.32 [1.27, 392.87]
Kim 2007	91	100	87	100	17.5%	0.66 [0.27, 1.63]
Tingart 2008	341	500	480	500	19.0%	11.19 [6.89, 18.18]
Zumstein 2006	23	29	24	26	13.7%	3.13 [0.57, 17.13]
Total (95% CI)		**834**		**851**	**100.0%**	**3.20 [1.02, 10.05]**
Total events	632		804			

Heterogeneity: Tau² = 1.73; Chi² = 38.05, df = 6 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.00 (P = 0.05)



NOTES: TKA = total knee arthroplasty; SD = standard deviation; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Tibial component alignment (reference: mechanical axis of leg)

Five studies (one randomised controlled study, one pseudo-randomised controlled study and three nonrandomised comparative studies) were identified that reported tibial component outcomes in relation to the mechanical axis of the leg (Anderson et al; 2005; Bäthis et al 2004b; Ensini et al 2006; Tingart et al 2008; Zumstein et al 2006).

Three studies (one RCT and two nonrandomised comparative studies) compared the postoperative deformity while two studies (one pseudo-randomised controlled study and one nonrandomised comparative study) compared the mean deviation between the conventional and computer-navigated total knee arthroplasty groups.

Postoperative deformity

Only one of the three studies, Anderson et al (2005), a nonrandomised comparative study, reported a statistically significant difference in postoperative deformity between the conventional and computer-navigated total knee arthroplasty groups. Anderson et al (2005) reported a statistically significant ($P < 0.05$) difference between the two techniques in favour of computer navigation.

In each of the three studies varus alignment was the predominant deformity observed. Each of the three conventional total knee arthroplasty study arms reported a mean varus deformity. Similarly two of the computer-navigated study arms reported a mean varus deformity while the third reported neutral alignment.

Deviation

Deviation of the tibial component from the mechanical axis of the leg in the frontal plane was defined as the deviation from the target angle of 90°, regardless of whether deviation was in the varus or valgus direction. One of the two studies reporting the deviation of the tibial component in relation to the mechanical axis of the leg, Tingart et al (2008), a nonrandomised comparative study, reported a statistically significant ($P < 0.01$) difference in favour of computer navigation.

Table 47 Radiological outcomes: tibial component alignment in reference to the mechanical axis of the leg

Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)
Level II studies				
Ensini 2006	…	Conventional (n = 60)	Varus 0.6° ± 1.4°	…
		Navigated (n = 60)	Varus 0.4° ± 1.3°	…
		P value	NS	…
Level III-1 studies				
Bäthis 2004b	…	Conventional (n = 80)	…	1.5° (95% CI: 1.2° to 1.7°)
		Navigated (n = 80)	…	1.2° (95% CI: 1.0° to 1.5°)
		P value	…	0.20
Level III-2 studies				
Tingart 2008	…	Conventional (n = 500)	…	2.0° ± 1.5° (valgus 4° to varus 6°)
		Navigated (n = 500)	…	1.1° ± 1.1° (valgus 5° to varus 8°)
		P value	…	< 0.01
Zumstein 2006	…	Conventional (n = 30)	Varus 1° ± 1.6° (valgus 4° to varus 2°) Variance: 2.6°	…
		Navigated (n = 30)	Varus 0.4° ± 1.9° (valgus 4° to varus 4°) Variance: 3.7°	…
		P value	0.434 (mean) 1.0 (variance)	…
Level III-3 studies				
Anderson 2005	2 weeks, 2, 3 and 6 months	Conventional (n = 51)	Varus 0.5° (valgus 3° to varus 4°)	…
		Navigated (n = 116)	Neutral 0° (valgus 4° to varus 3°)	…
		P value	< 0.05	…

NOTES: SD = standard deviation; … = not reported; NS = non significant; CI = confidence interval

Satisfactory alignment and outliers

Satisfactory postoperative alignment was defined as a tibial component within 3° varus or valgus of the target value (90°). Seven studies reporting this outcome were identified and considered suitable for cumulative meta-analysis.

Two randomised controlled trials reporting this outcome were identified (Chauhan et al 2004; Ensini et al 2006). Heterogeneity was low ($I^2 = 0\%$), so meta-analysis under a fixed-effects model was undertaken. This showed a non-statistically significant ($P = 0.26$) total odds ratio (non-event) of 2.59 (95% CI: 0.49 to 13.73) and indicated that while there are slightly greater odds that the tibial component will achieve satisfactory postoperative alignment with computer navigation than with conventional total knee arthroplasty, this is not significant (Figure 15).

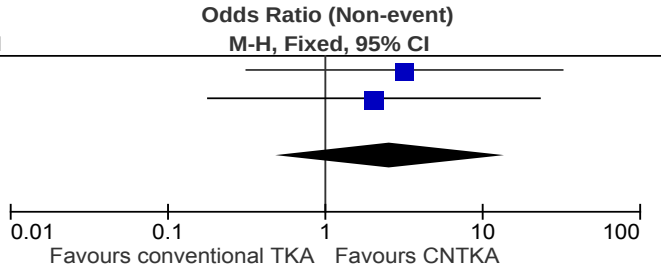
Two pseudo-randomised controlled trials were added to the meta-analysis and given the resultant increase in heterogeneity ($I^2 = 50\%$), a random effects model was employed (Bäthis et al 2004b; Kim et al 2007). This showed a smaller non-statistically significant ($P = 0.73$) odds ratio (non-event) of 1.24 (95% CI: 0.37 to 4.16) and indicated that while there are greater odds that the tibial component willl achieve satisfactory postoperative alignment with computer navigation than with conventional total knee arthroplasty, this is not significant (Figure 16).

