Universiteit Antwerpen

This item is the archived peer-reviewed author-version of:

Cost-effectiveness of bone SPECT/CT in painful total knee arthroplasty

uantwerpen.be

Cost-Effectiveness of Bone SPECT/CT in Painful Total Knee Arthroplasty

Tim Van den Wyngaert, MD, PhD [1,2]; Swetha R. Palli, MS [3]; Ryan J. Imhoff, MS [3]; Michael T. Hirschmann, MD [4,5]

[1] Nuclear Medicine, Antwerp University Hospital, Edegem, Belgium

[2] Faculty of Medicine and Health Sciences, University of Antwerp, Wilrijk, Belgium

[3] CTI Clinical Trial and Consulting Services, 100 E. RiverCenter Blvd
Covington, KY 41011 Tel: 513.598.9290 Fax: 513.7581710
SwethaRao.Palli@gmail.com, RImhoff@ctifacts.com

[4] Department of Orthopaedic Surgery and Traumatology, Kantonsspital Baselland (Bruderholz, Liestal, Laufen), Bruderholz, Switzerland Tel: +41 61 436 30 37
Fax: +41 61 436 36 50

[5] University of Basel, Basel, Switzerland, Michael.Hirschmann@unibas.ch

Corresponding author's Full affiliations:

Tim Van den Wyngaert, MD, PhD

Department of Nuclear Medicine
Antwerp University Hospital
Wilrijkstraat 10
2650 Edegem - Belgium

Molecular Imaging Center Antwerp (MICA)
University of Antwerp
Campus Drie Eiken - Building Uc
Universiteitsplein 1
2610 Wilrijk - Belgium

Tel: +32 3 821 34 97
Fax: +32 3 825 33 08

Email: tim.van.den.wyngaert@uza.be

Running title: Cost-utility of bone SPECT/CT in TKA

1

ABSTRACT

Purpose: To quantify the economic value of bone single-photon emission computed tomography (SPECT) with computed tomography (CT; SPECT/CT) versus CT or metal artifact reduction sequence (MARS) magnetic resonance imaging (MRI) for the diagnostic assessment of recurrent moderate-to-severe pain after total knee arthroplasty (TKA).

Methods: An Excel-based simulation model was developed to compare bone SPECT/CT versus CT or MARS-MRI from a payer perspective. Clinical endpoints (diagnosis – delayed or otherwise, and the subsequent treatment and complications) and their corresponding cost data (2017 United States dollars) were obtained by performing a best evidence review of the published literature. Studies were pooled and parameters weighted by sample size. A cost utility analysis was performed estimating the incremental cost per quality adjusted life years (QALYs) gained between bone SPECT/CT and the comparative scans. One-way (±25%) sensitivity analysis was performed to gauge the model robustness.

Results: For every 1,000 TKA patients, diagnostic bone SPECT/CT was expected to lead to three-year cost savings up to $1,867,695 vs. CT (or $622.6 per-patient-per-year) and $1,723,435 vs. MARS-MRI (or $574.5 per-patient-per-year) for a payer. With corresponding incremental QALY gains of 39.7 and 41.0 against CT and MARS-MRI, SPECT/CT can be considered as a cost-saving and dominant strategy in the work-up of persistent/recurrent pain in TKA patients. The model was limited by the still sparse literature data, was most sensitive to imaging-related sensitivity/specificity, but proved robust for varying prevalence of surgical/non-surgical causes of pain.

2

Conclusion: Bone SPECT/CT is a potentially highly cost-saving and dominant imaging intervention versus CT or MARS-MRI scanning in patients with recurrent and persistent knee pain after TKA.

INTRODUCTION

A record number of 4.7 million Americans were alive with a total knee arthroplasty (TKA) in 2010 and the annual number of procedures is projected to increase to 3.5 million by 2030 (*1,2*). In parallel, the TKA revision rate has increased 105.9% between 1991 and 2010 (*3*). With a cost that is 60% higher than the primary procedure, this poses a considerable budgetary challenge and emphasizes the need for careful patient selection (*4*). The most frequent indications for revision TKA are newly onset or persistent pain, (*5-7*) instability, stiffness or periprosthetic joint infection (*8*). Even though pain recurrence after TKA is well documented, the reported prevalence varies widely (between 4.8% to 44%). Identifying the precise cause of pain remains challenging as symptoms and history often lack specificity (*9-14*). This may delay a correct diagnosis, postpone optimal therapeutic intervention, increase the cost of the diagnostic work-up, and can potentially adversely affect patient outcome (*8*).

Current modalities used in TKA imaging include conventional radiographs, stress radiographs, computed tomography (CT), magnetic resonance imaging (MRI), planar bone scintigraphy with or without single photon emission computed tomography (SPECT), or [^{18}F]fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT (*14*). Multi-detector CT offers better bone and implant detail compared to radiographs, which are considered the preferred first-line imaging procedure (*15-17*). CT can assess the extent of osteolysis, periprosthetic fractures, and TKA malpositioning, but the technique is limited in differentiating inactive from active anatomic lesions (*15*). More recently, due to improvements in metal artifact reduction sequence (MARS) protocols, there is renewed interest in the use of MRI in this setting (*15*). In parallel, fully integrated

4

SPECT/CT devices have overcome the limited spatial resolution of SPECT-only imaging, resulting in significantly improved diagnostic accuracy and providing a unique combination of simultaneous evaluation of skeletal anatomy and physiology (*14,16*). Moreover, the use of bone-affine tracers with SPECT/CT offers the advantage of linking bone turnover patterns with biomechanical information on TKA placement and loading (*18*). This additional information can assist in selecting appropriate clinical management and assessing whether further surgical treatment is warranted (*14,16,17,19*). However, it is unclear whether these clinical benefits translate into successful economic and humanistic (e.g. quality-of-life [QoL]) outcomes. Therefore, this economic simulation study aimed to quantify the potential economic value and cost-utility of bone SPECT/CT compared to other imaging technologies (CT, MARS-MRI) in assessing persistent or recurrent knee pain after TKA from a payer perspective.

METHODS

Model scaffold

The diagnostic algorithm published by Park et al. combines physical examination, radiographs and lab work-up to stratify patients toward further diagnostic procedures (*6*). Following this decision-tree, instability/malposition and acute infection were not considered within the current model, as these conditions may be adequately characterized without advanced imaging techniques. However, additional imaging may be required for the accurate diagnosis of a) implant loosening/wear/osteolysis, b) chronic low grade infection, c) patellofemoral problems (includes anterior knee pain, extensor mechanism problems, avascular necrosis, and patellar overstuffing/maltracking). Based on an extensive literature review, the model focused

on the differential diagnosis of these three conditions as these represent the most frequent causes of post-TKA pain (Fig. 1) (*14,16,20-41*). The model also assumed: [1] one primary causal condition; [2] a non-diagnostic CT would be complemented with a MARS-MRI and vice versa, and an equal split between CT and MARS-MRI when bone SPECT/CT was non-diagnostic; [3] the second imaging procedure was always diagnostic (to avoid an infinite loop); [4] in case of a non-diagnostic scan, a subsequent scan was done following 6-month medical pain management regimen; [5] medical management involved a 70:30 mix of nonsteroidal anti-inflammatory drugs (NSAIDS) plus physiotherapy or steroid injections with occasional non-narcotic analgesics (e.g., acetaminophen); with regular office visits for pain-monitoring and treatment of any adverse events (including general, cardiovascular or gastrointestinal toxicity, skin flares or sepsis); [6] medical management did not result in long-term relief given the severity of the underlying condition and associated functional limitations.

