

Washington State Health Care Authority, HTA Program**Key Questions****Knee Joint Replacement or Knee Arthroplasty****Introduction**

HTA has selected Knee Joint Replacement/Knee Arthroplasty to undergo a health technology assessment where an independent vendor will systematically review the evidence available on the safety, efficacy, and cost-effectiveness. HTA posted the topic and gathered public input on all available evidence. HTA published the Draft Key Questions to gather public input about the key questions and any additional evidence to be considered in the evidence review. Key questions guide the development of the evidence report. HTA seeks to identify the appropriate topics (e.g. population, indications, comparators, outcomes, policy considerations) to address the statutory elements of evidence on safety, efficacy, and cost effectiveness relevant to coverage determinations.

Knee joint replacement or knee arthroplasty is surgery to replace a diseased knee joint with an artificial joint. It is an elective procedure, generally indicated for patients with significant loss of cartilage to bone, experiencing pain and limited range of motion. Questions primarily center on when the procedure is most appropriate and for whom, and whether certain types of procedures produce better results.

Draft Key Questions

When used in adult patients:

1. What is the evidence of efficacy and effectiveness of using computer-navigated TKA compared with conventional TKA? Outcomes to consider:
 - a. Primary: Clinical outcomes, Revision rates
 - b. Secondary: Radiographic, other reported outcomes
2. What is the evidence of efficacy and effectiveness of partial knee arthroplasty compared with conventional TKA? Include consideration of:
 - a. Unicompartmental
 - b. Bicompartmental
 - c. Bi-unicompartmental
3. What is the evidence of the safety of computer-navigated TKA or partial knee arthroplasty compared with standard total knee arthroplasty? Including consideration of:
 - a. Adverse events type and frequency (mortality, major morbidity, other)
 - b. Deep venous thrombosis
4. What is the evidence that TKA or partial knee arthroplasty has differential efficacy or safety issues in sub populations? Including consideration of:
 - a. Gender
 - b. Age
 - c. BMI
 - d. Diagnosis, including osteoarthritis versus rheumatoid arthritis
 - e. Psychological or psychosocial co-morbidities

- f. Other patient characteristics or evidence based patient selection criteria
 - g. Provider type, setting or other provider characteristics
 - h. Payor or beneficiary type, including worker's compensation, Medicaid, state employees
 - i. Bilateral TKA (simultaneous or staged)
5. What is the evidence of cost implications and cost-effectiveness of computer-navigated TKA or partial knee arthroplasty compared with knee joint arthroplasty?

Policy Context:

Knee joint replacement or knee arthroplasty is surgery to replace a diseased knee joint with an artificial joint. It is an elective procedure, generally indicated for patients with significant loss of cartilage to bone, experiencing pain and limited range of motion. Questions primarily center on when the procedure is most appropriate and for whom, and whether certain types of procedures produce better results.

Important questions remain about appropriate patient selection; timing; and clinical indications for knee replacement, as well as information on the use of different surgical approaches; prosthesis types and materials; and its safety and effectiveness and cost effectiveness compared to alternatives.

Public Comment and Response

HTA received one timely public comment and input from the technology assessment center. HTA reviewed the public comments, consulted technology assessment centers, and gathered follow up information from the nominating agencies. A summary of the input and modification to key questions is below.

Overall topic: Primary total knee arthroplasty is a well accepted technology and a preliminary review of evidence suggests that several quality analysis can be relied upon to describe the primary procedure, its indications, and its efficacy and safety profile; thus eliminating the proposed first key question and placing such information in the context section. Remaining Key questions were re-organized to account for this and narrow the focus to comparisons of different surgical approaches and prosthesis.

One commenter requested changes to the categorization of partial knee arthroplasty to match CPT coding; and categorization of surgical approach into minimally invasive and standard approach knee arthroplasty.

The key question categories were not altered to match CPT coding. Rather, the original categorization based on the preliminary literature search is used. However, the suggested categorizations and reasoning are included in materials for the evidence vendor to review when describing the technology or findings as appropriate, and a cross reference chart can be added if deemed necessary.



Paul A. Manner, M.D.

**Associate Professor
University of Washington School of Medicine
Seattle, Washington**

Specialty: Hip & Knee

College: B.Sc. Tufts University
Medical School: M.D. McGill University Faculty of Medicine
Internship: St. Luke's/Roosevelt Hospital Center, New York, NY, 1991-1993
Residency: McGill University, Montreal, QC, 1993-1996
Fellowship: Shriners Fellow, Orthopedic Research, Joint Diseases Laboratory, Shriners Hospital for Children, Montreal Unit 1996-1997.
Fellowship - Adult Reconstruction and Joint Replacement, University of Pittsburgh Medical Center, Pittsburgh, PA 1997-1998

Honors: Resident Teaching Award, Department of Orthopedic Surgery
The George Washington University Washington, DC, 2002-2003

Fellow, Leadership Fellows Program American Academy of Orthopedic Surgeons, 2005-2006

Board Certification: Board Certified

Memberships:

- Leadership Fellows Program, American Academy of Orthopedic Surgeons, 2005-2006
- American Association of Hip and Knee Surgeons
- Fellow of the Royal College of Surgeons - Canada
- Fellow American Academy of Orthopedic Surgeons
- Orthopedic Research Society
- Washington Orthopedic Society
- Canadian Orthopedic Association

Common Surgeries

Performed:

- Minimally invasive total hip replacement
- Total hip replacement
- Hemiresurfacing arthroplasty of the hip ("partial hip replacement")
- Open reduction internal fixation ("repair") of hip fractures
- Hemiarthroplasty for hip fracture
- Knee arthroscopy
- Knee osteotomy
- Minimally-invasive partial knee replacement (unicompartmental)
- Total knee replacement

Common Diagnoses Treated:

- Osteoarthritis (hip/knee)
- Rheumatoid arthritis (hip/knee)
- Avascular necrosis (osteonecrosis of the femoral head)
- Developmental dysplasia of the hip
- Metastatic disease to the hip/pelvis/knee
- Hip fracture
- Meniscus tears in the knee

Philosophy of care/General Information:

Many patients express interest in minimally invasive approaches to hip and knee surgery. I believe that this type of surgery, though technically challenging, offers many benefits to the patient, including less tissue injury, less post-operative pain, faster rehabilitation, and a shorter hospital stay.

My major interests relate to the care and treatment of osteoarthritis. My aim is to conduct clinical research that has a significant impact on the field while raising the clinical standards for optimal patient care. I want to reduce morbidity and improve outcomes in these patients not only through research but also by establishing a model of care that can be universally applied, easily adapted to both academic and community groups and led by outstanding trainees who can influence care throughout the world.

Scheduled Public Comments:

No PowerPoint Slides –

1. Dr. Bert Thomas and Tim Frandsen, Smith & Nephew (5 minutes)

With PowerPoint Slides –

1. N/A

Total Scheduled Public Comments = 5 minutes

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of \$10,000	X	
2.	Equity interests such as stocks, stock options or other ownership interests	X	
3.	Status or position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding		X
6.	Any other relationship, including travel arrangements	X	

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

I am an employee of Smith&Nephew from whom I receive a salary for my work as the Global Director of Surgical Navigation. As part of my employment with Smith&Nephew, my travel expenses are reimbursed when traveling to conduct work-related business, and I may also receive discretionary stock options from time to time.

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		

7. If yes, Provide Name and Funding Sources: _____

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X

10/14/2010

Tim Frandsen, PhD, MBA

Signature

Date

Print Name

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712



**Washington State
Health Care Authority**

Disclosure

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Potential Conflict Type		Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of \$10,000	x	
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5.	Research funding		x
6.	Any other relationship, including travel arrangements	x	

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

____ Consultant for Smith&Nephew _____

____ Travel Arrangements made by Smith&Nephew _____

Potential Conflict Type		Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		x

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X

Signature

Oct. 14, 2010
Date

Bert J. Thomas, M.D.
Print Name

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712



Agency Medical Director Comments

Total Knee Arthroplasty
October 22, 2010



TKA Treatment: Background

- TKA is an effective treatment for knee pain with loss of function caused by osteoarthritis (OA) or rheumatoid arthritis (RA) when other treatments have failed
- Evolution of conventional TKA to include computer navigation may improve on conventional techniques
- Less invasive procedures to replace only 1 or 2 (of 3) compartments may be alternatives to TKA



Agency Concerns

Safety Concerns (Low)

TKA has proven relatively safe and cost-effective.

Efficacy Concerns (Low)

Unclear benefit from new alternative procedures. Newer procedures potentially lead to broader usage.

Cost Concerns (Medium)

- TKA is a high cost procedure for knee OA.
- Any advances to TKA that increase cost should be demonstrated to be cost-effective in addition to being at least equally safe and effective.
- Australian HTA estimates CN-TKA adds \$1500.
- The number of procedures done each year is increasing (average of 12% increase per year for last 3 years, agency total).

Coverage Overview

Agency	TKA Coverage	Policy or Guideline	Unicompar tmental Coverage	Bicompartm ental Coverage	Computer Navigation Code
UMP	Yes	No	Yes	Yes	Not Covered**
L&I	Yes-UR/PA	Yes	Yes-UR/PA	No	Covered*
DSHS	Yes	No	Yes	Yes	Not Covered

*Add on CPT code is payable, \$234

**May be paid when UMP is secondary payer and primary covers

L&I Knee Guideline

Procedure	Conservative Care	Clinical Findings		
		Subjective	Objective	Imaging
<p>Knee Joint Replacement</p> <p>If only 1 compartment is affected, a unicompartmental or partial replacement is indicated</p> <p>If 2 of the 3 compartments are affected, a total joint replacement is indicated.</p>	<p>Medications</p> <p>OR</p> <p>Visco supplementation injections</p> <p>OR</p> <p>Steroid injection</p> <p>AND</p>	<p>Limited range of motion</p> <p>OR</p> <p>Night time joint pain</p> <p>OR</p> <p>No pain relief with conservative care</p>	<p>Over 50 years of age</p> <p>AND</p> <p>Body Mass Index of less than 35</p> <p>AND</p>	<p>Osteoarthritis on:</p> <p>Standing x-ray</p> <p>OR</p> <p>Arthroscopy</p>

Agency Utilization

Age	2006	2007	2008	2009	4 Yr Total
>=66	376	352	418	497	1649
51-65	595	640	747	853	2868
36-50	194	192	244	267	938
19-35	11	9	13	20	53
0-18	2	2	2	3	10
All	1178	1195	1424	1640	5518
Total Cost (million)	\$14.4	\$17.0	\$20.8	\$23.9	\$80.6

Agency Costs* 2009

Agency	Average/patient	Total
UMP	\$14,723	\$10,703,617
L&I	\$20,087	\$8,798,222
DSHS	\$11,505	\$4,410,825

* All costs are based on All Services, Day of Surgery figures. Patients may have had more than one procedure of the type specified but are counted only once per year.