A further three nonrandomised comparative studies were added to the analysis (Chang et al 2006; Tingart et al 2008; Zumstein et al 2006). Heterogeneity was high ($I^2 = 76\%$), so meta-analysis under a random effects model was undertaken. Again, this showed a non-statistically significant ($P = 0.19$) odds ratio (non-event) of 1.96 (95% CI: 0.72 to 5.32) and indicated that while there are slightly greater odds that the tibial component will achieve satisfactory postoperative alignment with computer navigation than with conventional total knee arthroplasty, this is not significant (Figure 17). This finding is consistent with the previous two meta-analyses and suggests no clear benefit of computer navigation.

Figure 15 Tibial component satisfactory postoperative alignment in reference to mechanical axis of the leg (RCTs only)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Fixed, 95% CI
Chauhan 2004	33	36	35	36	48.7%	3.18 [0.32, 32.14]
Ensini 2006	58	60	59	60	51.3%	2.03 [0.18, 23.06]
Total (95% CI)		**96**		**96**	**100.0%**	**2.59 [0.49, 13.73]**
Total events	91		94			

Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)

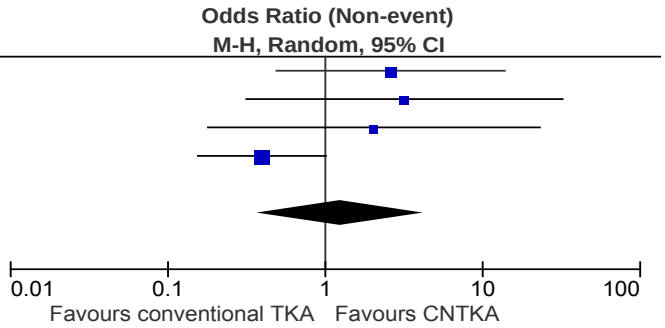


NOTES: TKA = total knee arthroplasty; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 16 Tibial component satisfactory postoperative alignment in reference to mechanical axis of the leg (RCTs & pseudo-RCTs)

Study or Subgroup	Conventional TKA Events	Total	CNTKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004a	75	80	78	80	26.0%	2.60 [0.49, 13.81]
Chauhan 2004	33	36	35	36	17.9%	3.18 [0.32, 32.14]
Ensini 2006	58	60	59	60	16.8%	2.03 [0.18, 23.06]
Kim 2007	93	100	84	100	39.2%	0.40 [0.15, 1.01]
Total (95% CI)		**276**		**276**	**100.0%**	**1.24 [0.37, 4.16]**
Total events	259		256			

Heterogeneity: Tau² = 0.75; Chi² = 6.04, df = 3 (P = 0.11); I² = 50%
Test for overall effect: Z = 0.34 (P = 0.73)

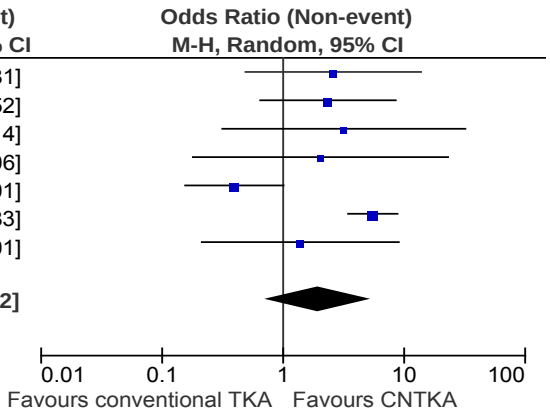


NOTES: TKA = total knee arthroplasty; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Figure 17 Tibial component satisfactory postoperative alignment in reference to mechanical axis of the leg (all studies)

Study or Subgroup	Conventional TKA Events	Total	Computer navigated TKA Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004b	75	80	78	80	13.5%	2.60 [0.49, 13.81]
Chang 2006	23	29	45	50	15.9%	2.35 [0.65, 8.52]
Chauhan 2004	33	36	35	36	10.0%	3.18 [0.32, 32.14]
Ensini 2006	58	60	59	60	9.5%	2.03 [0.18, 23.06]
Kim 2007	93	100	84	100	18.2%	0.40 [0.15, 1.01]
Tingart 2008	395	500	477	500	20.6%	5.51 [3.44, 8.83]
Zumstein 2006	26	29	24	26	12.3%	1.38 [0.21, 9.01]
Total (95% CI)		**834**		**852**	**100.0%**	**1.96 [0.72, 5.32]**
Total events	703		802			

Heterogeneity: Tau² = 1.21; Chi² = 25.37, df = 6 (P = 0.0003); I² = 76%
Test for overall effect: Z = 1.32 (P = 0.19)



NOTES: TKA = total knee arthroplasty; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty

Femoral component alignment (reference: femoral mechanical axis)

Eight studies (one randomised controlled study and seven nonrandomised comparative studies) were identified that reported femoral component outcomes in relation to the mechanical axis of the femur (Bäthis et al 2004a; Haaker et al 2005; Jenny et al 2005; Kim et al 2005; Malik et al 2007; Matziolis et al 2007; Rosenburger et al 2008; Yau et al 2008).