The study modeled a hypothetical cohort of 1,000 TKA patients experiencing recurrent moderate-to-severe pain over a three-year period. If diagnosed with a non-infectious cause, patients undergo a one-stage revision TKA: removal of TKA components and implantation of revision TKA (*42*). Primary patellar resurfacing was done in case of patellofemoral issues, while 13.8% of the loosening group also received secondary patellar resurfacing (Table 1) (*21*). For the chronic infection cohort, a two-stage exchange arthroplasty was performed: removal of all components, placement of a temporary antibiotic-laden cement spacer with subsequent extended intravenous and/or oral antibiotic regimen to eradicate the infection, followed by revision TKA (*43*). To model specificity, 10% of the cohort was assumed to have pain caused by other

6

conditions that did not require a surgical intervention, as first-line workup was expected to detect most of these patients before entering the modeled pathway (Fig. 1). The model also accounted for the risk of major and minor complications among the surgery patients (Table 2). Patients correctly treated with surgical intervention (true positives) were assumed to have no further treatment beyond the standard post-surgery management (e.g., physiotherapy and monitoring) and to remain pain-free for the duration of the study (Table 3). All improperly treated patients (i.e., the false positives and negatives) were assumed to have failed the treatment and to have derived no benefits. These patients continued to experience painful knees of undetermined origin and spend at least two years (*44*) in identifying the true cause of their condition before undergoing delayed TKA revision. During this wait-and-watch strategy, patients received [1] annual radiographs and a CT scan and [2] intensive medical management (70:30 mix of NSAIDS and steroid injections) with physiotherapy. Concurrently, quarterly visits to an orthopedic surgeon or general practitioner for consulting and management reasons were included. True negatives continued to be on a medical management pathway. These event pathways were constructed based on literature review and clinical expert opinion.

A best evidence review of PubMed articles published between 1/1/2006 and 3/31/2017 was performed to obtain default parameter values. Selection criteria included English language studies considered to be most relevant (e.g., adult human subjects, in vivo) to the clinical and imaging application(s) in question. Case reports and case series with sample size less than 15 (arbitrarily chosen) were excluded. For the imaging-related parameters, studies assessing sensitivity, specificity and/or non-diagnostic rates

7

were identified. Descriptive data from single modality series was used if direct comparison data was unavailable. Sample size weighted estimates were synthesized in case of multiple data sources to mitigate outlier bias (*45*).

Health states

Seven health states were considered in total (Fig. 2). Post-revision surgery, a transition was assumed within 3 months, to one of the following: full benefit state, an early failed/limited benefit state, or death. The latter was an absorbing state because of surgical mortality. A successfully revised patient was allocated to the full benefit health state until the end of the model. False positives and negatives entered the failed/limited benefit state. After the implementation of the 'wait-and-watch' strategy, they would be correctly treated for the underlying cause of the pain, before transitioning to the full-benefit state.

Utilities

Utility factors (0=death; 1=perfect health) were assigned to all health states (based on orthopedic literature data) to adjust survival for QoL and were expressed as quality-adjusted life years (QALYs) by multiplying the length of time spent in a health state with its corresponding utility (Table 4) (*46*). To represent the short-term negative impact of TKA revision on QoL (*47*) (reduced mobility, pain, and non-lethal complications after surgery), a one-time deduction was applied by multiplying the acute procedure toll with the recovery time (3 months) to the patient QALYs in the procedure year (*48*). Based on published evidence, the disutility of having a revision TKA was set at −0.19 with no distinction placed on the aseptic and septic cause given the low prevalence of chronic infection in our model (16.7%).

Cost estimates

To represent the payer's perspective, the 2017 national average Medicare professional and technical fees were extracted based on the specific Current Procedural Terminology (CPT) codes for each modality (*49*). Baseline revision arthroplasty procedure cost was derived from 2014 Healthcare Cost and Utilization Project data (*50*) with add-on costs for each additional complexity (e.g., antibiotic-laden spacer and antibiotic regimen for infectious patient,(*51*) patellar resurfacing,(*52*) and any perioperative complication(s) (*27,40,41,47,53-55*). Medical management costs accrued during the three-month post-surgery period accounting for care provided in inpatient settings, physician services, and post-acute care facilities (e.g., skilled nursing or rehabilitation facilities, home health, hospice, and/or long-term care) were included. Cost estimates were inflated to 2017 United States (US) dollars using the Bureau of Labor Statistics' US Medical Care Consumer Price Index (*56*). Non-Medicare (commercial) payments were calculated for persons aged ≤ 65 based on Medicare payments. Given the study's short time-frame, discounting was not considered.

Outcomes

For each imaging modality: the *total three-year cost burden* was the cumulative cost of [1] diagnostic imaging scan and re-scans; [2] revision surgery (surgery, perioperative complications) and post-surgical management; [3] medical management (office visits, physiotherapy, NSAIDs, injections, analgesics and any potential adverse events associated with these treatments); and [4] monitoring (radiographs, CT, surgeon consultations, office visits) during the 'wait-and-watch' approach. *Total QALYs* was

calculated as the sum of the utility of each of the seven health states multiplied by the time spent in each health state.

Cost-effectiveness of SPECT/CT was defined as the ratio of incremental difference in costs and QALYs between SPECT/CT and the comparator technique, and expressed as the incremental cost-effectiveness ratio of SPECT/CT per QALY gained.

Sensitivity analysis

In order to assess the impact of the individual model parameters and robustness of the findings, a one-way sensitivity analysis was conducted by varying each model parameter by ±25% of its basecase estimate. Further, the impact of the 10% prevalence of non-surgical causes on the results was explored in a separate sensitivity analysis, to increase the applicability of the model's findings in other care settings. This model was built using Excel 2013 (Microsoft Corporation. Redmond, WA, USA).

RESULTS

For every 1,000 TKA patients experiencing recurrent and persistent moderate-to-severe pain and undergoing diagnostic bone SPECT/CT, CT or MARS-MRI, the total three-year burden was expected to be $37,133,788, $39,001,483 and $38,857,223 respectively (Fig. 3). Therefore, SPECT/CT was found to result in $1,867,695 lesser costs for a payer versus CT over three years or $622.6 per-patient-per-year. SPECT/CT's lower costs against CT appeared to be primarily driven by its improved accuracy, thus avoiding undue surgeries and ad-hoc medical management for the major duration of the study period. Switching from MARS-MRI was also found to save the payer approximately $1,723,435 ($574.5 per-patient-per-year). SPECT/CT's relatively higher sensitivity and specificity reduced overall utilization which in turn, lowered costs

for the hybrid technology cohort. A total of 908, 926 and 914 revision surgeries were performed in the SPECT/CT, CT and MARS-MRI cohorts respectively, of which 1.7%, 18.8% and 16.9% were deemed as late/delayed procedures owing to a false negative diagnosis, respectively.

In terms of QALYs, SPECT/CT, CT and MARS-MRI were found to be associated with QALYs of 2,287.8, 2,248.1 and 2,246.8, respectively: i.e., QALY gains of 39.7 and 41.0 for SPECT/CT versus CT and MARS-MRI, respectively. The life-years gained were a direct function of the bone SPECT/CT cohort receiving the highest successful revision surgery rate early during the study period. CT's non-optimal management owing to its lower diagnostic rate and specificity was also found to have contributed to its lower QALYs. Since SPECT/CT was found to lower costs and improve QALYs, this imaging modality can be considered as a highly cost-effective and dominant strategy for diagnosing recurrent and persistent knee pain in TKA patients.