Evidence: Safety and Efficacy

Treatment	Comparator	Safety	Efficacy
CN-TKA	Conv-TKA	Possibly lower risk of embolism, longer surgery time	At least equal
Uni-compartmental	Conv-TKA	About equal	About equal
Bi-compartmental	UKA	Very limited evidence	Very limited evidence

Evidence: Differential efficacy

Treatment	Factors
Conv-TKA:	Equivalent effectiveness including: age, sex, obesity, other co-morbidities, hospital or surgeon volume.
Uni-compartmental	Younger age associated with higher revision rate (same as TKA), otherwise no consistent effects.
Staged vs simultaneous	No difference in pain, function or revision. <u>Increase in mortality for simultaneous TKA</u>

Cost-effectiveness

Treatment	Comparator	C/E
CN-TKA	Conv-TKA	Evidence is insufficient to show CN- cost-effectiveness
Uni-compartmental	Conv-TKA	Evidence suggests Uni- may be as cost-effective as TKA
Bi-compartmental	UKA	No evidence



AMDG Recommendations

When TKA or UKA are medically necessary-

Coverage with criteria:

- TKA- covered for patients with 2 or 3 compartments when conservative treatment has failed.
- Uni-compartmental- for patients with only 1 diseased compartment and who have failed conservative treatment.
- Per FDA approved indications and contraindications
- No age limitation
- No BMI limitation
- CN-TKA- not covered due to: limited data on cost-effectiveness, and evidence that CN-TKA reduces risk of unsatisfactory alignment, but alignment is not linked to functional outcomes.
- Bi-compartmental- not covered due to limited evidence base.

Knee Arthroplasty Technology Assessment

Spectrum Research, Inc.

Joseph R. Dettori, PhD, MPH
Erika Ecker, BS
Daniel Norvell, PhD
Robin Hashimoto, PhD
Nora B. Henrikson, PhD, MPH
Lisa Kercher, PhD, MPH,
Kara McMullen, MPH
Annie Raich, MS, MPH

**Health Technology Clinical Committee Meeting
WS Health Technology Assessment Program
Seattle, Washington**

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Scope of Report

**This report evaluates relevant
published research describing the
use of knee arthroplasty**

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Background

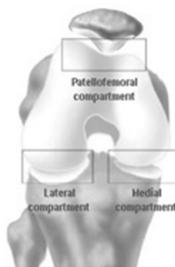
- Conventional total knee arthroplasty (CONV-TKA) is an effective treatment for end stage knee arthritis
- Overtime, technologies to improve CONV-TKA have been introduced
- Whether these technologies to improve CONV-TKA are efficacious or cost-effective is uncertain
- Two of these technologies, computer-navigated total knee arthroplasty (CN-TKA) and partial knee arthroplasty are the subject of this HTA

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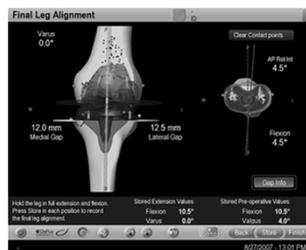


Background

CONV-TKA



CN-TKA

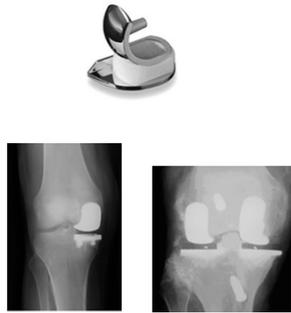


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Partial Knee Arthroplasty

Unicompartmental



Bicompartmental



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Indications

For CN-TKA – similar to CONV-TKA

- Moderate to severe arthritic knee pain that has not adequately responded to a prolonged course of nonsurgical treatment, **and**
- Radiological evidence of joint damage, **and**
- Lower quality of life due to clinically significant limitations in function

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Indications

For partial knee arthroplasty

- Similar as with TKA except that the arthritis must be limited to one compartment (medial or lateral for unicompartmental) or to two compartments (medial or lateral and patellofemoral for bicompartamental)

Note: Partial knee arthroplasty traditionally reserved for relatively inactive elderly patients, but is being used with increasing frequency in younger, more active patients.

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Key Questions

When used in adult patients

1. What is the evidence of efficacy and effectiveness of using CN-TKA compared with CONV-TKA?
2. What is the evidence of efficacy and effectiveness of partial knee arthroplasty compared with CONV-TKA?
3. What is the evidence of the safety of CN-TKA or partial knee arthroplasty compared with CONV-TKA?
4. What is the evidence that TKA or partial knee arthroplasty has differential efficacy or safety issues in sub populations?
5. What is the evidence of cost implications and cost-effectiveness of CN-TKA or partial knee arthroplasty compared with CONV-TKA?

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Study Inclusion Criteria

Study parameters

- Population: adults with primary knee arthroplasty for arthritis
- Intervention: CN-TKA, UKA or bicompartamental knee arthroplasty
- Comparator: CONV-TKA or high tibial osteotomy (for UKA)

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Outcomes

Efficacy/effectiveness

- Revision rate
- Time to revision
- Clinician reported and patient reported outcomes
- Radiographic alignment for computer navigation (secondary outcome)

Safety

- Complications and adverse effects
- Infections
- Fractures
- Blood loss
- Thromboembolic event

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Studies Included

Study design

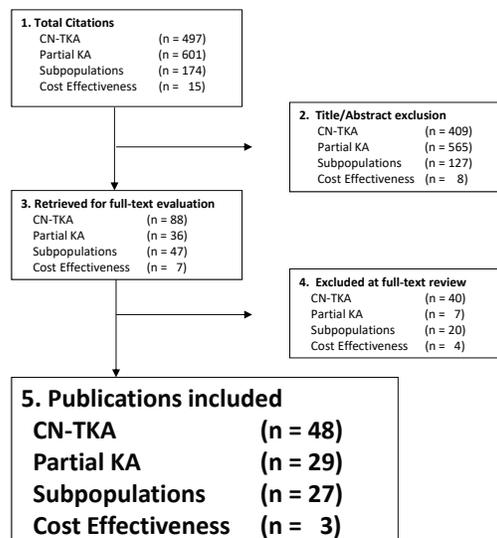
Key Questions 1-4:

- Meta-analyses
- RCTs
- Comparative observational studies
- Registry studies to assess long term revision rates and special populations

Key Question 5:

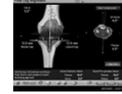
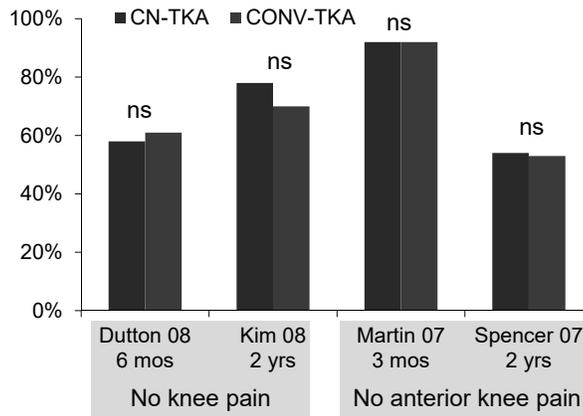
- Economic analyses

Literature Search



Key Question 1: Efficacy of CN-TKA vs. CONV-TKA

No pain



Key Question 1: Efficacy of CN-TKA vs. CONV-TKA

PROs*

	CN-TKA	CONV-TKA	p-value	Follow-up
Oxford Knee Score				
Dutton 08	20	22	ns	6 mos
Ensini 07	20.0 ±7.2	18.8 ±6.6	ns	2 years
Spencer 07	26.7 ±21.8	20.1 ±15	ns	2 years
WOMAC				
Luring 08	7 ±9	7 ±6	ns	3 mos
Seon 09	31.3	32.2	ns	2 years
Spencer 07	23.4 ±21.5	13.6 ±13.0	ns	2 years

* 6 RCTs – 5 with total scores shown here. Decking 05, 07 had component scores for the WOMAC with no difference between groups at 3 mos and 1 year.

Key Question 1: Efficacy of CN-TKA vs. CONV-TKA CBOs*



	CN-TKA	CONV-TKA	p-value	Follow-up
Knee Society Score				
Martin 07	173 ±19	169 ±20	ns	3 mos
Martin 09	160 ±24	160 ±22	ns	3 mos
Matziolis 07	149 ±34	144 ±29	ns	6 mos
Spencer 07	156 ±33	159 ±29	ns	2 years
Hospital for Special Surgery Scale				
Boehling 05	82	83	ns	7 mos
Seon 09	92	91	ns	2 years
Kim 07	90	89	ns	2 years

* 11 RCTs – 7 with total scores shown here; four others with component scores. There were no significant differences between groups in any component score.

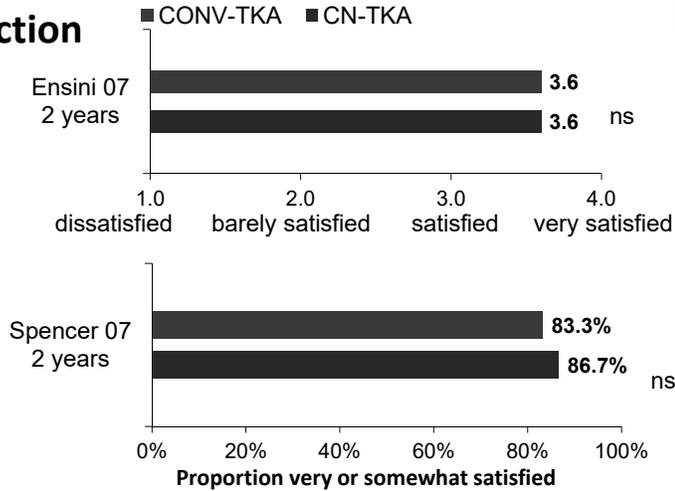
Key Question 1: Efficacy of CN-TKA vs. CONV-TKA QoL



	CN-TKA	CONV-TKA	p-value	Follow-up
SF-36 or SF-12* physical (mean or median)				
Dutton 08	46	43	ns	6 mos
Spencer 07	57	70	ns	2 years
Choong*	43	38	ns	1 year
SF-36 or SF-12* mental (mean or median)				
Dutton 08	57	58	ns	6 mos
Spencer 07	75	80	ns	2 years
Choong*	47	45	ns	1 year
EuroQoL (median)				
Lutzner 10	70	65	ns	2 years