Five studies (all nonrandomised comparative studies) compared the postoperative deformity while three studies (one randomised comparative study and two nonrandomised comparative studies) compared the mean deviation between the conventional and computer-navigated total knee arthroplasty groups (Table 48).

Postoperative deformity

Three studies (Haaker et al 2005; Kim et al 2005; Rosenburger et al 2008), all nonrandomised comparative studies, reported statistically significant differences between the two techniques. Kim et al (2005) and Rosenburger et al (2008) both reported statistically significant differences in favour of the computer-navigated technique. In contrast, Haaker et al (2005) reported a statistically significant ($P < 0.001$) difference in favour of the conventional technique.

Unlike the femoral component alignment in reference to the mechanical axis of the leg, there was no predominant deformity. Out of the five conventional study arms, two reported varus alignment and three reported valgus alignment. Of the five computer-navigated study arms, three reported varus alignment and two reported valgus alignment.

Deviation

Deviation of the femoral component from the mechanical axis of the femur in the frontal plane was defined as the deviation from the target angle of 90°, regardless of whether deviation was in the varus or valgus direction. While all three of the studies reporting the mean deviation from the mechanical axis of the femur demonstrated a smaller deviation in the computer-navigated group, this difference was statistically significant in two studies only (Matziolis et al 2007; Jenny et al 2005).

Table 48 Radiological outcomes: femoral component alignment in reference to the femoral mechanical axis

Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)
Level II studies				
Matziolis 2007	…	Conventional (n = 28)	…	2.2° ± 3.2°
		Navigated (n = 32)	…	1.0° ± 0.6°
		P value	…	0.008
Level III-2 studies				
Bäthis 2004a	…	Conventional (n = 50)	...	2.0° ± 1.6°
		Navigated (n = 50)	…	1.6°± 1.1°
		P value	…	> 0.05 (NS)
Haaker 2005	3 weeks	Conventional (n = 100)	Valgus 0.49° ± 2.54° (valgus 10° to varus 4°; 95% CI: varus 0.01° to valgus 1.0°)	…
		Navigated (n = 100)	Varus 0.57° ± 1.29° (86° to 94°; 95% CI: varus 0.81° to varus 0.30°)	…
		P value	< 0.001	…
Malik 2007	…	Conventional (n = 14)	Varus 1.05° ± 1.96°	…
		Navigated (n = 14)	Varus 0.69° ± 1.64°	…
		P value	0.445	…
Level III-2/3 studies				
Kim 2005	4 months in navigated group (or 1 year if missed) and at regular yearly follow-ups in the conventional group	Conventional (n = 78)	Valgus 0.8° ± 2.1° (12.4°)	…
		Navigated (n = 69)	Valgus 0.1° ± 1.0° (5.5°)	…
		P value	0.005	…
Level III-3 studies				
Jenny 2005	6 and 12 weeks	Conventional (n = 235)	…	1.6° ± 1.6° (0° to 9°)
		Navigated (n = 235)	…	1.1° ± 1.3° (0° to 7°)
		P value	…	< 0.001
Rosenburger 2008	…	Conventional (n = 50)	Varus 0.44° ± 2.69° (valgus 6.6° to varus 6.5°)	…
		Navigated (n = 50)	Varus 0.03° ± 1.53° (valgus 2.9° to varus 4.4°)	…
		P value	< 0.001	…
Yau 2008	6 weeks, repeated radiographs ≥ 1 week apart (where necessary)	Conventional (n = 33)	Valgus 0.3° ± 1.7°	…
		Navigated (n = 33)	Valgus 0.3° ± 1.9°	…
		P value	0.999	…

NOTES: SD = standard deviation; … = not reported; NS = non significant; CI = confidence interval

Satisfactory alignment and outliers

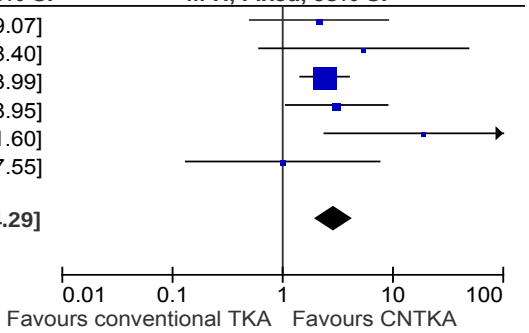
Satisfactory postoperative alignment was defined as a femoral component within 3° varus or valgus of the target value (90°). Six studies (one pseudo-randomised controlled study and five nonrandomised comparative studies) reporting this outcome were identified and considered suitable for cumulative meta-analysis (Bäthis et al 2004a; Bolognesi et al 2005; Jenny et al 2005; Martin et al 2007; Rosenburger et al 2008; Yau et al 2008). Heterogeneity was low ($I^2 = 4\%$), so meta-analysis under a fixed effects model was undertaken. This showed a statistically significant total odds ratio (non-event) of 2.87 (95% CI: 1.92 to 4.29) in favour of computer navigation ($P < 0.00001$). This indicates that the odds of the femoral component achieving satisfactory alignment are 2.87 times greater with computer navigation than with conventional total knee arthroplasty (Figure 18).