Sensitivity analyses

The model was most sensitive to imaging-related parameters, especially sensitivity/specificity, and 'wait-and-watch' period related costs (Fig. 4). SPECT/CT was found to be always cost-saving/neutral even with a ±25% change in their basecase parameter values. In addition, changing the prevalence of non-surgical causes of painful TKA affected the cost-savings and QALYs gained by SPECT/CT over CT and MARS-MRI in a proportional way, but it remained cost-saving and dominant (Supplemental Fig. 1).

11

DISCUSSION

Despite plateauing TKA failure times (mean 5.9 years),(*57-59*) increasing primary TKAs rates are driving the growing number of revision procedures (approximately 101,290 in the US in 2017) (*2*). With an average hospitalization cost of $29,584,(*50*) the total inpatient revision TKA burden in 2017 alone aggregated to nearly $3 billion, highlighting the impact on budgets and increasing strain on surgeons, patients, and health systems (*2,50*). A prompt and accurate diagnosis is pivotal, as the outcome of revision is very poor (failure rate up to 80%) if the root cause is left undetermined prior to surgery (*60*). Diagnostic algorithms to streamline the work-up and maximize their yield firmly rely on imaging procedures (*6,14*). It is therefore not surprising that imaging services account for 18.2% of payments of knee osteoarthritis-related healthcare expenditure, exceeding the cost of outpatient office evaluations and prescription non-narcotic analgesic medications (*61*). Hence, interventions that can improve diagnostic accuracy and assist surgeon decision-making will be of paramount importance for optimal patient management, long-term outcomes, and budget control. Integrated bone SPECT/CT is the newest entry in this space and is considered superior to conventional bone SPECT imaging because of its improved resolution, attenuation and scatter correction, and accurate anatomical localization (*62*). Indeed, very high diagnostic accuracies of bone SPECT/CT have recently been reported for evaluating knee prosthesis patients, translating into a change in diagnosis and/or treatment plan in nearly 50.7% (16-85.5%) of cases (*14,16,17,19*) compared to the impact of MRI or CT which was only 36-48.8% (*24,63,64*). The current study, to our knowledge, is the first to evaluate the value of bone SPECT/CT from a cost perspective.

For every 1,000 patients experiencing moderate-to-severe persistent pain post-TKA, the three-year burden was calculated to be $37.1, $39.0 and $38.9 million for diagnostic SPECT/CT, CT or MARS-MRI, respectively. SPECT/CT's cost savings (per-patient-per-year of $622.6 and $574.5 versus CT and MARS-MRI, respectively) are driven by its higher diagnostic accuracy and reduction of unnecessary revision surgeries (18 and 6 procedures for every 1000 CT/MARS-MRI patients switching to SPECT/CT). In addition, avoiding surgeries saved 17 (vs. CT) and 14 (vs. MARS-MRI) more lives, thereby improving SPECT/CT cohort's survival by 2% and 1%, respectively. SPECT/CT was also found to be associated with QALY gains of 39.7 and 41.0 compared to CT and MARS-MRI making it a dominant intervention. The additional life-years gained by the SPECT/CT cohort are likely realized by redirecting patients sooner to the appropriate surgical intervention compared to other techniques, while CT's non-optimal management (e.g., high non-diagnostic rate) further lowered QALYs in that group. Indeed, early and timely management at relieving pain may prevent the domino effect of a chronic failed state on a patient's QoL. Conservatively, our model did not assume an increase in pain severity during the two-year 'wait-and-watch' period, even though this may be important (*44,65*).

Incorporating novel imaging techniques like SPECT/CT in the pre-surgery work-up may contribute to improved selection of appropriate surgical approach. Indeed, identifying the origin of the pain and whether or not it has a surgically rectifiable cause is critical to optimize patient management. Coupled with the anticipated rise in revision procedures, SPECT/CT may prove to be an important component to optimize revision arthroplasty effectiveness. We recognize that the management of painful TKA requires a

multidisciplinary approach involving surgeons, physiotherapists, and pain management teams (*7*) and the optimal use of SPECT/CT will require a further intensive collaboration of the referring orthopedic surgeon and the nuclear medicine physician and/or radiologist (*14*). This could be facilitated by the introduction of multi-disciplinary team discussions, similar to those ubiquitously established in the oncology setting.

Limitations

Like every economic analysis, this model is limited by its simplistic real-world representation. In particular, it focuses only on the top three of most common intrinsic pathologies requiring surgery, and assumes a singular causal condition. Conflicting reports exist in implicating aseptic (polyethylene wear, prosthetic loosening, and instability) and septic indications as the primary mechanism for failed TKA. Variability also exists across patient characteristics, failure modes, procedure types, and utilization across hospitals and regions, which the model does not address (*21*). The reader should therefore carefully assess the applicability of our findings to their own context. It should also be acknowledged that available literature evaluating the accuracy of imaging tests is relatively sparse, the published studies often had small patient numbers, and differed with respect to image acquisition protocols (which may evolve over the time) and reference standards (typically a composite of clinical, radiological, laboratory and surgical follow-up). None of the included studies on SPECT/CT or CT implemented MAR techniques that may further improve their accuracy. However, this limitation in our dataset applied to both techniques and did not favor one above the other. Taken together, our results are subject to the heterogeneity present in current literature data but are sufficiently provocative to merit further research.

CONCLUSION

For every 1,000 patients experiencing moderate-to-severe persistent pain post-TKA, the total three-year burden was calculated to be $37.1, $39.0 and $38.9 million for bone SPECT/CT, CT or MARS-MRI, respectively leading to SPECT/CT's per-patient-per-year cost savings of $622.6 (vs. CT) and $574.5 (vs. MARS-MRI). With corresponding incremental QALY gains of 39.7 and 41.0 against CT and MARS-MRI, SPECT/CT can be considered as a cost-saving and dominant strategy for orthopedic knee diagnostic purposes. Future evaluation of this technique in a larger number of patients and multiple centers, possibly in a prospective and controlled fashion, would help to more confidently address the value of this technique.

Disclosures

This study was sponsored by GE Healthcare. Dr. Van den Wyngaert has nothing to disclose. Swetha R. Palli and Ryan J. Imhoff are employees of CTI Clinical Trial and Consulting Services, Inc. which is a paid consultant to GE Healthcare. Dr. Hirschmann reports personal fees from DepuySynthes, Lima, Symbios, Smith&Nephew, and Arthrex, as well as grants from Finceramica, Italy, outside the submitted work.

15

REFERENCES

1. Maradit Kremers H, Larson DR, Crowson CS, et al. Prevalence of total hip and knee replacement in the united states. *J Bone Joint Surg Am.* 2015;97:1386-1397.

2. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the united states from 2005 to 2030. *J Bone Joint Surg Am.* 2007;89:780-785.

3. Cram P, Lu X, Kates SL, Singh JA, Li Y, Wolf BR. Total knee arthroplasty volume, utilization, and outcomes among medicare beneficiaries, 1991-2010. *JAMA.* 2012;308:1227-1236.

4. Burns AW, Bourne RB, Chesworth BM, MacDonald SJ, Rorabeck CH. Cost effectiveness of revision total knee arthroplasty. *Clin Orthop Relat Res.* 2006;446:29-33.

5. Baker PN, van der Meulen JH, Lewsey J, Gregg PJ. The role of pain and function in determining patient satisfaction after total knee replacement. Data from the national joint registry for England and Wales. *J Bone Joint Surg Br.* 2007;89:893-900.