Key Question 1: Efficacy of CN-TKA vs. CONV-TKA

Satisfaction

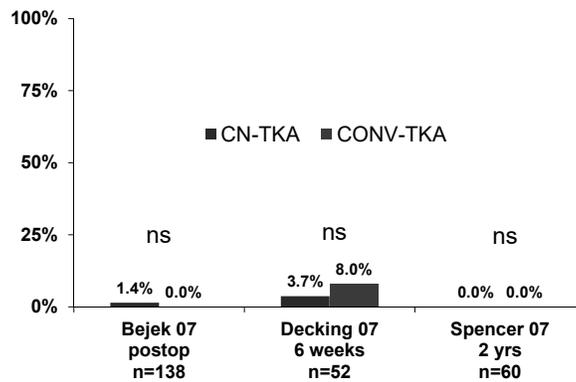


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Key Question 1: Efficacy of CN-TKA vs. CONV-TKA

Revision



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Key Question 1: Efficacy of CN-TKA vs. CONV-TKA

ROM reported by 6 RCTS

- No significant differences between groups in 5 studies either postop or at 2 years
CN-TKA range: 102° to 129°
CONV-TKA range: 100° to 129°
- One study recorded slightly greater flexion in the CN-TKA group (132° vs. 125°), p=.001



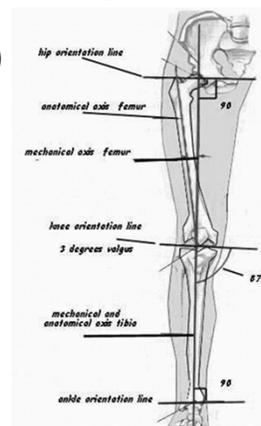
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Radiographic Alignment

We report mechanical axis alignment from 2 meta-analyses:

1. Bauwens et al 2007 (33 studies; N = 3432)
 - 10 RCTs
 - 8 qRCTs
 - 15 nonrandomized trials
2. Australian HTA 2009 (43 studies)
 - 15 RCTs
 - 7 qRCTs
 - 21 nonrandomized trials



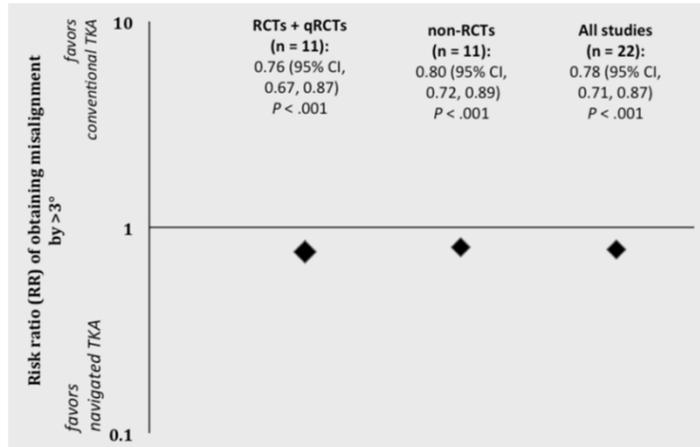
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Radiographic Alignment



1. Risk ratio of obtaining misalignment by $>3^\circ$ (Bauwens 07)



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Radiographic Alignment



2. Odds ratio of achieving satisfactory alignment defined as $\leq 3^\circ$ from the mechanical axis (Australian HTA)

- 25 studies (5 RCTs, 6 quasi-RCTs, and 14 cohort studies)
- Of these, 10 studies were also reported in the Bauwens et al
- CN-TKA had 4.14 times higher odds of achieving satisfactory alignment compared with CONV-TKA (odds ratio: 4.14; 95% CI, 3.03, 5.66; $P < .00001$).

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Summary CN-TKA Efficacy



1. CN-TKA reduces the proportion of patients with misalignment
2. However, this does not appear to have an effect on short term pain or functional outcomes
3. Whether CN-TKA improves long term outcomes to include revision rates is not yet known

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Key Question 2: Efficacy of PKA vs. CONV-TKA



One RCT comparing UKA vs. TKA (Newman et al 1998)

	UKA	TKA	P-value	F/U
OUTCOME				
Knee Scores:	76 (34/45)	57 (26/46)	ns	5 yrs
BKS Excellent results, % (n/N)	71 (15/21)	53 (10/19)	ns	15 yrs
BKS pain score, Excellent results, % (n/N)	89 (40/45)	83 (38/46)	ns	5 yrs
ROM \geq 120 flexion, % (n/N)	69 (31/45)	17 (8/46)	< .01	5 yrs
Revision, % (n/N)	13 (3/23)	16 (4/25)	ns	15 yrs
Survival (end point: failure), % (n/N)	89.8	78.7	ns	15 yrs

BKS = Bristol Knee Score

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Key Question 2: Effectiveness of UKA



	UKA	TKA	F/U (range of means)
PATIENT REPORTED KNEE SCORES			
Oxford Knee Score (range of means)			
4 cohort studies	18-38	22-26	.5 -2.3 years
CLINICIAN BASED KNEE SCORES			
Knee Society Score			
Knee Score (range of means)			
5 cohort studies	82-99	84-96	1-6 years
Function score (range of means)			
4 cohort studies	80-100	76-96	1-5 years
PATIENT SATISFACTION			
Satisfied or very satisfied (%)			
2 cohort studies	88-93	80-93	2-6 years

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Key Question 2: Effectiveness of UKA



Revision/survival

	UKA	TKA	F/U
Revision, %, (n/N)			
Ackroyd 02	6.1 (25/408)	3.8 (20/531)	5.7 years
Furnes 02	8.4 (192/2288)	6.7 (204/3032)	10 years
Robertsson 99	7.0 (752/10,624)	3.7 (568/15,437)	NR
Survival rate (endpoint = revision)			
Ackroyd 02	87.5%	89.6%	5.7 years
Amin 2006	88%	100%	5 years
Gioe 03	92.6%	97.9%	5 years
Gioe 07	88.6%	94.8%	10 years
Gioe 07	67.7%	84.5%	14 years
Koskinen 08	73%	90%	10 years
	60%	80%	15 years

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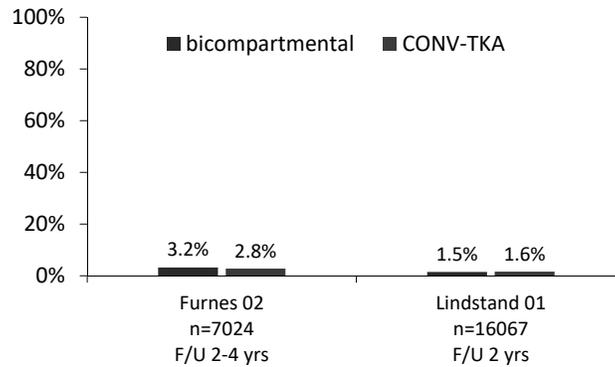


Key Question 2: Bicompartamental Knee Arthroplasty



No RCTs found

2 registry studies assessing revision:



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Key Question 2: Bi-UKA



No RCTs found

One small retrospective cohort study:

- No diff in functional scores at a minimum of 4 years follow-up
- No revisions recorded in either group

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Summary PKA Efficacy/Effectiveness



1. With limited evidence, we found similar functional outcomes between UKA and TKA
2. UKA revision rates tended to be higher than TKA revision rates at 10 and 15 years following surgery

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Key Question 3: Safety of CN-TKA



CN-TKA

25 RCTs and 14 nonrandomized studies provided safety data

VTE:

CN-TKA, which does not use intramedullary alignment rods, may lead to fewer embolic events

1 RCT used Mayo Clinic score to assess the degree of embolic shower

- Amount of right atrium filled by echogenic particles
- Duration of echogenesis during one minute video segments looking at time to peak intensity
- Diameter of largest echogenic particle

	CONV-TKA		
CN-TKA	IM femur guide	IM femur & tibia guide	p-value
4.2	5.1	5.4	.02, .04

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Key Question 3: Safety of CN-TKA



	CN-TKA	TKA	P-value
VTE (range of proportions)			
DVT – 8 studies	0-8%	0-10%	ns
PE – 5 studies	0-2%	0-3%	ns
Ischemic events (range of proportions)			
Acute MI – 1 study	2%	2%	ns
Transient ischemia – 1 study	0%	3%	ns
Confusion - 2 studies	0-3%	4-28%	.007
Wound complications (range of proportions)			
Deep infection – 14 studies	0-4%	0-2%	ns
Superficial infection – 6 studies	0-7%	0-8%	ns
Tourniquet time, min (range of means)			
9 studies	59-105	44-100	< .002 (7/9)

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Key Question 3: Safety of UKA



1 RCTs and 9 nonrandomized studies provided safety data

	UKA	TKA	P-value
VTE (range of proportions)			
DVT – 4 studies (n=366)	0-5%	2-10%	ns
PE – 2 studies (n=172)	0-7%	0-5%	ns
Wound complications (range of proportions)			
Delayed wound healing – 2 studies (n=332)	0%	2-4%	ns

32



Key Question 3: Safety of Bi-UKA, Bicomparmental KA



2 cases (9%) of intraoperative fracture of the tibial spine in 1 retrospective cohort study of bi-UKA

No complication data available from the 2 registry studies of bicomparmental knee arthroplasty

33



Key Question 4: Differential Efficacy/Safety



CONV-TKA:

- Diagnosis of RA vs. OA associated with greater improvement in function compared with baseline (may be related to lower baseline function)
- No other factors consistently associated with outcome to include: age, sex, obesity, comorbidities, hospital or surgeon volume

34



Key Question 4: Differential Efficacy/Safety



CN-TKA:

- Morbid obesity (BMI >40) was associated with greater blood and hemoglobin loss and superficial infection compared with non obesity (BMI <30) in 1 retrospective study

UKA:



- Younger age was consistently associated with higher revision rates among several large registries and cohort studies (<65 vs >65)
- Similar association for CONV-TKA (not differential)
- No other characteristics were associated with failure to include obesity, sex or provider facility

35



Key Question 4: Differential Efficacy

Simultaneous vs. staged bilateral TKA

No RCTS, 11 cohort studies

- No difference in pain or function in 5 cohort studies at follow-up from 3-15 years
- Revision and prosthesis survival was similar in 2 studies, one with 3 year and one with 10 year F/U
- Mortality appears to be higher among those receiving simultaneous TKA vs. staged.