Figure 18 Femoral component satisfactory postoperative alignment in reference to mechanical axis of the femur (all studies)

	Conventional TKA		Computer navigated TKA			Odds Ratio (Non-event)	Odds Ratio (Non-event)
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
Bathis 2004a	44	50	47	50	8.7%	2.14 [0.50, 9.07]	
Bolognesi 2005	45	50	49	50	3.0%	5.44 [0.61, 48.40]	
Jenny 2005	181	235	209	235	65.7%	2.40 [1.44, 3.99]	
Martin 2007	86	100	95	100	14.1%	3.09 [1.07, 8.95]	
Rosenburger 2008	36	50	49	50	2.4%	19.06 [2.40, 151.60]	
Yau 2008	31	33	31	33	6.2%	1.00 [0.13, 7.55]	
Total (95% CI)		**518**		**518**	**100.0%**	**2.87 [1.92, 4.29]**	
Total events	423		480				

Heterogeneity: Chi² = 5.23, df = 5 (P = 0.39); I² = 4%

Test for overall effect: Z = 5.16 (P < 0.00001)



NOTES: TKA = total knee arthroplasty; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty. * Martin 2007 is the highest level evidence for this outcome (Level III-1, pseudo-RCT)

Tibial component alignment (reference: tibial mechanical axis)

Eight studies (one randomised controlled study and seven nonrandomised controlled studies) were identified that reported tibial component outcomes in relation to the mechanical axis of the tibia (Bäthis et al 2004; Haaker et al 2005; Jenny et al 2005; Kim et al 2005; Malik et al 2007; Matziolis et al 2007; Rosenburger et al 2008; Yau et al 2008).

Five studies (all nonrandomised comparative studies) compared the postoperative deformity while three studies (one randomised comparative study and two nonrandomised comparative studies) compared the mean deviation between the conventional and computer-navigated total knee arthroplasty groups (Table 49).

Postoperative deformity

Four studies (Haaker et al 2005; Kim et al 2005; Rosenburger et al 2008; Yau et al 2008), all nonrandomised comparative studies, reported statistically significant differences between the two techniques. Three of the four studies (Haaker et al 2005; Kim et al 2005; Rosenburger et al 2008) reported statistically significant differences in favour of the computer-navigated technique. In contrast, Yau et al (2008) reported a statistically significant ($P = 0.01$) difference in favour of the conventional total knee arthroplasty technique.

Unlike the tibial component alignment in reference to the mechanical axis of the leg, there was no predominant deformity. Of the five conventional study arms valgus alignment was reported once, varus alignment twice and neutral alignment once. Of the five computer-navigated study arms, valgus alignment was reported three times and varus alignment reported twice.

Deviation

Deviation of the tibial component from the mechanical axis of the tibia in the frontal plane was defined as the deviation from the target angle of 90°, regardless of whether deviation was in the varus or valgus direction. While all three of the studies reporting the mean deviation from the mechanical axis of the tibia demonstrated a small deviation in the computer navigation group, this difference was statistically significant in one study only ($P = 0.03$; Jenny et al 2005).

Table 49 Radiological outcomes: tibial component alignment in reference to the tibial mechanical axis

Study	Outcome time point	Treatment group	Postoperative deformity Mean ± SD (range)	Deviation Mean ± SD (range)
Level II studies				
Matziolis 2007	…	Conventional (n = 28)	…	2.0° ± 1.7°
		Navigated (n = 32)	…	1.4° ± 0.9°
		P value	…	0.646
Level III-2 studies				
Bäthis 2004a	…	Conventional (n = 50)	…	1.5° ± 1.2°
		Navigated (n = 50)	…	1.1° ± 0.9°
		P value	…	> 0.05 (NS)
Haaker 2005	3 weeks	Conventional (n = 100)	Varus 0.67° ± 1.56° (valgus 2° to varus 6°; 95% CI: 89.03° to 89.66°)	…
		Navigated (n = 100)	Valgus 0.17° ± 1.14° (valgus 4° to varus 4°; 95% CI: valgus 0.4° to varus 0.06°)	…
		P value	< 0.001	…
Malik 2007	…	Conventional (n = 14)	Valgus 0.65° ± 2.14°	…
		Navigated (n = 14)	Valgus 0.84° ± 1.96°	…
		P value	0.413	…
Level III-2/3 studies				
Kim 2005	4 months in navigated group (or 1 year if missed) and regular yearly follow-up in conventional group	Conventional (n = 78)	Varus 1.0° ± 1.9° (9.1°)	…
		Navigated (n = 69)	Varus 0.5° ± 1.3° (7.0°)	…
		P value	0.04	…
Level III-3 studies				
Jenny 2005	6 and 12 weeks	Conventional (n = 235)	…	1.3° ± 1.4° (0° to 6°)
		Navigated (n = 235)	…	1.0° ± 1.3° (0° to 6°)
		P value	…	0.03
Rosenburger 2008	…	Conventional (n = 50)	Varus 1.47° ± 1.94° (valgus 3.4° to varus 6.3°)	…
		Navigated (n = 50)	Valgus 0.01° ± 1.62° (valgus 4.1° to varus 3.0°)	…
		P value	0.037	…
Yau 2008	6 weeks, repeated radiographs ≥ 1 week apart (where necessary)	Conventional (n = 33)	0° ± 2°	…
		Navigated (n = 33)	Varus 1° ± 2°	…
		P value	0.01	…