6. Park CN, White PB, Meftah M, Ranawat AS, Ranawat CS. Diagnostic algorithm for residual pain after total knee arthroplasty. *Orthopedics.* 2016;39:e246-252.

7. Toms AD, Mandalia V, Haigh R, Hopwood B. The management of patients with painful total knee replacement. *J Bone Joint Surg Br.* 2009;91:143-150.

8. Mandalia V, Eyres K, Schranz P, Toms AD. Evaluation of patients with a painful total knee replacement. *J Bone Joint Surg Br.* 2008;90:265-271.

9. Elson DW, Brenkel IJ. A conservative approach is feasible in unexplained pain after knee replacement: A selected cohort study. *J Bone Joint Surg Br.* 2007;89:1042-1045.

10.   Brander VA, Stulberg SD, Adams AD, et al. Predicting total knee replacement pain: A prospective, observational study. *Clin Orthop Relat Res.* 2003:27-36.

11.   Meftah M, Ranawat AS, Ranawat CS. The natural history of anterior knee pain in 2 posterior-stabilized, modular total knee arthroplasty designs. *J Arthroplasty.* 2011;26:1145-1148.

12.   Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: Prevalence, sensory qualities, and postoperative determinants. *Pain.* 2011;152:566-572.

13.   Hirschmann MT, Becker R. *The unhappy total knee replacement: A comprehensive review and management guide.* 1st ed. Cham, Switzerland: Springer International Publishing; 2015: XXVI, 823.

14.   Hirschmann MT, Amsler F, Rasch H. Clinical value of spect/ct in the painful total knee arthroplasty (TKA): A prospective study in a consecutive series of 100 tka. *Eur J Nucl Med Mol Imaging.* 2015;42:1869-1882.

15.   Sneag DB, Bogner EA, Potter HG. Magnetic resonance imaging evaluation of the painful total knee arthroplasty. *Semin Musculoskelet Radiol.* 2015;19:40-48.

16.   Hirschmann MT, Konala P, Iranpour F, Kerner A, Rasch H, Friederich NF. Clinical value of SPECT/CT for evaluation of patients with painful knees after total knee arthroplasty--a new dimension of diagnostics? *BMC Musculoskelet Disord.* 2011;12:36.

17.   Al-Nabhani K, Michopoulou S, Allie R, et al. Painful knee prosthesis: Can we help with bone SPECT/CT? *Nucl Med Commun.* 2014;35:182-188.

18.   Rasch H, Falkowski AL, Forrer F, Henckel J, Hirschmann MT. 4D-SPECT/CT in orthopaedics: A new method of combined quantitative volumetric 3D analysis of

SPECT/CT tracer uptake and component position measurements in patients after total knee arthroplasty. *Skeletal Radiol.* 2013;42:1215-1223.

19. Arican P, Okudan Tekin B, Sefizade R, Naldoken S, Bastug A, Ozkurt B. The role of bone spect/ct in the evaluation of painful joint prostheses. *Nucl Med Commun.* 2015;36:931-940.

20. Niinimaki T, Eskelinen A, Makela K, Ohtonen P, Puhto AP, Remes V. Unicompartmental knee arthroplasty survivorship is lower than TKA survivorship: A 27-year Finnish registry study. *Clin Orthop Relat Res.* 2014;472:1496-1501.

21. Bozic KJ, Kamath AF, Ong K, et al. Comparative epidemiology of revision arthroplasty: Failed tha poses greater clinical and economic burdens than failed TKA. *Clin Orthop Relat Res.* 2015;473:2131-2138.

22. Mortazavi SM, Molligan J, Austin MS, Purtill JJ, Hozack WJ, Parvizi J. Failure following revision total knee arthroplasty: Infection is the major cause. *Int Orthop.* 2011;35:1157-1164.

23. Dalury DF, Pomeroy DL, Gorab RS, Adams MJ. Why are total knee arthroplasties being revised? *J Arthroplasty.* 2013;28:120-121.

24. Vessely MB, Frick MA, Oakes D, Wenger DE, Berry DJ. Magnetic resonance imaging with metal suppression for evaluation of periprosthetic osteolysis after total knee arthroplasty. *J Arthroplasty.* 2006;21:826-831.

25. Patil N, Lee K, Huddleston JI, Harris AH, Goodman SB. Aseptic versus septic revision total knee arthroplasty: Patient satisfaction, outcome and quality of life improvement. *Knee.* 2010;17:200-203.

26.   Robertsson O, W-Dahl A. The risk of revision after tka is affected by previous HTO or UKA. *Clin Orthop Relat Res.* 2015;473:90-93.

27.   Schairer WW, Vail TP, Bozic KJ. What are the rates and causes of hospital readmission after total knee arthroplasty? *Clin Orthop Relat Res.* 2014;472:181-187.

28.   Lyons MC, MacDonald SJ, Somerville LE, Naudie DD, McCalden RW. Unicompartmental versus total knee arthroplasty database analysis: Is there a winner? *Clin Orthop Relat Res.* 2012;470:84-90.

29.   Johnson AJ, Sayeed SA, Naziri Q, Khanuja HS, Mont MA. Minimizing dynamic knee spacer complications in infected revision arthroplasty. *Clin Orthop Relat Res.* 2012;470:220-227.

30.   Kim KT, Lee S, Ko DO, Seo BS, Jung WS, Chang BK. Causes of failure after total knee arthroplasty in osteoarthritis patients 55 years of age or younger. *Knee Surg Relat Res.* 2014;26:13-19.

31.   Sharkey PF, Lichstein PM, Shen C, Tokarski AT, Parvizi J. Why are total knee arthroplasties failing today--has anything changed after 10 years? *J Arthroplasty.* 2014;29:1774-1778.

32.   Parratte S, Lunebourg A, Ollivier M, Abdel MP, Argenson JN. Are revisions of patellofemoral arthroplasties more like primary or revision TKAs. *Clin Orthop Relat Res.* 2015;473:213-219.

33.   Baker P, Cowling P, Kurtz S, Jameson S, Gregg P, Deehan D. Reason for revision influences early patient outcomes after aseptic knee revision. *Clin Orthop Relat Res.* 2012;470:2244-2252.

34.   Le DH, Goodman SB, Maloney WJ, Huddleston JI. Current modes of failure in TKA: Infection, instability, and stiffness predominate. *Clin Orthop Relat Res.* 2014;472:2197-2200.

35.   Metsna V, Vorobjov S, Martson A. Prevalence of anterior knee pain among patients following total knee arthroplasty with nonreplaced patella: A retrospective study of 1778 knees. *Medicina (Kaunas).* 2014;50:82-86.

36.   Kasahara Y, Majima T, Kimura S, Nishiike O, Uchida J. What are the causes of revision total knee arthroplasty in japan? *Clin Orthop Relat Res.* 2013;471:1533-1538.

37.   Koh IJ, Cho WS, Choi NY, Kim TK. Causes, risk factors, and trends in failures after TKA in Korea over the past 5 years: A multicenter study. *Clin Orthop Relat Res.* 2014;472:316-326.

38.   van Kempen RW, Schimmel JJ, van Hellemondt GG, Vandenneucker H, Wymenga AB. Reason for revision TKA predicts clinical outcome: Prospective evaluation of 150 consecutive patients with 2-years followup. *Clin Orthop Relat Res.* 2013;471:2296-2302.

39.   Hossain F, Patel S, Haddad FS. Midterm assessment of causes and results of revision total knee arthroplasty. *Clin Orthop Relat Res.* 2010;468:1221-1228.