36



Simultaneous vs. staged bilateral TKA

Mortality

	F/U	Bilateral TKA		2 nd op.	p-value
		Simultaneous	Staged		
Stefansdottir	30 days	.97% (11/1139)	.15% (5/3432)	1 yr	.003
Ritter 03	12 mos	1.2% (25/2050)	.7% (1/152)	1 yr	ns
Ritter 97	30 days	.99% (128/12922)	.48% (21/4354)	6 wks	.0012
			.29% (13/4524)	3 mos	.000
			.31% (30/9829)	6 mos	.000
			.36% (113/31401)	12 mos	.000

37



Key Question 5. Cost effectiveness

CN-TKA

- Limited data
- One US study calculating ICER (\$45,554 per QALY)

Australian HTA 2009

(assumption: CONV-TKA 10 yr revision rate = 6%)

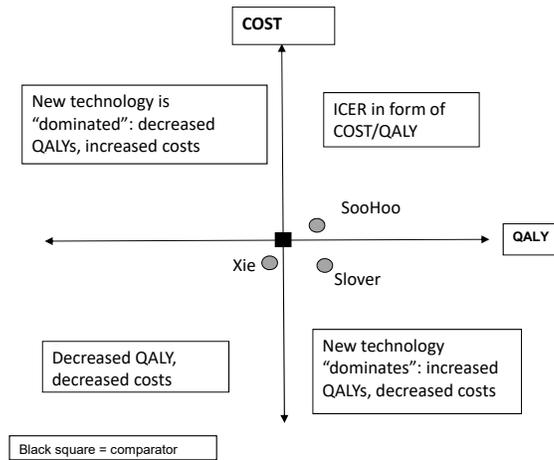
	CN-TKA 10 year revision rate	Cost effective (<\$50K/QALY)
Scenario 1	6%	no
Scenario 2	5% (17% improvement)	no
Scenario 3	4% (33% improvement)	after 15 years
Scenario 4	3% (50% improvement)	after 10 years

38



UKA

- 3 studies
- Varying assumptions



39

Points to Consider:



CN-TKA

1. CN-TKA reduces the risk of unsatisfactory alignment of the mechanical axis ($> 3^\circ$) compared with CONV-TKA.
2. Despite this, there is no evidence in the short term (< 3 years) that CN-TKA results in better patient reported, clinical or QoL outcomes.
3. Only short term revision rates are available from small studies and they are inconsistent. To determine the effect of CN-TKA on revision rates, longer follow-up is needed.

40

Points to Consider:



CN-TKA

4. There appears to be fewer emboli following CN-TKA than CONV-TKA as measured by the Mayo Clinic Score. This is attributed in part to the absence of use of the femoral IM guide in CONV-TKA. However, its clinical importance is not known.
5. VTE events are similar between CN-TKA and CONV-TKA as are wound and other complications.
6. Postoperative transient confusion occurred slightly less frequently one RCT and markedly less frequently in a second among those receiving CN-TKA.

41



Points to Consider:



UKA and bicompartamental KA

1. Pain and function appear to be similar comparing UKA and TKA in patients with unicompartmental disease. ROM is consistently higher in patients receiving UKA.
2. Revision rates tend to be slightly higher in the UKA vs. TKA group in most studies up to 10 years of follow-up. Likewise, prosthesis survival slightly favors TKA at 10-14 year follow-up.
3. The safety profile with respect to mortality, VTE, wound complications and other complications is similar between UKA and TKA.

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Points to Consider:



UKA and bicompartamental KA

4. Bicompartamental knee arthroplasty in two large registry studies had similar survival 2-4 years following surgery. The longer term effect is not known.
5. The safety profiles of bicompartamental knee arthroplasty and bi-UKA are not known.

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Points to Consider:

Differential Efficacy

1. Younger age at the time of UKA is associated with higher revision rates. This is thought to be related to activity level. The age cut off used by many studies was 65years; however, there is some evidence of a dose response.
2. Though there is an association between age and revision, this is not differential; that is, lower age is also associated with higher revision rates in TKA.

44



Points to Consider:

Differential Efficacy

Mortality is slightly higher among patients receiving simultaneous bilateral TKA compared with staged. However, whether this difference is real or a function of selection bias is not known. These data are taken from registries and only individuals completing the second stage were included in the staged group. Therefore, a “healthy patient” bias may result.

45



Points to Consider:

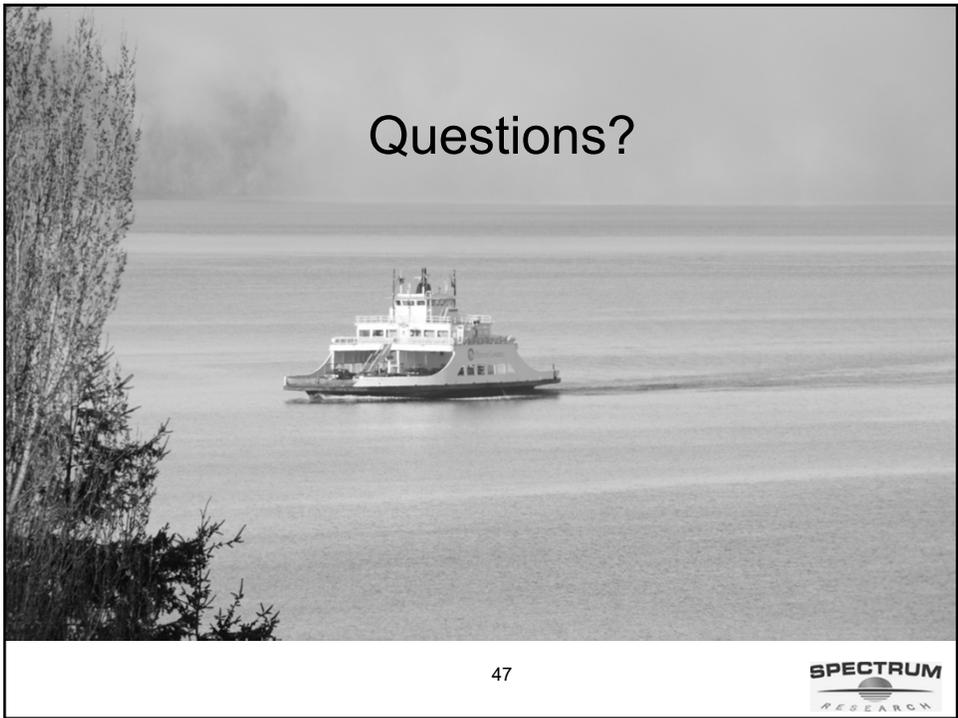
Cost Effectiveness

1. There is insufficient revision data to conclude whether CN-TKA is cost effective. Modeling suggest that the 10 year revision rate would need to be reduced between 33%-50% of CONV-TKA for potential cost savings.
2. There is some evidence that UKA and TKA have similar cost and QALY outcome profiles in older patients (mean age of 70 years), but this evidence depends on assumption that need verification with longer studies.

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Questions?



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Health Technology Assessment

Peer Review, Public and Washington State Agency Comments & Responses

Total Knee Arthroplasty

September 22nd, 2010

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1. SPECTRUM RESEARCH RESPONSE TO PEER REVIEW COMMENTS

No formal peer review comments were received by the closing date.
No comments were received from the Washington State Agency.
Letters to the editor were submitted by Mr. Mike L. McClure, Director/Strategic Reimbursement, Smith and Nephew, Inc. after the closing date. Those letters are included below.

2. SPECTRUM RESEARCH RESPONSE TO PUBLIC COMMENTS

Response to Dr. Bert J. Thomas, M.D.; Professor of Orthopaedic Surgery; Chief, Joint Replacement Service; David Geffen School of Medicine at UCLA

Comment 1

We chose the two metaanalyses that contained the most robust number of randomized trials (though non-randomized trials were also included).

Comment 2

We did not include data from case series.

Comment 3

We did not evaluate the one month outcomes of independent ambulation.

Comment 4

We updated our report with the p-value in table for Ek and a comment in the text on page 62.

Comment 5

Longstaff evaluates function and alignment in those that received CONV-TKA (no CN-TKA). We included the article by Choong that also evaluates the association between alignment and function using both CN-TKA and CONV-TKA.

Comments 6, 7

These outcomes were not part of our inclusion criteria.

Comment 8

This study is from an administrative database. In general, administrative databases contain data that have been gathered as a by-product of some other process; the data may be collected and entered by hundreds of individuals at many locations; usually, there are few, if any, quality checks on the data; records may have different lengths and structures within the same database; and missing data are common.(Lange, 1993; Baron, 2000)
One of the most obvious disadvantages is that these systems were not created for research

purposes and, in most cases, researchers did not have input into the design or types of information collected by the systems. They may lack some of the details that researchers might want.(Cowper, 1999) These characteristics of large databases lead to the controversy over their use in epidemiologic and health services research and point to the need to consider validity and reliability issues.(Connell, 1987; Flood, 1990)

References:

Lange, L. L., Jacox, A.: Using large data bases in nursing and health policy research. *J Prof Nurs*, **9**: 204, 1993

Baron, J. A., Weiderpass, E.: An introduction to epidemiological research with medical databases. *Ann Epidemiol*, **10**: 200, 2000

Cowper, D. C., Hynes, D. M., Kubal, J. D. et al.: Using administrative databases for outcomes research: select examples from VA Health Services Research and Development. *J Med Syst*, **23**: 249, 1999

Connell, F. A., Diehr, P., Hart, L. G.: The use of large data bases in health care studies. *Annu Rev Public Health*, **8**: 51, 1987

Flood, A. B.: Peaks and pits of using large data bases to measure quality of care. *Int J Technol Assess Health Care*, **6**: 253, 1990

Comment 9,10

These references are from the Proceedings of meetings. We included only peer-reviewed articles.

\

3. Public Comments

1. Bert J. Thomas, M.D

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To whom it may concern:

I am the chief of the joint replacement service at UCLA, and over the past 25 years have developed some rather strong opinions regarding hip, knee, and shoulder replacements, and how they should be performed. The improvement in patients' lives after unicompartamental, bicompartamental, and total knee arthroplasty, are nothing short of a miracle. My vision is to make these procedures so reproducible that every patient will be able to achieve the same outstanding results. Computer navigation and robotic assisted surgery are tools that can help to achieve this goal.

I believe that in the near future, computer technology will assist with virtually every orthopaedic reconstructive procedure, and that young surgeons will wonder how anyone could ever have considered not using these 'smart tools'. I have therefore, signed on as a consultant with Smith&Nephew as a consultant to help this belief to become a reality, and must disclose this as a potential conflict of interest.