NOTES: SD = standard deviation; … = not reported; NS = non significant; CI = confidence interval

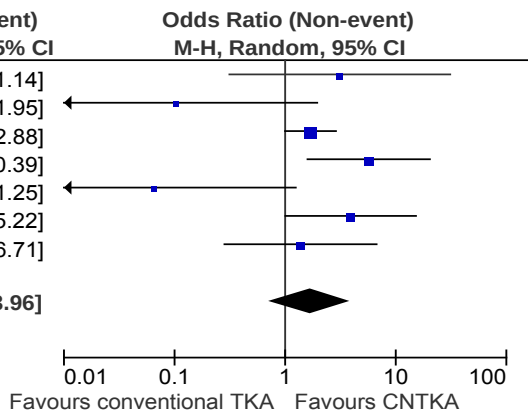
Satisfactory alignment and outliers

Satisfactory postoperative alignment was defined as a tibial component within 3° varus or valgus of the target value (90°). Six studies (one pseudo-randomised controlled study and five nonrandomised comparative studies) reporting this outcome were identified and considered suitable for cumulative meta-analysis (Bäthis et al 2004a; Bolognesi et al 2005; Jenny et al 2005; Martin et al 2007; Rosenburger et al 2008; Yau et al 2008). Heterogeneity was high (I^2 = 55%), so meta-analysis under a random effects model was undertaken. This showed a non-statistically significant total odds ratio (non-event) of 1.68 (95% CI: 0.71 to 3.96) (Figure 19).

Figure 19 Tibial component satisfactory postoperative alignment in reference to mechanical axis of the tibia (all studies)

Study or Subgroup	Conventional Events	Conventional Total	Computer navigated TKA Events	Computer navigated TKA Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Bathis 2004a	47	50	49	50	9.5%	3.13 [0.31, 31.14]
Bolognesi 2005	50	50	46	50	6.6%	0.10 [0.01, 1.95]
Jenny 2005	194	235	209	235	27.1%	1.70 [1.00, 2.88]
Martin 2007	85	100	97	100	18.1%	5.71 [1.60, 20.39]
Matziolis 2007	5	28	0	32	6.6%	0.07 [0.00, 1.25]
Rosenburger 2008	40	50	47	50	17.2%	3.92 [1.01, 15.22]
Yau 2008	3	33	4	33	14.9%	1.38 [0.28, 6.71]
Total (95% CI)		**546**		**550**	**100.0%**	**1.68 [0.71, 3.96]**
Total events	424		452			

Heterogeneity: Tau² = 0.63; Chi² = 13.48, df = 6 (P = 0.04); I² = 55%
Test for overall effect: Z = 1.19 (P = 0.23)



NOTES: TKA = total knee arthroplasty; CI = confidence interval, df = degrees of freedom; CNTKA = computer-navigated total knee arthroplasty. * Martin 2007 is the highest level evidence for this outcome (Level III-1, pseudo-RCT)

Appendix P Other clinical outcomes

Table 50 Clinical and peri-hospital outcomes: other clinical outcomes

Study	Outcome time point	Treatment group	Other outcomes Mean ± SD (range)
Level II studies			
Church 2007	Intraoperative	Conventional (n = 12)	Modified Mayo Clinic Embolic score[8]: 6.15 (4 to 8)
		Navigated (n = 14)	Modified Mayo Clinic Embolic score: 4.89 (3 to 7)
		P value	0.004
Decking 2005 & Decking 2007*	3 months; 12 months	Conventional (n = 25)	WOMAC score 3 months pain: 1.9 ± 1.7 12 months pain: 1.2 ± 1.0 3 months stiffness: 2.8 ± 1.9 12 months stiffness: 2.0 ± 1.8 3 months physical function: 2.3 ± 1.5 12 months physical function: 1.9 ± 1.8
		Navigated (n = 27)	WOMAC score 3 months pain: 1.9 ± 2.0 12 months pain: 0.9 ± 0.9 3 months stiffness: 2.3 ± 1.8 12 months stiffness: 2.0 ± 2.1 3 months physical function: 2.0 ± 1.6 12 months physical function: 1.6 ± 1.5
		P value	3 months pain: 0.53 12 months pain: 0.67 3 months stiffness: 0.27 12 months stiffness: 0.78 3 months physical function: 0.37 12 months physical function: 0.36

[8] The modified mayo Clinic grading system for echogenic emboli gives a total score of three to nine points depending on the percentage of the atrium filled (1-3 points), the duration of echogenesis (1-3 points) and the diameter of the largest particles (1-3 points).