40.   Gooding CR, Masri BA, Duncan CP, Greidanus NV, Garbuz DS. Durable infection control and function with the prostalac spacer in two-stage revision for infected knee arthroplasty. *Clin Orthop Relat Res.* 2011;469:985-993.

41.   Greidanus NV, Peterson RC, Masri BA, Garbuz DS. Quality of life outcomes in revision versus primary total knee arthroplasty. *J Arthroplasty.* 2011;26:615-620.

42. Peersman G, Jak W, Vandenlangenbergh T, Jans C, Cartier P, Fennema P. Cost-effectiveness of unicondylar versus total knee arthroplasty: A Markov model analysis. *Knee.* 2014;21 Suppl 1:S37-42.

43. Lichstein P, Su S, Hedlund H, et al. Treatment of periprosthetic knee infection with a two-stage protocol using static spacers. *Clin Orthop Relat Res.* 2016;474:120-125.

44. Piscitelli P, Iolascon G, Innocenti M, et al. Painful prosthesis: Approaching the patient with persistent pain following total hip and knee arthroplasty. *Clin Cases Miner Bone Metab.* 2013;10:97-110.

45. Toney LK, Kim RD, Palli SR. The economic value of hybrid single-photon emission computed tomography with computed tomography imaging in pulmonary embolism diagnosis. *Acad Emerg Med.* 2017;24:1110-1123.

46. Soohoo NF, Sharifi H, Kominski G, Lieberman JR. Cost-effectiveness analysis of unicompartmental knee arthroplasty as an alternative to total knee arthroplasty for unicompartmental osteoarthritis. *J Bone Joint Surg Am.* 2006;88:1975-1982.

47. Mather RC, 3rd, Hug KT, Orlando LA, et al. Economic evaluation of access to musculoskeletal care: The case of waiting for total knee arthroplasty. *BMC Musculoskelet Disord.* 2014;15:22.

48. Slover J, Espehaug B, Havelin LI, et al. Cost-effectiveness of unicompartmental and total knee arthroplasty in elderly low-demand patients. A Markov decision analysis. *J Bone Joint Surg Am.* 2006;88:2348-2355.

49.   Centers for Medicare & Medicaid Services. Physician fee schedule. 2017.

https://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx

Accessed April 24, 2017.

50.   Agency for Healthcare Research and Quality. Healthcare Cost and Utilization

Project – 2014 data. https://hcupnet.ahrq.gov/#setup. Accessed February 27, 2017.

51.   Kalore NV, Maheshwari A, Sharma A, Cheng E, Gioe TJ. Is there a preferred

articulating spacer technique for infected knee arthroplasty? A preliminary study. *Clin*

Orthop Relat Res. 2012;470:228-235.

52.   N.C. Industrial Commission Medical Fees Section. CPT codes and fees (cpt code

27438). http://www.ic.nc.gov/ncic/pages/00000a.htm. Accessed April 24, 2017.

53.   Losina E, Paltiel AD, Weinstein AM, et al. Lifetime medical costs of knee

osteoarthritis management in the united states: Impact of extending indications for total

knee arthroplasty. *Arthritis Care Res (Hoboken).* 2015;67:203-215.

54.   Iribarne A, Burgener JD, Hong K, et al. Quantifying the incremental cost of

complications associated with mitral valve surgery in the united states. *J Thorac*

Cardiovasc Surg. 2012;143:864-872.

55.   Jarvenpaa J, Kettunen J, Miettinen H, Kroger H. The clinical outcome of revision

knee replacement after unicompartmental knee arthroplasty versus primary total knee

arthroplasty: 8-17 years follow-up study of 49 patients. *Int Orthop.* 2010;34:649-653.

56.   United States Bureau of Labor Statistics. Us medical care consumer price index.

2017. http://data.bls.gov/cgi-bin/surveymost?cu Accessed May 24, 2017.

57.   Schroer WC, Berend KR, Lombardi AV, et al. Why are total knees failing today?

Etiology of total knee revision in 2010 and 2011. *J Arthroplasty.* 2013;28:116-119.

58. Lombardi AV, Jr., Berend KR, Adams JB. Why knee replacements fail in 2013: Patient, surgeon, or implant? *Bone Joint J.* 2014;96-B:101-104.

59. Bozic KJ, Kurtz SM, Lau E, et al. The epidemiology of revision total knee arthroplasty in the united states. *Clin Orthop Relat Res.* 2010;468:45-51.

60. Laskin RS. The painful knee. *Orthopedics.* 1999;22:869-870.

61. Weick JW, Bawa HS, Dirschl DR. Hyaluronic acid injections for treatment of advanced osteoarthritis of the knee: Utilization and cost in a national population sample. *J Bone Joint Surg Am.* 2016;98:1429-1435.

62. Huellner MW, Strobel K. Clinical applications of spect/ct in imaging the extremities. *Eur J Nucl Med Mol Imaging.* 2014;41 Suppl 1:S50-58.

63. Horger M, Eschmann SM, Pfannenberg C, et al. Added value of SPECT/CT in patients suspected of having bone infection: Preliminary results. *Arch Orthop Trauma Surg.* 2007;127:211-221.

64. Sofka CM, Potter HG, Figgie M, Laskin R. Magnetic resonance imaging of total knee arthroplasty. *Clin Orthop Relat Res.* 2003:129-135.

65. Hoogeboom TJ, van den Ende CH, van der Sluis G, et al. The impact of waiting for total joint replacement on pain and functional status: A systematic review. *Osteoarthritis Cartilage.* 2009;17:1420-1427.

66. American Hospital Association. Trendwatch chartbook 2016. Trends affecting hospitals and health systems. http://www.aha.org/research/reports/tw/chartbook/2016/2016chartbook.pdf. Accessed April 24, 2017.

67. Zajonz D, Wuthe L, Tiepolt S, et al. Diagnostic work-up strategy for periprosthetic joint infections after total hip and knee arthroplasty: A 12-year experience on 320 consecutive cases. *Patient Saf Surg.* 2015;9:20.

68. He C, Lu Y, Jiang M, Feng J, Wang Y, Liu Z. Clinical value of optimized magnetic resonance imaging for evaluation of patients with painful hip arthroplasty. *Chin Med J (Engl).* 2014;127:3876-3880.

69. Sutter R, Hodek R, Fucentese SF, Nittka M, Pfirrmann CW. Total knee arthroplasty MRI featuring slice-encoding for metal artifact correction: Reduction of artifacts for stir and proton density-weighted sequences. *AJR Am J Roentgenol.* 2013;201:1315-1324.

70. Termaat MF, Raijmakers PG, Scholten HJ, Bakker FC, Patka P, Haarman HJ. The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: A systematic review and meta-analysis. *J Bone Joint Surg Am.* 2005;87:2464-2471.

71. Plodkowski AJ, Hayter CL, Miller TT, Nguyen JT, Potter HG. Lamellated hyperintense synovitis: Potential mr imaging sign of an infected knee arthroplasty. *Radiology.* 2013;266:256-260.

72. Li AE, Sneag DB, Greditzer HGt, Johnson CC, Miller TT, Potter HG. Total knee arthroplasty: Diagnostic accuracy of patterns of synovitis at mr imaging. *Radiology.* 2016;281:499-506.

73. Ruiz D, Jr., Koenig L, Dall TM, et al. The direct and indirect costs to society of treatment for end-stage knee osteoarthritis. *J Bone Joint Surg Am.* 2013;95:1473-1480.