I have had the privilege of reviewing the Washington State's Health Technology Assessment Report, and appreciate the opportunity to make the following observations.

While the Health Technology Assessment Report has done a thorough and exhaustive review of the available literature on computer-assisted/navigated surgery, given the growing body of evidence evaluating the improved patient outcomes provided by computer-assisted navigation on TKA, it can be argued that certain clinical results are not captured in the report. I believe that these additional results are relevant to the reimbursement decision for computer-assisted navigation of TKA and should be considered when rendering the final decision.

The specific relevant studies and data points that are not included in the Health Technology Assessment Report include:

Mason et al. (2007) and Brin et al. (2010) both undertook meta-analyses of the clinical literature and concluded that component orientation and postoperative limb alignment were improved with surgical navigation. These studies were referenced but not reported by the Health Technology Assessment Report, which only reports the two meta-analyses that include the most clinical trials. However, both the Mason study as well as the Brin study report on a greater number of TKAs than either of the two studies reported by the committee. Mason reports the results of 3,437 procedures and Brin reports the results of 4,199

procedures; while the two studies reported by the committee include 2,482 procedures and 3,423 procedures.

The Health Technology Assessment Report does not include data from Tingart et al. (2008) who conducted a prospective case series involving 1,000 patients. In the computer-assisted group 94.8% of patients had a postoperative leg axis within range of $\pm 3^\circ$ compared to 74.4% in the conventional group.

The Health Technology Assessment Report includes the non-significant data from Dutton et al. (2008), but provides no discussion of the fact that patients who underwent navigated TKA had shorter hospital stays, and at one month follow-up significantly more patients in the navigated group were able to walk independently for more than 30 minutes.

In reporting the results of the study performed by Ek et al. (2008), the Health Technology Assessment Report includes the improved SF-12 scores in the computer navigation group, but does not additionally include the improved International Knee Score in the navigated group.

The Health Technology Assessment Report does not include data from Longstaff et al. (2009), whose data demonstrate that short-term function is improved by better alignment of the limb after TKR.

The Health Technology Assessment Report does not include data from Dillon et al. (2009), who used gait analysis to demonstrate that computer-assisted TKA improves knee function as compared to standard instruments.

The Health Technology Assessment Report does not include data from Saragaglia (2006), Han (2008), or Hakki (2009), all of which reported that computer navigation may allow a more quantifiable approach to soft-tissue balance, which according to Engh (2003) is a critical factor in restoring function after TKA, where failure to release contracted collateral ligaments can lead to accelerated implant wear.

The Health Technology Assessment Report does not include data from Browne (2010), who compared the early postoperative outcomes of computer navigated TKA to standard conventional TKA using a large nationwide database of 101,596 patients who underwent TKA in 2005. These authors reported no differences in postoperative mortality or complications, but did report a shorter length of stay and a lower rate of postoperative cardiac complications.

The Health Technology Assessment Report does not include data from Chambers et al. (2008), who found that patients who underwent TKR with surgical navigation on average reached oxygen saturation levels on air faster than the non-navigated group. These authors also reported that there was a lower need for oxygen and shorter length of hospital stay in the computer navigated group during the early post-operative period.

The Health Technology Assessment Report does not include data from Song et al. (2010), who reported mid-term clinical and radiographic outcomes of navigated TKR's as compared to the conventional technique. These authors reported that prosthetic loosening increases significantly when postoperative alignment exceeds 3° and implant survivorship improved when properly aligned.

Key Question 1: Evidence of efficacy and effectiveness of using computer-navigated total knee arthroplasty (CN-TKA) compared with conventional TKA

Overall Leg Alignment

The importance of varus/valgus alignment in total knee arthroplasty (TKA) has been documented extensively in the orthopedic literature over the years and is well accepted (Insall, 1985; Hungerford and Krackow, 1985; Moreland, 1988). In fact, Moreland went as far as to state that "Prosthetic alignment is the most important factor influencing postoperative loosening and instability... the major mechanisms of failure in TKA". Other investigators have further quantified the relationship between alignment and clinical

outcomes, indicating that varus/valgus alignment in excess of 3° is strongly correlated to poor postoperative clinical results (Laskin, 1990; Ritter, 1994; Kumar and Dorr, 1997; Insall, 2002).

Ritter (1994) demonstrated that the highest rate of aseptic loosening occurred in knees with greater than $\pm 4^\circ$ of mal-alignment relative to the mechanical axis, and Jeffery (1991) demonstrated that the incidence of loosening over an 8-year period was 24% with a mechanical axis of greater than 3° , but only 3% with a mechanical axis of less than 3° . In regards to the relationship between alignment and survival of the implant, Rand and Coventry (1988) demonstrated a 10 year survival rate in excess of 90% with a varus/valgus alignment of less than 4° , which decreased dramatically to 73% with a varus/valgus alignment of more than 4° . In short, there is a significant body of clinical data to support the importance of postoperative leg alignment after total and partial knee replacement, where, for example, the above cited authors reported that:

The rate of implant loosening over 8 years was 24% in the mal-aligned group (with mal-aligned being defined as the mechanical axis exceeding $\pm 3^\circ$ from neutral), but only 3% in the group where alignment was within 3° .

The 10-year survival rate of the implant was in excess of 90% when leg alignment was $\pm 3^\circ$ but only 73% when in excess of $\pm 3^\circ$

Given the importance of postoperative leg alignment and its impact on implant longevity, anything that improves post-operative alignment should similarly impact implant longevity.

Many authors contend that computer navigation improves the accuracy of implanting the total knee prosthesis and therefore improves implant longevity. Published data also suggests that the incidence of implant mal-alignment is high and therefore a problem that must be addressed. For example, in 2004 Perlick reported a staggering 28% incidence of mal-alignment and Bathis similarly reported a 22% incidence of mal-alignment. There is a significant amount of evidence in the form of randomized controlled trials, prospective and retrospective case series and published reviews demonstrating that there is improved alignment when compared to conventional approaches (Jenny et al., 2001; Ritschl et al., 2002; Sparmann, et al., 2003; Bathis et al., 2004; Bolognesi and Hofmann, 2005; Chin, et al., 2005; Decking, et al., 2005; Haaker, et al., 2005; Keene, et al., 2006; Matziolis et al., 2007; Kamat et al., 2009; Luring et al., 2009; Weng, et al., 2009). Some authors have also reported that the use of computer navigation is associated with longer surgical times (Decking, et al. 2005; Bolognesi and Hofmann, 2005), as well as there being no difference in functional scores (such as Kamat et al., 2009). Most recently, Song et al. (2010) reported mid-term (5 years or greater) clinical and radiographic outcomes of navigated TKR's as compared to the conventional technique. The authors reported that prosthetic loosening increases significantly when post-operative alignment exceeds 3° and implant survivorship improved when properly aligned.

Other recent studies have similarly demonstrated that the use of computer navigation results in improved mechanical axis and component alignment, where there is a growing body of evidence to support previous findings. For example, Tingart et al. (2008) conducted a prospective case series involving 1000 patients (500 underwent computer navigated TKA and 500 underwent a conventional approach). In the computer-assisted group 94.8% of patients had a postoperative leg axis within range of $\pm 3^\circ$ compared to 74.4% in the conventional group. Similarly, Dutton et al. (2008) published the results of a prospective randomized trial (n=108) also demonstrating the benefit of computer navigation in improving postoperative alignment without short-term complications. The patients who underwent conventional TKA had shorter operating times, but longer hospital stays. These authors also reported that at one month significantly more patients in the navigated group were able to walk independently for more than 30 minutes compared to the conventional group. The difference was not significant at three and six months, and at six months similar improvements were noted in the mean scores of both groups, including the Oxford knee score, Knee Society score, and Short Form-36 scores.

A meta-analysis was undertaken by Mason et al. (2007) to examine alignment outcomes in computer-assisted TKR versus conventional TKR, where a systematic review of literature from 1990 to 2007 was performed. Based on the results, these authors concluded that alignment outcomes were significantly improved when surgical navigation is used. A meta-analysis was similarly performed by Brin et al. (2010), where 23 publications were reviewed. These authors also concluded that component orientation and

postoperative limb alignment were improved with surgical navigation is used when performing TKA (analysis of component orientation included 3,058 TKAs, and analysis of limb alignment included 4,199 TKAs).

Functional Outcomes

In a prospective randomized trial of 108 patients, Dutton et al. (2008) reported that those patients who underwent navigated TKA had shorter hospital stays, and at one month follow-up significantly more patients in the navigated group were able to walk independently for more than 30 minutes. Another group of authors has reported that improved alignment from computer navigated TKR correlated with improved knee function scores and quality of life. Choong and colleagues (2009) reported the results of a randomized controlled trial comparing the alignment, function and patient quality-of-life outcomes between patients who underwent conventional and computer-assisted TKA (=115). Mean operating time was longer for the computer-assisted group, although there was no difference in blood loss between groups. Mean length of stay was 6 days for both groups. A total of 88% from the navigated group versus 61% of the conventional group achieved a mechanical axis within 3° of neutral. Patients with a mechanical axis within 3° demonstrated superior total International Knee Society (IKS) scores and Short-Form 36 scores at 6 weeks, 3 months, 6 months, and 12 months following surgery.

Another group of authors similarly reported improved functional and quality of life outcomes. Ek et al. (2008) reported the results of a matched-controlled retrospective study of 100 patients (50 in the navigated TKA group and 50 in the non-navigated group), in which the use of computer navigation resulted in better SF-12 and IKS scores, as compared to the non-navigated group. Longstaff et al. (2009) similarly reported that short-term function is improved by better alignment of the limb after TKR. In another recent study that was presented at the 2009 AAOS, clinical data was presented also demonstrating that computer-assisted TKA improves knee function as compared to standard instruments. In this study, Dillon et al. (2009) compared navigated, non-navigated, and non-TKR knee function as assessed by gait analysis. These authors reported that at 8 months maximum knee flexion was significantly better in the navigated group during walking, chair rising/sitting, and stairs ascent/stairs descent. Moreover, when analyzing other outcomes that are associated with normal daily activities (detection of a biphasic moment pattern, mean double stance support time, etc.), the computer navigated group was more similar to the control group (the non-TKR group).

Lastly, it is well recognized that soft-tissue balance and accurate gap balancing is a critical factor in restoring function after TKR. Engh (2003) reported that the failure to release contracted collateral ligaments can lead to accelerated implant wear, especially when treating severe deformity. Moreover, gap symmetry in both flexion and extension, joint line position, and posterior femoral offset needs to be fairly accurate for the joint to function optimally postoperatively. All of these parameters are interrelated, and the surgeon must ensure accuracy and precision while performing each stage of the procedure. To that end, Mullaji and colleagues (2009) reported that computer-assisted TKA provides excellent information regarding gap equality and symmetry throughout the knee ROM, and allows for precise release for deformities. Numerous other studies have similarly reported that computer navigation may allow a more quantifiable approach to soft-tissue balance (Saragaglia et al., 2006; Han et al., 2008; Hakki et al., 2009).