Table 50 continued Clinical and peri-hospital outcomes: other clinical outcomes

Study	Outcome time point	Treatment group	Other outcomes Mean ± SD (range)
Level II studies			
Ensini 2006	28 months (mean)	Conventional (n = 60)	Oxford score[9]: 18.8 ± 6.6 Patellofemoral joint score[10]: 22.1 ± 4.5 Satisfaction score[11]: 3.6 ± 0.6
		Navigated (n = 60)	Oxford score: 20.0 ± 7.2 Patellofemoral joint score: 22.9 ± 3.9 Satisfaction score: 3.6 ± 0.8
		P value	Oxford score: NS Patellofemoral joint score: NS Satisfaction score: NS
Kalairajah 2006	Day 1; Day 3	Conventional (n = 10)	Mental test score, day 3 (mean ± SEM): 9.3 ± 0.21 Respiratory rate, day 3 (mean ± SEM): 19.0 ± 0.3 Oxygen saturation, day 3 (mean ± SEM): 96.8 ± 0.44 Pulse rate, day 3 (mean ± SEM): 81.1 ± 4.65 Systolic blood pressure, day 3 (mean ± SEM): 130.1 ± 5.76 Diastolic blood pressure, day 3 (mean ± SEM): 68.4 ± 3.28 Temperature, day 3 (mean ± SEM): 37.78 ± 0.23
		Navigated (n = 14)	Mental test score, day 3 (mean ± SEM): 9.57 ± 0.2 Respiratory rate, day 3 (mean ± SEM): 19.07 ± 0.2 Oxygen saturation, day 3 (mean ± SEM): 97.71 ± 0.16 Pulse rate, day 3 (mean ± SEM): 89.5 ± 3.28 Systolic blood pressure, day 3 (mean ± SEM): 136.29 ± 4.75 Diastolic blood pressure, day 3 (mean ± SEM): 75.86 ± 3.5 Temperature, day 3 (mean ± SEM): 37.69 ± 0.17
		P value	Mental test score, day 3: 0.24 Respiratory rate, day 3: 0.88 Oxygen saturation, day 3: 0.097 Pulse rate, day 3: 0.13 Systolic blood pressure, day 3: 0.35 Diastolic blood pressure, day 3: 0.24 Temperature, day 3: 0.75

[9] The Oxford score assessed patient perception of TKA with 12 question regarding pain and knee function. Score of 1-5 for each question (1 = best; 5 = worst). Range from 12 (very bad) to 60 (very good).
[10] The Patellofemoral joint score measured anterior knee pain (0-15), ability to rise and sit on a chair (0-5), ability to ascend and descend stairs (2-5) and muscle strength at the quadriceps (1-5; excluded because survey conducted over the phone). Range from 2 to 25 (very good).
[11] The Satisfaction score: 1 = dissatisfied; 2 = barely satisfied; 3 = satisfied; 4 = very satisfied.

Table 50 continued Clinical and peri-hospital outcomes: other clinical outcomes

Study	Outcome time point	Treatment group	Other outcomes Mean ± SD (range)
Level II studies			
Spencer 2007	24 months	Conventional (n = 30)	WOMAC score[12]: 13.6 ± 13.0 Oxford score: 20.1 ± 15 Bartlett Patellar score[13]: 23.8 ± 4.7 Clinically significant pain: 2 (7%) Anterior knee pain: 14 (47%) Satisfaction[14]: 25 (83.3%) SF-36[15]
		Navigated (n = 30)	WOMAC score: 23.4 ± 21.5 Oxford score: 26.7 ± 21.8 Bartlett Patellar score: 23.0 ± 5.8 Clinically significant pain: 5 (16%) Anterior knee pain: 14 (44%) Satisfaction: 26 (86.7%) SF-36
		P value	WOMAC score: 0.061 Oxford score: 0.607 Bartlett Patellar score: 0.161 Clinically significant pain: 0.427 Anterior knee pain: … Satisfaction: …
Level III-1 studies			
Böhling 2005	7 months (mean)	Conventional (n = 50)	Hospital for Special Surgery score[16]: median: 83.0 (62 to 97)
		Navigated (n = 50)	Hospital for Special Surgery score: median: 82.0 (39 to 64)
		P value	Hospital for Special Surgery score: 0.883

[12] The Western Ontario and McMaster (WOMAC) Universities osteoarthritis index ranges from 0 to 96, where a lower score indicates a better outcome.
[13] The Bartlett patellar score measures anterior knee pain, quadriceps strength, ability to rise from a chair and stair climbing ability. Score is out of 30 where a lower score indicates a better result.
[14] Locally-designed patient satisfaction questionnaire. Scale from 1 (very dissatisfied) to 5 (very dissatisfied).
[15] No summary scores reported for the SF-36 Health Survey. However, the SF-36 scores showed no statistical difference between the computer navigation and conventional groups in seven of the eight parameters at each review.
[16] The Hospital for Special Surgery score measures, pain, function, range of motion, muscle strength, flexion deformity and instability. Subtractions are made for walking aids, extension lag, and varus/valgus deformity. Maximum score 100. 85-100 (excellent), 70-84 (good), 60-69 (fair) and < 60 poor.