74. Pasquale MK, Louder AM, Cheung RY, et al. Healthcare utilization and costs of knee or hip replacements versus pain-relief injections. *Am Health Drug Benefits.* 2015;8:384-394.

75. Desmeules F, Dionne CE, Belzile E, Bourbonnais R, Fremont P. The burden of wait for knee replacement surgery: Effects on pain, function and health-related quality of life at the time of surgery. *Rheumatology (Oxford).* 2010;49:945-954.

76. Hatoum HT, Fierlinger AL, Lin SJ, Altman RD. Cost-effectiveness analysis of intra-articular injections of a high molecular weight bioengineered hyaluronic acid for the treatment of osteoarthritis knee pain. *J Med Econ.* 2014;17:326-337.

77. Winther SB, Foss OA, Wik TS, et al. 1-year follow-up of 920 hip and knee arthroplasty patients after implementing fast-track. *Acta Orthop.* 2015;86:78-85.

78. Odum SM, Troyer JL, Kelly MP, Dedini RD, Bozic KJ. A cost-utility analysis comparing the cost-effectiveness of simultaneous and staged bilateral total knee arthroplasty. *J Bone Joint Surg Am.* 2013;95:1441-1449.
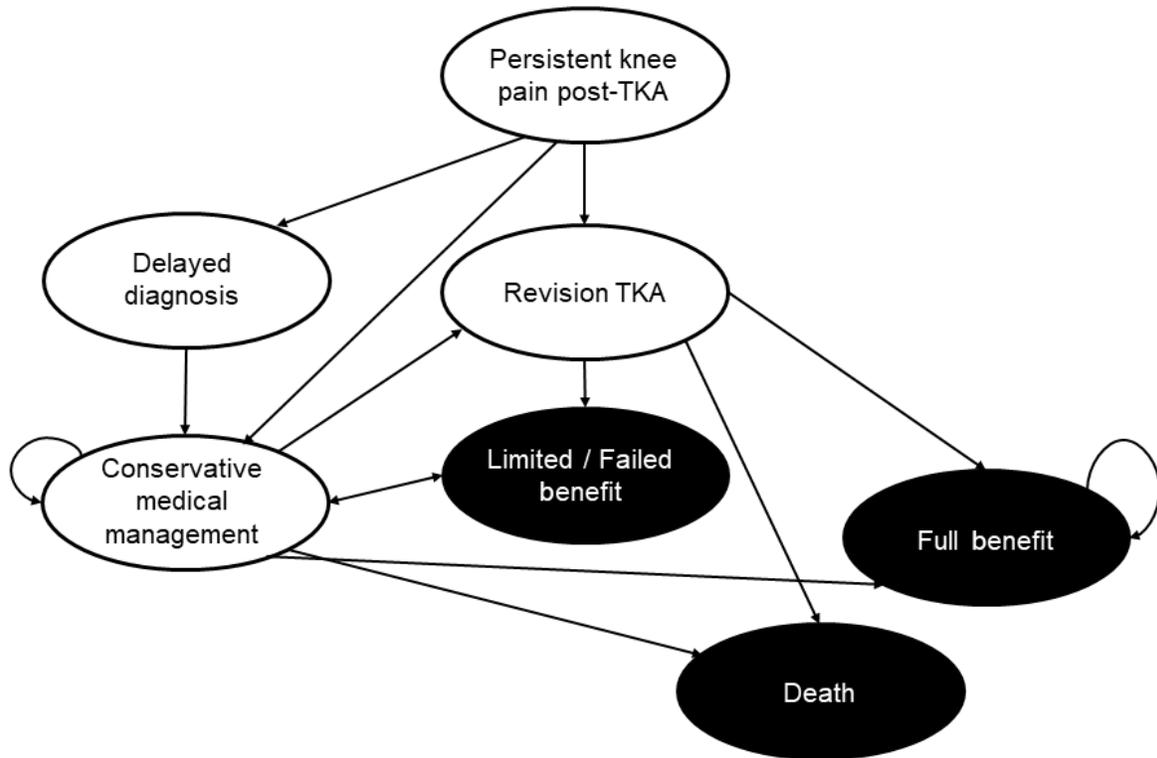
Figure 1. Model scaffold: proposed care pathway

Abbreviations: CT: computed tomography; MARS-MRI: metal artifact reduction sequence magnetic resonance imaging; SPECT/CT: single-photon emission computed tomography with computed tomography; TKA: total knee arthroplasty; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: white blood cells.
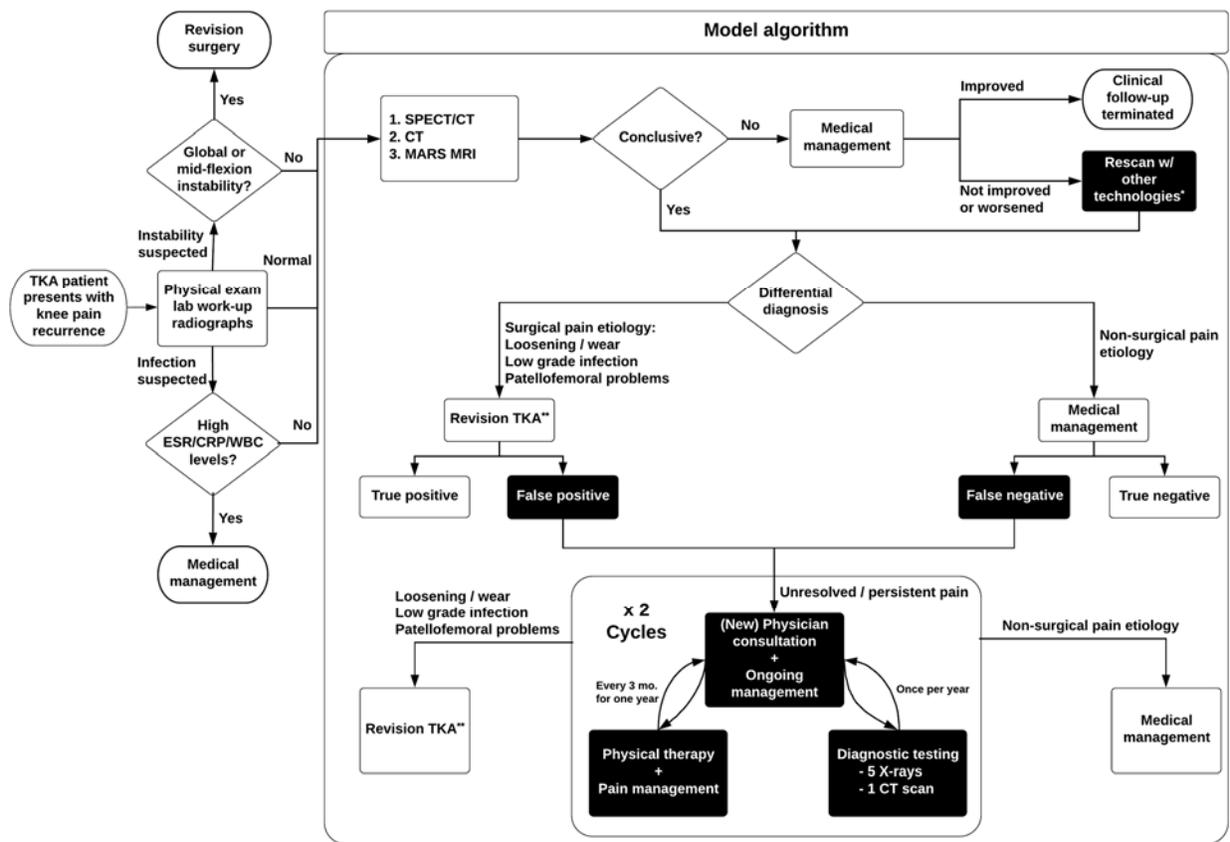