Key Question 3: Evidence of the safety of computer-navigated TKA or partial knee arthroplasty

Blood Loss and Transfusions

The blood loss that accompanies total knee arthroplasty (TKA) can be substantial. Many patients need perioperative blood transfusions. To avoid anemia and transfusion-related complications, the amount of blood loss and need for blood transfusions must be reduced. In a randomized controlled trial by Kalairajah et al. (2005) in which blood loss and rate of transfusions were assessed in a group of navigated TKA patients versus non-navigated TKA patients, blood loss was lower and fewer patients required blood

transfusions in the navigated group. In more recent studies by Conteduca, et al. (2009) and Hinarejos et al. (2009) the investigators reported that intraoperative blood loss for patients who underwent navigated TKA was less than that of those who underwent conventional TKA. Most recently, in a study of 500 patients undergoing TKA, Schnurr et al. (2010) reported that the average blood loss in the drainages and the calculated total blood loss were significantly reduced in the computer navigated group. Moreover, these authors reported that the transfusion rate of the navigated group was almost halved.

Browne et al. (2010) compared the early postoperative outcomes of computer navigated TKA to standard conventional TKA using a large nationwide database and reported that after adjustment for patient characteristics. Using multivariate regression analysis the authors found no differences in postoperative mortality or complications for the majority of the measured outcomes, but nevertheless reported that computer navigation was associated with less postoperative cardiac complications in addition to a shorter length of stay and a trend toward fewer hematomas.

Emboli

In addition to reducing blood loss, studies have also shown that the use of computer navigation is correlated with a reduction in thromboemboli (Kalairajah et al., 2006; Ooi et al., 2008). Church et al. (2007) and Kalairajah et al. (2006) also reported a reduction in systemic emboli (as measured by trans-esophageal echocardiography) in a navigated TKR group as compared to a non-navigated group. Other authors have reported a reduction in post-operative confusion in patients who have received navigated TKR (Chauhan et al. 2004). There is also some evidence that the C-reactive protein level, a marker of systemic inflammatory response, is reduced with a navigated TKR (Shen et al. 2009). Lastly, a prospective study by Chambers et al. (2008) found that patients who underwent TKR with surgical navigation on average reached oxygen saturation levels on air faster than the non-navigated group. These authors also reported that there was a lower need for oxygen and a shorter length of hospital stay in the computer navigated group during the early post-operative period.

In summary, upon review of the clinical literature, it is clear that there are many benefits of navigated TKR as compared to the traditional technique. Some of these benefits include:

Reduced blood loss and incidence blood transfusion (Kalairajah et al., 2005; Conteduca, et al., 2009; Hinarejos et al., 2009; Schmurr et al., 2010)

Less postoperative cardiac complications in addition to a shorter length of stay and a trend toward fewer hematomas (Browne et al., 2010)

A reduction in the incidence of thromboemboli/systemic emboli (Kalairajah et al., 2006; Church et al., 2007; Ooi et al., 2008)

Key Question 5: Evidence of cost implications and cost-effectiveness of computer navigated

TKA or partial knee arthroplasty

Given the current healthcare economic environment which is characterized by increasing pressures to reduce the cost of care and/or improve efficiencies, the question has arisen as to whether the use of computer-assisted surgery can be a cost-effective tool to justify its added cost. Although variability in published outcomes introduces some level of uncertainty in determining the cost-effectiveness, Novak et al. (2007) demonstrated that computer-assisted surgery achieved cost-savings if the added cost of using the device is \$629 or less per operation. As this seems to be within the range of what the navigation system manufacturers are willing to charge on a per-use basis, it may be that the use of surgical navigation for knee arthroplasty is cost-effective. Moreover, this cost savings is calculated based only on the probability of increased rate of revision (as a function of mal-alignment), and does not account for additional sources of

additional cost savings such as the decreased cost of blood products and the reduced risk of venous thromboemboli.

In summary, computer technology offers a cost-effective tool to prevent outliers, decrease emboli, blood loss, cardiac complications, and hospital stay, while increasing the survival of knee reconstruction with unicompartmental, bicompartamental or total knee replacement.

Sincerely,

Bert J. Thomas, M.D.
Professor of Orthopaedic Surgery
Chief, Joint Replacement Service
David Geffen School of Medicine at UCLA

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2. Mr. Mike L. McClure

From: McClure, Michael [mailto:Michael.McClure@smith-nephew.com]
Sent: Tuesday, September 07, 2010 8:27 AM
To: Santoyo, Denise (HCA)
Cc: Frandsen, Tim; William Alkire
Subject: RE: HTA Updates: Total Knee Arthroplasty and Routine Ultrasound Draft Evidence Reports

Ms. Santoya,

I hope this email finds you well. I look forward to the October meeting regarding knee arthroplasty. I am fully aware the time has past for comments which could alter the draft assessment but I wanted to make you aware of an issue brought to my attention by Tim Frandsen Ph.D. M.B.A. who has responsibility for Computer Assisted Surgery at Smith & Nephew. I am providing a link to a response to an article concerning several meta analysis cited by Spectrum. The use and understanding of these meta-analyses leaves CAS in an unnecessarily unflattering light due to information in the analyses being interpreted incorrectly in the draft assessment. The link explains the issues with interpreting results of both Bauwens and Mason meta analysis. This is a fairly serious error in judging the evidence and presenting a fair and unbiased assessment of CAS to your panel.

I apologize for the tardiness of this information but there was insufficient time to respond to the initial draft assessment due to its length and complexity.

<http://www.ejbs.org/cgi/eletters/89/2/261#3881>

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Letters to the Editor to:

Scientific Articles:

Kai Bauwens, Gerrit Matthes, Michael Wich, Florian Gebhard, Beate Hanson, Axel Ekkernkamp, and Dirk Stengel

Navigated Total Knee Replacement. A Meta-Analysis

J Bone Joint Surg Am 2007; 89: 261-269

[\[Abstract\]](#) [\[Full text\]](#) [\[PDF\]](#)

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Electronic letters published:

▼ **Dr. Katz & Dr. Losina comment on Navigated Total Knee Replacement.**

Jeffrey N. Katz, M.D., MSc, Elena Losina, Ph.D. (17 September 2007)

▼ **"Review of Navigated Total Knee Replacement: A Meta Analysis by Bauwens et al."**

J. Bohannon Mason, M.D., Thomas Fehring, M.D., and Kyle Fahrback, Ph.D. (25 July 2007)

▼ **Dr. Stengel et al. respond to Dr. Mason.**

Dirk Stengel, M.D., Ph.D, MSc., Kai Bauwens, M.D, Gerrit Matthes, M.D., Michael Wich, M.D., Florian Gebhard, M.D., PhD, Beate Hanson, M.D., MPH, Axel Ekkernkamp, M.D., PhD. (25 July 2007)

▼ **Navigated Total Knee Arthroplasty--a Meta-analysis**

Alberto Gregori, Graeme Holt. (27 March 2007)

▼ **Dr. Stengel & Dr. Bauwens respond to Dr. Gregori & Dr. Holt**

Dirk Stengel, M.D., Ph.D., MSc, Kai Bauwens, M.D. (27 March 2007)

Dr. Katz & Dr. Losina comment on Navigated Total Knee Replacement.

17 September
2007



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Send letter to
journal:
[Re: Dr. Katz & Dr.
Losina comment
on Navigated
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[E-mail](#) Jeffrey N.
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To The Editor:

In their meta-analysis of the effectiveness of navigated total knee replacement, Bauwens et al.(1) found that navigation was associated with favorable results in terms of several radiographic parameters. The data were insufficient to evaluate effects on complication rates or functional outcomes. The article stimulated the above letter from Mason et al.(2) and a letter from Gregori and Holt(3), which prompted additional letters of clarification from Bauwens et al.(1).

Caught in the crossfire, readers might well ask why a meta-analysis led to such editorial dueling. Of note, controversy over meta-analysis is long-standing(4). The debates stem in part from the methodological complexity of meta-analysis, a powerful but challenging analytic technique that permits pooling of estimates across studies. We will discuss a few of the many methodological complexities of meta-analysis to put the correspondence about navigated total knee replacement in perspective.

Why Pool? Meta-Analysis Compared with Traditional Literature Review

If pooling raises so many questions, why bother to pool estimates quantitatively across studies? In many reviews, the authors simply array the findings of separate studies in evidence tables without attempting to synthesize them quantitatively into single estimates of effect. A key rationale for pooling is that the available evidence may consist of small studies that show positive (or negative) effects but lack power to establish the associations with significance. Pooling these smaller studies may avoid false-negative results due to Type-II error.

A useful example of this application of meta-analysis was provided by Felson and Anderson in a meta-

analysis of the effect of cytotoxic therapy and corticosteroids compared with that of corticosteroids alone for patients with lupus nephritis(5). Prior small studies had suggested a beneficial effect of cytotoxic therapy. The meta-analysis overcame the small sample sizes of the component studies and illustrated the beneficial effect of cytotoxic therapy across studies.

Pooling also permits the investigator to examine whether particular study characteristics are associated with the principal outcome. This technique is termed metaregression. The investigator develops a regression model in which each study serves as a single observation, contributing a single estimate of outcome and of each covariate. The investigator can weight studies differentially in order to give greater importance in the regression to those that have larger sample sizes or that are of higher methodological quality. Metaregression can yield insights about sources of variability in outcome measures across studies. For example, it may be that trial designs are associated with larger effects and nonrandomized designs, with smaller effects, or vice versa.

Why Not Pool?

Pooling the results of separate studies into single estimates of effect involves several assumptions that frequently are not satisfied by the literature under review. Clearly, the outcome variable must be consistent across studies. This constraint poses no problem when the outcome is unambiguously defined, such as thirty-day all-cause mortality following hip replacement. However, when studies measure satisfaction, pain relief, functional status, and other such complex outcome variables, the task becomes more complicated. These domains are often measured with different tools in different studies, or different cutoffs are used to define success. For example, the authors of some studies of the outcome of total knee replacement might use the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) as the principal outcome measure whereas others might use the SF-36 (Short Form-36) or the Knee Society Scale. Attempting to synthesize results in these

circumstances involves essentially combining apples and oranges and is not advisable. Standardization of outcome assessment and reporting in specific fields would assist investigators who wish to perform meta-analysis.