Table 50 continued Clinical and peri-hospital outcomes: other clinical outcomes

Study	Outcome time point	Treatment group	Other outcomes Mean ± SD (range)
Level III-1 studies			
Kim 2007	…	Conventional (n = 100)	Hospital for Special Surgery score Total: 89 (76 to 100) Functional sub-score: 17 (12 to 22) Pain sub-score: 25 (21 to 30) Postoperative pain None: 70 (70%) Mild: 30 (30%) Postoperative walking distance < 1 block: 34 (34%) 1 to 5 blocks: 33 (33%) 5 to 10 blocks: 23 (23%) Unlimited: 10 (10%) Postoperative walking support None: 83 (83%) 1 cane: 17 (17%) Stairs Normal: 30 (30%) Without support: 70 (70%)
		Navigated (n = 100)	Hospital for Special Surgery score Total: 90 (75 to 100) Functional sub-score: 15 (11 to 22) Pain sub-score: 25 (20 to 30) Postoperative pain: None: 78 (78%) Mild: 21 (21%) Moderate: 1 (1%) Postoperative walking distance < 1 block: 34 (34%) 1 to 5 blocks: 33 (33%) 5 to 10 blocks: 23 (23%) Unlimited: 10 (10%) Postoperative walking support None: 83 (83%) 1 cane: 17 (17%) Stairs Normal: 30 (30%) Without support: 70 (70%)
		P value	Hospital for Special Surgery score: 0.433 Postoperative pain: … Postoperative walking distance: … Postoperative walking support: … Stairs: …

Table 50 continued Clinical and peri-hospital outcomes: other clinical outcomes

Study	Outcome time point	Treatment group	Other outcomes Mean ± SD (range)
Level III-1 studies			
Martin 2007	3 months	Conventional (n = 100)	Anterior drawer test Stable: 89 (89%) Unstable: 11 (11%) Feeling of instability No: 98 (98%) Yes: 2 (2%) Step test Positive: 74 (74%) Negative: 26 (26%) Instability during step test No: 86 (86%) Yes: 14 (14%) Anterior knee pain No: 92 (92%) Yes: 8 (8%)
		Navigated (n = 100)	Anterior drawer test Stable: 88 (88%) Unstable: 12 (12%) Feeling of instability No: 93 (93%) Yes: 7 (7%) Step test Positive: 83 (83%) Negative: 17 (17%) Instability during step test No: 88 (88%) Yes: 12 (12%) Anterior knee pain No: 92 (92%) Yes: 8 (8%)
		P value	Anterior drawer test: NS Feeling of instability: NS Step test: … Instability during step test: … Anterior knee pain: NS
Song 2007	…	Conventional (n = 44)	Modified Hospital for Special Surgery score: 65.0 ± 5.9
		Navigated (n = 42)	Modified Hospital for Special Surgery score: 67.2 ± 4.3
		P value	0.732
Level III-2 studies			
Chang 2006	3 months	Conventional (n = 29)	Oxford score: 22.1 ± 2.8
		Navigated (n = 50)	Oxford score: 20.9 ± 1.1
		P value	0.663

NOTES: SD = standard deviation; * 3-month data from Decking et al (2005), 12-month data from Decking et al (2007). Same patient cohort; NS = non significant; SEM = standard error of the mean; WOMAC = Western Ontario and McMaster Universities osteoarthritis index; SF-36 = short form – 36; … = not reported

Appendix Q Unicompartmental knee arthroplasty

Introduction

The literature search identified studies which compared both navigated and conventional total and unicompartmental knee arthroplasty. Four studies, including two case-control studies and two comparative studies reported results in patients undergoing unicompartmental knee arthroplasty.

Effectiveness

Relevant outcomes for computer-navigated unicompartmental knee arthroplasty were reported in two case-control studies (Jenny & Boeri 2003(a); Jenny & Boeri 2003(b)) and two concurrent comparative studies (Cossey & Spriggins 2005; Jenny 2005).

Comparable coronal plane alignment outcomes were reported at three months postoperatively by three of the studies (Jenny & Boeri 2003(a); Jenny & Boeri 2003(b); Jenny 2005), while Cossey and Spriggins (2005) utilised Kennedy's Protocol for assessment of the postoperative mechanical axis.

The femorotibial axis, orientation of femoral component angle and orientation of tibial component angle after computer-navigated unicompartmental knee arthroplasty in 80 patients was compared to that of another 80 patients undergoing conventional unicompartmental knee arthroplasty (Table 51, Table 52 and Table 53). Only one of the three studies reporting these outcomes statistically compared the results of the two groups (Jenny & Boeri 2003a).

Additionally, the number of prostheses determined to be in the desired angular range postoperatively was reported for each outcome. This desired angular range was zero to five degrees for the femorotibial mechanical angle, and $90° \pm 2°$ for the femoral and tibial components.

In mean measurements of all the reported anatomical angles, prostheses implanted utilising computer navigation appeared to result in similar postoperative coronal plane angles to those implanted using conventional techniques. The differences between the two groups did not reach statistical significance in the one study that applied statistical tests. However, the measures of variability around the mean angles (standard deviation and range) were notably larger in the conventional UKA groups, indicating that CNUKA resulted in consistently greater accuracy of prosthesis placement and resultant joint angles across the CNUKA population as a whole.

This is supported by the number of prostheses found to be in the desired angular range postoperatively. There were substantially more CNUKA patients with prostheses in the desired range than conventional UKA patients. This result was significant for each outcome measure in the one study reporting statistical testing.