* For secondary rescan among the nondiagnostic patients, the imaging choice would be either CT or MRI. In the SPECT/CT arm, a 50:50 split between CT and MRI scans is assumed for the nondiagnostic cases
** Revision due to low-grade infection involves prosthesis removal, insertion of a temporary spacer , antibiotic treatment, and placement of new prosthesis; revision due to patelofemoral problems includes primary patellar resurfacing

Figure 2. Health state diagram representation
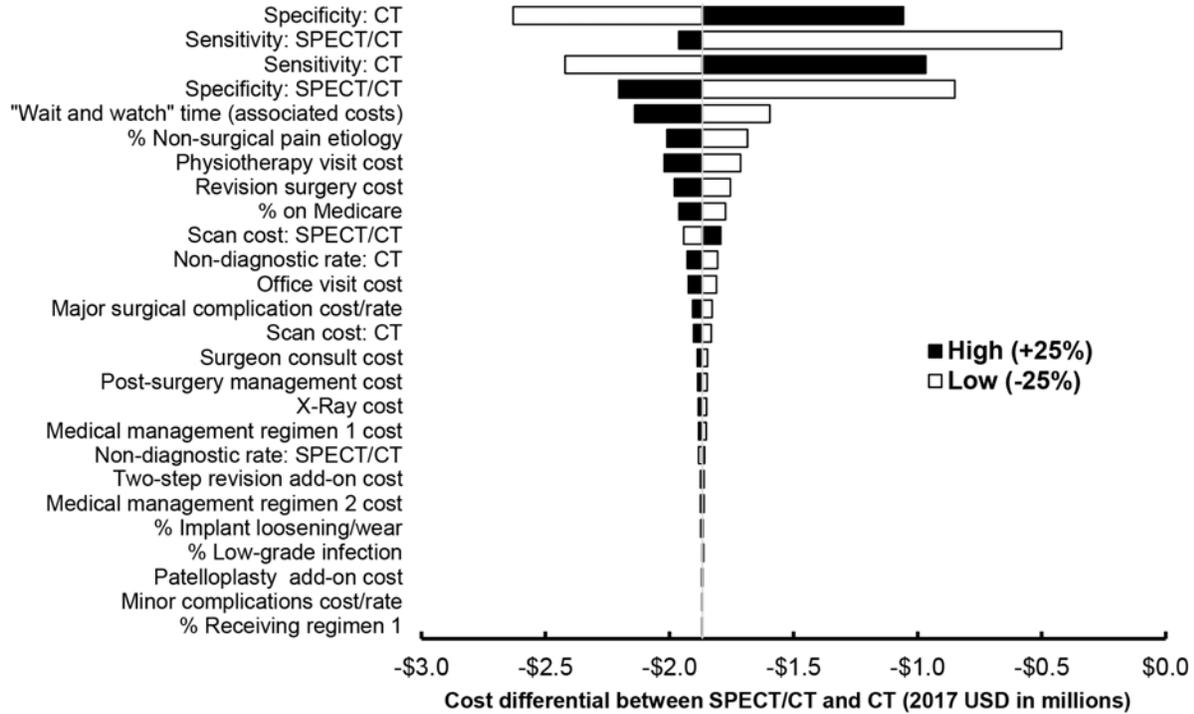

Abbreviations: TKA: total knee arthroplasty

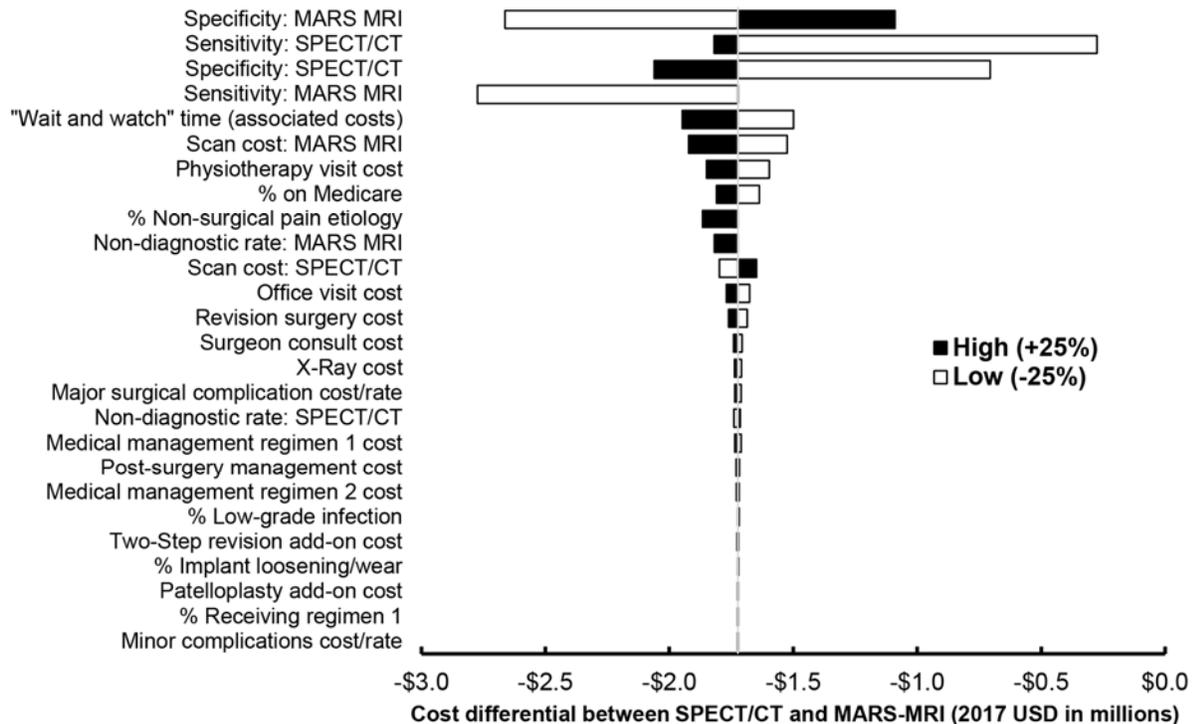**Figure 3.** Economic burden and QALYs, by imaging type
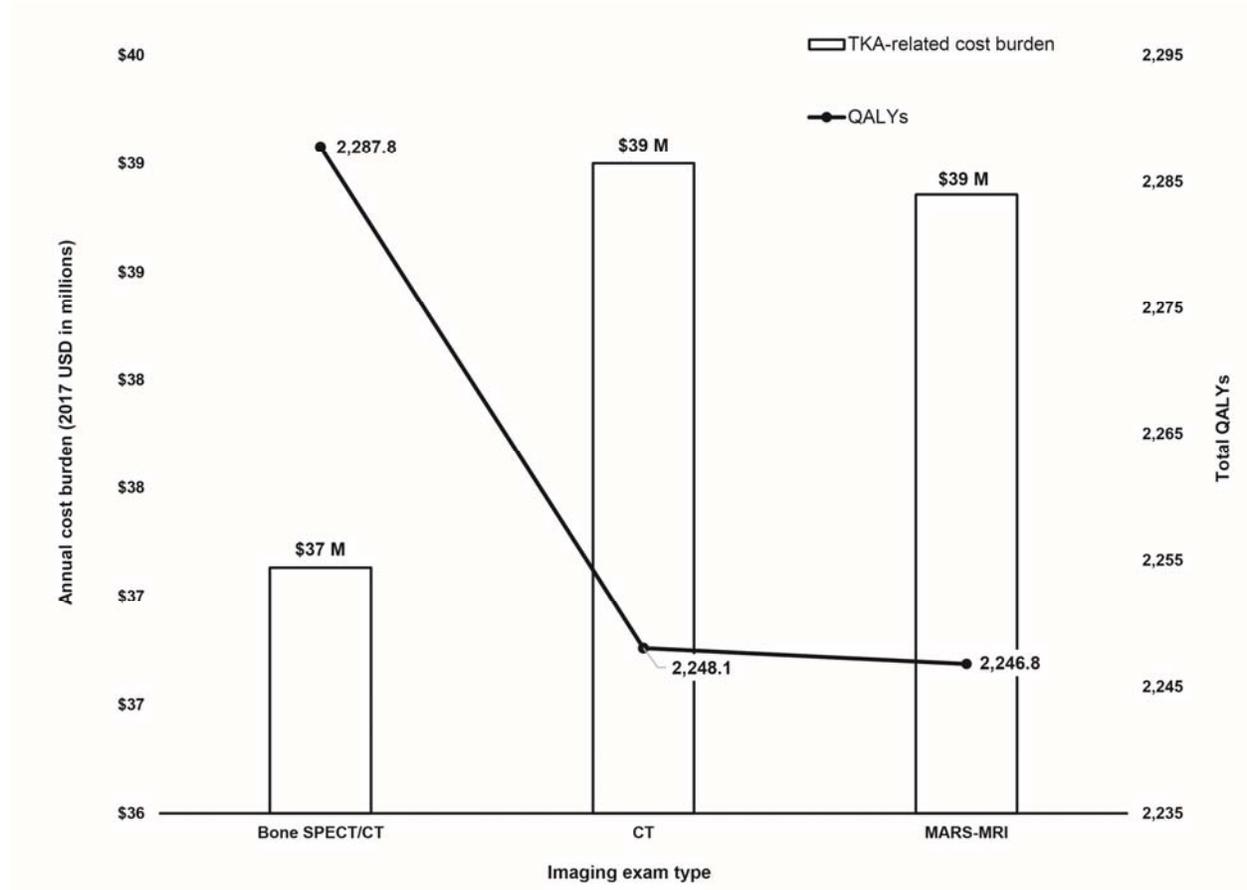
Abbreviations: QALYs: quality adjusted life years