In addition, the underlying statistical methodology of meta-analysis assumes that each of the studies to be synthesized represents one observation from a single distribution of studies. This assumption is validated with tests of homogeneity of the odds ratios (or other effect estimates) across studies. If the group of studies to be synthesized appears to emanate from a single distribution, the homogeneity criterion is met and the studies may be synthesized in a meta-analysis. If, on the other hand, the assumption of homogeneity is not met, and the studies appear to be heterogeneous, then the investigators should be cautious about pooling. The investigators could simply choose not to pool the studies quantitatively. Alternatively, the investigators might wish to perform a metaregression to identify sources of heterogeneity. For example, it may be that higher-quality studies or a particular study design (e.g., trials) are associated with higher effect estimates.

What to Pool?

A meta-analysis is essentially an observational study of individual studies(6). As with all observational studies, the results are influenced by the selection criteria that dictate which studies are included in the meta -analysis and which are excluded. An issue that arises frequently, and was a major focus of contention about the paper by Bauwens et al.(1), is whether to include unpublished studies. Excluding unpublished studies risks publication bias, a form of selection bias in meta-analyses that arises because positive studies are, on the average, more likely to be published than negative studies. However, including unpublished studies that have not passed peer review risks the inclusion of studies with results that may not be credible.

Another important decision is whether to restrict the analysis to randomized controlled trials or to include

observational designs. The advantage of restricting the analysis to randomized controlled trials is that randomization greatly reduces the risk of selection bias in each component study of the meta-analysis. Including observational studies permits the meta-analysis to simply propagate the biases inherent in the component studies. The disadvantage of restricting the sample to randomized controlled trials is that for many clinical problems, including navigated total knee replacement, there are few randomized controlled trials and most of the relevant literature includes observational designs.

Returning to Navigated Total Knee Replacement

Bauwens et al.(1) handled most of the above-mentioned issues with sophistication. They decided to pool because they were concerned that multiple underpowered studies would fail to establish an effect that might become apparent in a pooled analysis. They included nonrandomized trials because they were not comfortable restricting the analysis to randomized controlled trials. (An alternative approach would be to use metaregression to examine whether the magnitude of effect differed between randomized and observational studies; if it did, the meta-analysis could be done in subgroups.) The authors weighted the studies according to sample size and quality. They used appropriate analytic techniques to look for publication bias and, finding no evidence of such a bias, they restricted the analysis to published studies. In addition to stating the results of these analyses of publication bias, displaying the graphical evidence would have been helpful to readers.

Bauwens et al.(1) concluded that the studies that they wished to synthesize were heterogeneous. Having established heterogeneity, the authors could have simply decided not to pool the studies at all. Alternatively, they could have developed a metaregression model, which would have been useful in identifying and ultimately controlling for sources of heterogeneity. They could have stratified according to such characteristics and tested whether the stratified meta-analysis would have yielded less heterogeneity. The authors did indeed perform a metaregression, but they did not use it to identify

strata in which studies were more homogeneous, as discussed here. By documenting heterogeneity and not doing anything about it, the authors in a sense, made a diagnosis without offering a remedy.

Data Sharing

Synthesizing the results of various studies is ultimately a collaborative activity. The investigator will often wish to contact other scientists who have access to original trial data or who themselves have attempted a data synthesis. These collaborations can help move the field forward. In fact, the National Institutes of Health (NIH) and other research sponsors have developed specific provisions for facilitating data sharing in order to best leverage the precious data garnered in NIH-funded studies. In this regard, we were particularly impressed by the willingness of Bauwens et al.(1) to share their data and we were disappointed that Mason et al.(2) chose to communicate their observations in a letter to The Journal without discussing the findings with the original authors. Readers, and ultimately patients, were not served well by this failure to behave collaboratively.

Concluding Remarks

The meta-analysis by Bauwens et al.(1) prompted questions about selection of studies, choice of common outcome measures across studies, assessment and management of heterogeneity, interpretation of results, and approaches to collaboration. The lessons learned from these studies of navigated total knee replacement are that investigators should make individual studies as definitive as possible by using the most rigorous designs feasible, powering studies adequately, and using standardized measures of outcome. Pooling is a powerful method for aggregating information across studies, but it is ultimately a collaborative effort. Leaders in the field should designate standard measures of outcome to facilitate pooling, and investigators should work collaboratively with one another so that data syntheses move the field forward, bringing quality and value to patients.

The authors did not receive any outside funding or grants in support

of their research for or preparation of this work. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

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"Review of Navigated Total Knee Replacement: A Meta Analysis by Bauwens et al."

25 July
2007



J. Bohannon
Mason, M.D.,

To The Editor:

OrthoCarolina Hip
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Thomas Fehring,
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Fahrbach, Ph.D.

Send letter to
journal:

Re: "[Review of
Navigated Total
Knee
Replacement: A
Meta Analysis by
Bauwens et al.](#)"

[E-mail](#) J.
Bohannon Mason,
M.D., et al.

We read with interest and concern the article, Navigated Total Knee Replacement: A Meta Analysis by Bauwens et al.(1). We submitted a similar meta-analysis to the Journal of Bone Surgery over one year ago, which was appropriately rejected for publication due to the inclusion of abstracts and uncontrolled case series data. The reviewers and editors also expressed concern that our finding of an advantage for navigated total knee arthroplasty (TKA) versus conventional TKA based on radiographic alignment endpoints needed to be balanced against the lack of evidence comparing the two procedures on cost-effectiveness, complication rates, and long term outcomes.

We were in the process of updating our meta-analysis in light of more recent publications (excluding abstract and uncontrolled case series data), when the study by Bauwens et al.(1) was published. Having reviewed essentially the same database, we were perplexed by the authors' conclusions that "navigated knee replacement provided few advantages over conventional surgery on the basis of radiographic endpoints", as our own meta-analysis revealed a significant improvement in radiographic endpoints with computer-assisted navigation.

Our concerns about the discrepancies between our findings and those of Bauwens et al. prompted us to investigate their source data. We contacted them, and they graciously provided us with the raw data for all studies included in their meta-analysis. Upon further review, we discovered multiple inaccuracies of data extraction and/or data entry in their analysis:

In four of the studies reviewed in the Bauwens article(2-5) the data for conventional techniques was entered into the navigated data set for analysis while the data for the navigated set was entered under conventional techniques.

In four additional studies(6-9) we were able to determine errors of data extraction, data entry, patient count or patient group assignment.

One paper(10) was included and counted as reporting mechanical axis data when this was not reported in the study.

A kinship study (i.e., a study sharing overlapping data with an already included study) was included that should have been excluded(11).

There were two additional studies (12,13) in which the numbers we extracted were slightly different from those in Bauwens et al; we note these only as discrepancies (not errors) in extraction.

Our further review of their paper also suggests that their labeling and description of results was misleading. Specifically, they describe their meta-analyses as those of “relative risk of malalignment”, and label their figures accordingly. Yet, in the discussion, they state that “the available data suggest that navigation reduces the relative risk of 3 degrees of malalignment by 25%”. This statement is in error, because their meta-analysis was not of the relative risk of malalignment, but rather the relative risk of alignment, (i.e., the chance that a patient has alignment after the procedure). It would, therefore, have been accurate for them to state that conventional total knee arthroplasty decreases the relative chance of alignment by 25%. When misfit is the outcome of choice, instead of fit, the results are quite different from those reported by Bauwens et al. Correctly stated, the risk of malalignment is approximately three times that with conventional replacement relative to CAS.

In conclusion, our findings of data extraction and entry errors cause us to challenge the conclusions in the article regarding the meta-analysis of radiographic endpoints in conventional versus navigated knee replacement surgery. A correct data analysis demonstrates overwhelming evidence of a much lower error rate with navigation. Reversal of some of the extracted data and misreporting relative risks for fit as risks of malalignment is partially responsible for the muted difference that Bauwens described between navigated and conventional total knee arthroplasty. These errors, however, do not obviate Bauwens’ other discussion

points regarding methodological limits of the available trials, including a dearth of evidence on long term outcomes, quality of life, and costs.

While we recognize and understand the challenges inherent in performing meta-analyses, our intent is to bring these errors to the attention of the readers of the Journal to correct any erroneous impression this work may have left with the readership.

In support of their research for or preparation of this work, one or more of the authors received, in any one year, outside funding or grants in excess of \$10,000 from Depuy, and Johnson & Johnson. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

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Dr. Stengel et al. respond to Dr. Mason.

25 July
2007



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Send letter to
journal:

[Re: Dr. Stengel et
al. respond to Dr.
Mason.](#)

[E-mail](#) Dirk
Stengel, M.D.,
Ph.D, MSc., et al.

We read with great interest the letter from Dr. Mason and colleagues. Since they raised substantial concerns about the validity of our findings, we carefully reviewed the dataset that formed the basis for all analyses and figures presented in the Journal.

We reviewed our references 2-5 and found that there was no data shift between the conventional and navigated groups. This was unlikely, since the forest plots consistently showed an advantage for the navigated cohort.

Mason et al. also claimed that they found additional errors of data extraction from our references 6 to 9, but unless they are more specific in their criticisms, we cannot respond properly.

We would refer the Dr. Mason et al. to the Methods Section of our paper, where we stressed that the numbers of patients were extracted from histograms whenever possible. This may explain most differences eventually noted between their and our dataset. Additional differences might be related to different handling of the unit of interest, that is, the patient or the knee. Indeed, Bolognesi and Hofmann(1) reported the alignment of the femoral and the tibial component rather than the mechanical axis. However, if navigation improves both femoral and tibial component alignment, it is very likely that the resulting mechanical axis will be optimized as well. Since the observed effects were consistent with others, we decided to include the study in our analysis. We definitely identified and excluded some kinship studies, but could not retrieve a dual publication published by Mielke and colleagues(2).

When posing a null-hypothesis it is important to define the accepted standard of care. Risk ratios and other relative measures are asymmetric. This was the reason why we also provided risk differences, that can be used for calculating the number needed

to treat. Currently, navigation is an experimental add-on, and may either decrease the risk of malalignment, or increase the chance of alignment. It is, however, not justified to argue that conventional surgery would increase the relative risk of malalignment over navigated component placement. With regard to health policy decisions, this is a dangerous statement, since it would imply that all patients who are not operated on with computer assistance are at a higher risk of malalignment when compared to those who undergo conventional TKA by an experienced surgeon.