Table 51 Femorotibial mechanical axis

	Jenny and Boeri 2003a n = 30/30	Jenny and Boeri 2003b n = 20/40	Jenny 2005 n = 30/30
Femorotibial mechanical angle (mean ± SD) [range]*			
CNUKA	1.5 ± 2.2 [-4-5]	1 ± 2 [-4-5]	1.5 ± 2.2 [-4-5]
Conventional UKA	0.7 ± 3.9 [-10-10]	1 ± 4 [-10-10]	0.9 ± 4.0 [-6-7]
P value	*0.42*	…	…
Femorotibial mechanical angle (number of prostheses in desired angular range†)			
CNUKA	26/30 (87%)	18/20 (90%)	25/30 (83%)
Conventional UKA	20/30 (67%)	27/40 (68%)	20/30 (67%)
P value	*<0.05*	…	…

NOTES: SD = standard deviation; CNUKA computer-navigated unicompartmental knee arthroplasty; UKA unicompartmental knee arthroplasty; *normal femorotibial angle = 0°; … not reported; †desired angular range 0-5°

Table 52 Femoral component angle – coronal plane alignment

	Jenny & Boeri 2003a n = 30/30	Jenny & Boeri 2003b n = 20/40	Jenny 2005 n = 30/30
Orientation of femoral component (mean ± SD) [range]*			
CNUKA	89.1 ± 1.3 [85-90]	89 ± 1 [85-90]	89.1 ± 1.4 [85-92]
Conventional UKA	88.1 ± 2.8 [80-94]	88 ± 3 [80-94]	88.0 ± 2.9 [82-95]
P value	*0.13*	…	…
Orientation of femoral component (number of prostheses in desired angular range†)			
CNUKA	27/30 (90%)	16/20 (80%)	26/30 (87%)
Conventional UKA	19/30 (63%)	20/40 (50%)	21/30 (70%)
P value	*<0.02*	…	…

NOTES: SD = standard deviation; CNUKA computer-navigated unicompartmental knee arthroplasty; UKA unicompartmental knee arthroplasty;*normal femoral component angle = 90°; … not reported; †desired angular range 90±2°

Table 53 Tibial component angle – coronal plane alignment

	Jenny & Boeri 2003a n = 30/30	Jenny & Boeri 2003b n = 20/40	Jenny 2005 n = 30/30
Orientation of tibial component (mean ± SD) [range]*			
CNUKA	89.2 ± 1.2 [87-90]	89 ± 1 [87-90]	89.1 ± 4 [86-92]
Conventional UKA	88.1 ± 2.5 [80-94]	88 ± 3 [80-94]	88.2 ± 2.6 [79-96]
P value	*0.07*	…	…
Orientation of tibial component (number of prostheses in desired angular range†)			
CNUKA	26/30 (87%)	18/20 (90%)	28/30 (93%)
Conventional UKA	19/30 (63%)	20/40 (50%)	6/30 (20%)
P value	*<0.05*	…	…

NOTES: SD = standard deviation; CNUKA computer-navigated unicompartmental knee arthroplasty; UKA unicompartmental knee arthroplasty;*normal tibial component angle = 90°; … not reported; †desired angular range 90±2°

These three studies also reported on the number of satisfactorily or optimally implanted prostheses, although a precise definition of these terms was not provided. The number of satisfactorily or optimally implanted prostheses was higher in the CNUKA groups than the conventional groups in every study. This was tested and reported as statistically significant by Jenny and Boeri (2003a) with 18/30 (60%) and 6/30 (20%) satisfactorily implanted prostheses in the CNUKA and conventional groups respectively ($P < 0.01$).

Utilising Kennedy's Protocol to analyse postoperative zone alignment demonstrated that CNUKA resulted in more joints with desired zone alignment than conventional UKA (Table 54). The authors stated that ' analysis…showed a *P* value of less than 0.05 when comparing the computer-assisted navigation group with the non-navigated group', but did not report which zone/s this was for.

Table 54 Mechanical axis – Kennedy's Protocol

	Zone alignment results* (number of postoperative knees)		
	Zone 2	Zone C	Zone 3
CNUKA	10/15 (67%)	5/15 (33%)	0/15 (0%)
Conventional UKA	7/15 (47%)	4/15 (27%)	4/15 (27%)
P value	…	…	…

NOTES: CNUKA computer-navigated unicompartmental knee arthroplasty; UKA unicompartmental knee arthroplasty; *alignment in zones 2 & C results in a more 'biomechanically friendly' environment, reducing the wear rate of the prosthesis. Alignment in zone 3 indicates over-correction.

Safety

Three of the four studies reported some safety outcomes. Jenny and Boeri (2003a) and Jenny and Boeri (2003b) reported technical outcomes only, stating that no complication occurred in relation to the navigation system and that no conversion to conventional technique was required. Cossey and Spriggins (2005) reported adverse events, with two deep vein thrombi below the knee and one superficial wound infection amongst the 15 patients in the CNUKA group. Of the 15 patients in the conventional UKA group, there was one deep vein thrombosis and one superficial wound infection reported.

Summary

The limited evidence available on unicompartmental knee arthroplasty using computer navigation suggests that the technique does not provide a clear benefit in terms of postoperative overall limb or component alignment. The studies presented, however, demonstrate that a greater proportion of patients achieved alignment within the desired range using computer navigation for both the overall and individual component alignment. In terms of safety, the limited evidence did not allow for an accurate comparison between the two techniques.

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