Importantly, our analyses and plots showed a significant advantage of navigated over conventional knee replacement in radiological surrogates, so we are in complete agreement with Dr. Mason. Yet, unless these advantages are consistent with improved outcomes, we feel that our conclusion "Navigated knee replacement provides few advantages over conventional surgery on the basis of radiographic end points" is valid.

Finally, we regret that Dr. Mason, after receiving our dataset (which shows our openness and willingness to engage in scientific debate), did not contact us again to compare both datasets, and to discuss, explore and resolve any possible differences jointly before submitting a Letter to the Editor challenging our scientific reputation. We are sorry that Dr. Mason's group could not publish their paper, but we are deeply disappointed in their behavior.

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Navigated Total Knee Arthroplasty-- a Meta-analysis

27 March
2007

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Graeme Holt.

To The Editor:

In their recent meta-analysis(1), Bauwens et al. concluded that "navigated knee replacement provides few advantages.....on the basis of radiographic end points". However, our analysis of this paper suggests that this conclusion is invalid.

Send letter to
journal:

[Re: Navigated
Total Knee
Arthroplasty--a
Meta-analysis](#)

[E-mail](#) Alberto
Gregori, et al.

While meta-analysis of randomised controlled trials represents the gold standard in validation of surgical interventions, overcoming the reduced statistical power of small sample sizes, it cannot compensate for poor scientific methodology in the analyzed papers. The authors (1) included not only randomised, but also quasi-randomized controlled trials, non- randomized cohort studies, studies with historical cohorts, and studies investigating the outcome of CT or image-free navigation systems for both unicompartmental and total knee arthroplasty.

A meta-analysis must use a predefined, documented search strategy allowing assessment of its completeness; this was not reported. "Mean straightness of mechanical axes" is an inappropriate outcome measure. The mean mechanical axis says nothing about the distribution of values that it represents without reporting standard deviations and range, though 95% confidence intervals were stated. However, two groups may have significantly different distributions of alignment values centered about similar mean values.

Navigation reduces the number of implants with a predetermined variance from the true mechanical axis, commonly defined as $\pm 3\sigma$. The authors estimate a risk ratio of a deviation of $>3^\circ$ with navigated versus conventional knee arthroplasty at 0.79 and 0.76 for a threshold of 2σ . Navigation reduced the relative risk of $>3^\circ$ malalignment by 25% thus avoiding one additional patient with unfavorable component positioning in any five patients managed with computer-assisted instead of jig-based methods.

The authors conclude that “the benefits of navigation diminished rapidly with increasing thresholds of proper implant positioning”. If we were to accept a deviation of up to 6 degrees from the true mechanical axis then both conventional jig and navigation based arthroplasty are almost equally efficacious; however, this degree of error is greater than most arthroplasty surgeons would accept.

Navigated total knee arthroplasty improves implant alignment, but consequent improved implant survival remains unproven. We are concerned that this meta-analysis(1) will be regarded by many as definitive evidence even though its methodological shortcomings and interpretation of results do not justify the conclusions reached.

The authors did not receive any outside funding or grants in support of their research for or preparation of this work. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. A commercial entity (Biomet & BBraun) paid or directed in any one year, or agreed to pay or direct, benefits in excess of \$10,000 to a research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

Reference:

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**Dr. Stengel & Dr. Bauwens respond
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27 March
2007



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[Re: Dr. Stengel &](#)

We read with great interest the comments of Alberto Gregori and Graeme Holt on our meta-analysis. We believe all the issues they raise were clearly addressed in the printed article and the electronic appendix, but we will be happy to respond to their letter in a point-to-point fashion.

1. We do not agree that the conclusion of the abstract conflicts with current best evidence. Most trials focused on alignment, not function, quality of life, or cost. We feel that all would agree that higher

[Dr. Bauwens
respond to Dr.
Gregori & Dr. Holt](#)

[E-mail](#) Dirk
Stengel, M.D.,
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precision in restoring the physiological limb axis is an advantage of navigated over conventional total knee replacement, but patient-centered and health-economic values have more weight in clinical and political decision making. In the Discussion, we stressed the need for high-quality trials aiming at investigating clinically relevant outcomes.

2. Meta-analyses (especially in orthopedics) are often criticized for including only RCT, thereby limiting the external validity of the results. We are very much aware of the discrepancy between methodological and clinical demands. In the methods section, we clearly pointed out that we conducted a meta-regression analysis to account for different study designs. There was no meaningful difference in effect estimates between RCT and other study settings.

All key features of our search strategy were mentioned in the methods section. Specifically, we (i) reported all databases searched, (ii) tried diligently to avoid a tower of Babel bias by including studies of all languages, (iii) did a manual search, (iv) reported the study selection in a QUOROM flow-chart, (v) assessed methodological features by two or more independent raters, (vi) tested for publication bias and statistical heterogeneity. If we had missed any important quality criterion of a valid meta-analysis (or a relevant paper that contradicts our findings), we would be pleased to be informed by Drs.Gregori and Holt.

4. In the Discussion, we admitted the limits of the chosen endpoints- however, as indicated in their letter, this was not a shortcoming of the quantitative summary, but the lack of reporting of other endpoints in the original manuscripts.

Dr. Gregori and Dr. Holt conclude that navigated total knee arthroplasty improves implant alignment, but consequent improved implant survival remains unproven. We are happy about this conclusion, since it perfectly agrees with the findings of our meta-analysis.

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective¹ as expressed by the following standards.²

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.³

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

¹ Based on Legislative mandate: See RCW 70.14.100(2).

² The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

³ The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. *Availability of Evidence:*

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. *Sufficiency of the Evidence:*

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence⁴ using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. *Factors for Consideration - Importance*

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

Medicare Coverage and Guidelines

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
<p>CMS National Policy Decisions – WA HTA Page: 39</p> <p>Centers for Medicare and Medicaid Services</p>		No NCD	No	
<p>Guidelines – WA HTA Page: 36</p> <p><i>National Guideline Clearinghouse</i></p>		No specific guidelines were found that addressed unicompartmental, bicompartamental, bi-unicompartmental, total knee arthroplasty, or computed-assisted knee arthroplasty for the treatment of end-state knee arthritis.		
<p>Guidelines – WA HTA Page: 36</p> <p><i>National Institute for Health and Clinical Excellence (NICE)</i></p>		No specific guidelines were found that addressed unicompartmental, bicompartamental, bi-unicompartmental, total knee arthroplasty, or computer-assisted knee arthroplasty for the treatment of end-stage knee arthritis from the National Institute for Health and Clinical Excellence (NICE), which provides guidance on health technologies and clinical practice for the National Health Service in England and Wales.		
<p>Guidelines – WA HTA Page: 36-37</p> <p><i>NIH Consensus Statement on Total Knee Replacement</i></p>	2003	<p>Technical factors in performing surgery may influence both the short- and long-term success rates. Proper alignment of the prosthesis appears to be critical in minimizing long-term wear, risk of osteolysis, and loosening of the prosthesis. Computer navigation may eventually reduce the risk of substantial malalignment and improve soft tissue balance and patellar tracking. However, the technology is expensive, increasing operating room time, and the benefits remain unclear.</p> <p>There is clear evidence of racial/ethnic and gender disparities in the provision of TKR in the United States. The limited role of economic and other access factors in these racial or ethnic disparities can be demonstrated by significant differences in the rate of procedures in the VA system, where cost and access are assumed equivalent across race or ethnic groups.</p>	Evidence cited	

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
<p>Guidelines – WA HTA Page: 37</p> <p><i>Ontario Health Technology Advisory Committee (OHTAC)</i></p>	<p>2004</p>	<p>Concluded that computer-assisted arthroplasty using navigation systems is considered to be in the investigational stage. Current studies have only assessed short-term outcomes, and long-term effectiveness (need for revision, implant longevity, pain, and functional performance) has not been demonstrated.</p>		
<p>Guidelines – WA HTA Page: 37</p> <p><i>Osteoarthritis Research Society International (OARSI)</i></p>		<p>OARSI published 23 treatment guidelines for the management of hip and knee osteoarthritis identified from a literature search, including six opinion based, five evidence-based and 12 based on both expert opinion and research evidence. Relevant guidelines for this report are:</p> <p>Unicompartmental knee replacement is effective in patients with knee osteoarthritis restricted to a single compartment.</p> <p>For the young and physically active patient with significant symptoms from unicompartmental knee osteoarthritis, high tibial osteotomy may offer an alternative intervention that delays the need for joint replacement some 10 years.</p>	<p>Evidence cited</p>	
<p>Guidelines – WA HTA Page: 37</p> <p><i>American Academy of Orthopedic Surgeons (AAOS)</i></p>		<p>No specific clinical guidelines for knee arthroplasty were found; however, recommendations are due to be published in September 2010.</p>		

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

Safety Outcomes	Safety Evidence
Mortality	
Morbidity	
Venous Thromboembolism (VTE) <ul style="list-style-type: none"> ▪ Deep Vein Thrombosis (DVT) ▪ Pulmonary Embolism (PE) 	
Ischemic Events	
Wound Complications	
Tourniquet Time	
Operative Time	
Revision and removal rates	
Infections	
Other Adverse Events	
Efficacy – Effectiveness Outcomes	Efficacy / Effectiveness Evidence
Pain Relief <ul style="list-style-type: none"> - Short term - Med term - Long term 	
Functional improvement <ul style="list-style-type: none"> - Short term - Med/long term 	
Quality of Life <ul style="list-style-type: none"> - Short term - Med/long term 	
Revision or Failure	
Range of Motion	

Patient Satisfaction	
Prosthesis Survival	
Radiographic & Motion Outcomes	
Return to work (employment)	
Other Patient outcomes	
Special Population / Considerations Outcomes	Special Population Evidence
Type of Arthritis <ul style="list-style-type: none"> ▪ Rheumatoid arthritis ▪ Osteoarthritis 	
Gender	
Age	
BMI / Obesity	
Provider Facility	
Surgeon Volume	
Co-morbidities <ul style="list-style-type: none"> ▪ Psychological ▪ Psychosocial 	
Preoperative Pain Levels	
Patient Selection	
Payer or Beneficiary Type	
Cost	Cost Evidence
Cost Implications	
Cost Effectiveness	

Clinical Committee Evidence Votes

First voting question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective				
Safe				
Cost-effective				

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____ Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

- 1) Does the committee have enough information to identify conditions or criteria?
 - Refer to evidence identification document and discussion.
 - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
 - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.
- 2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
 - What are the known conditions/criteria and evidence state
 - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
 - Direct outcome or surrogate measure
 - Short term or long term effect
 - Magnitude of effect
 - Impact on pain, functional restoration, quality of life
 - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
 - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
 - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
 - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?