Figure 4. One-way sensitivity analysis (tornado diagram) for SPECT/CT vs (A) CT and

(B) MARS-MRI.

A) SPECT/CT vs CT

B) SPECT/CT vs MARS-MRI

Abbreviations: CT: computed tomography; MARS-MRI: metal artifact reduction sequence magnetic resonance imaging; SPECT/CT: single-photon emission computed tomography with computed tomography

Table 1. Demographic, Disease, and Imaging Model Parameters

Parameter	Basecase	Range	References
Demographics			
Age < 65 years	40.4%	0-100%	
Medicare-to-Commercial reimbursement conversion factor	1.5	1.17 - 1.95	AHA's Aggregate Hospital Payment-to-cost Ratio (*66*)
Disease Related			
Prevalence of loosening / wear	70.38%	10 - 94.95%	(*14,16,20-26,28,30-32,34-41*)
Prevalence of low grade infection	16.68%	14.81 - 80.52%	(*14,16,20-25,28,30,31,34-41,51,63*)
Prevalence of patellofemoral problems	12.94%	0 - 68.75%	
Imaging Scan Related			
SPECT/CT			
Scan Cost	$239.38	-	Medicare National Payment Amount for CPT code 78320 (*49*)
Sensitivity	98.42%	97 - 100%	(*14,16,17*)
Specificity	91.34%	68.5 - 100%	(*17*)
Non-Diagnostic Rate	3.17%	0 - 8.83%	(*14,16,17*)
CT			

Parameter	Basecase	Range	References
Scan Cost	$115.20	-	Medicare National Payment Amount for CPT code 72190 (*49*)
Sensitivity	80.60%	80 - 81%	(*67,68*)
Specificity	74%	50 - 98%	(*69,70*)
Non-Diagnostic Rate	16.13%	12.1 - 20.2%	(*63*)
MARS-MRI			
Scan Cost	$646.72	-	Medicare National Payment Amount for CPT code 73725 / 73721 or 73723 plus OR (*49*)
Sensitivity	82.87%	67 - 100%	(*24,67,69,71,72*)
Specificity	84.52%	83 - 88%	(*71,72*)
Non-Diagnostic Rate	8.47%	0 - 16.1%	(*63,71*)

CPT: Current Procedural Terminology; CT: computed tomography; MARS-MRI: metal artifact reduction sequence

magnetic resonance imaging; OR: operating room; SPECT/CT: single-photon emission computed tomography with

computed tomography

Table 2. Revision Surgery and Unresolved Pain Basecase Model Parameters

Parameter	Basecase	Range	References
Revision surgery cost	$22,693	$12,063 - 27,136	2014 Healthcare Cost and Utilization Project Database (ICD-9 Proc primary codes: 00.80, 00.81, 00.82, 00.83, 00.84, 80.06, 81.55)(*50*)
Medicare Payment-to-cost %	88.50%	2.1 - 3.5%	(*66*)
Medicare Reimbursement	$20,083	$10,675 - 24,015	(*66*)
Private Payer Payment-to-cost %	143.70%	2.1 - 3.5%	(*66*)
Private Payer Reimbursement	$32,610	$17,334 - 38,994	(*66*)
Spacer cost	$4,466	$4,255 - 4,677	(*51*)
Patelloplasty cost	$2,719	$2,039 - 3,399	(*52*)
Proportion of loosening patients receiving patella resurfacing	13.80%	10.4 - 17.3%	(*21*)
Risk and costs associated with Medical complications			
Probability of MI	4.41%	0.8 - 7.7%	(*27,40,53*)
MI cost	$21,308	$15,981 - 26,635	(*53*)
Probability of Pneumonia	1.36%	1.4 - 15.4%	(*40,53*)
Pneumonia cost	$11,926	$10,684 - 31,793	(*53,54*)
Probability of PE/DVT	4.90%	0.8 - 10.71%	(*27,40,41,53,55*)
PE/DVT cost	$12,770	$9,578 - 15,963	(*53*)

Parameter	Basecase	Range	References
Probability of infection (joint, UTI, or Sepsis)	5.36%	0.7 - 15.4%	(40,53)
Infection cost	$26,219	$19,664 - 32,773	(53)
Probability of RF	7.95%	1.7 - 15.4%	(27,40,41)
RF cost	$38,305	$34,821 - 41,789	(54)
Probability of GI Bleed	4.41%	4.3 - 7.7%	(27,40)
GI Bleed cost	$16,533	$11,063 - 22,004	(54)
Probability of death	0.96%	0.01 - 1.2%	(47,53)
Cost of death	$16,910	$12,683 - 21,138	(53)
Post-surgery medical management including physiotherapy	$3,366	$2,524 - 4,207	(73,74)
Unresolved Pain			
Office Visit			
Probability	100%	0 – 100%	Assumption
Number per year	1	-	Assumption
Cost per visit	$127.59	$109 – 146	Medicare National Payment Amount for CPT codes 99214-99215 (49)
Surgeon consult			
Number per year	1	-	Assumption

34

Parameter	Basecase	Range	References
Cost per consult	$187.70	$166 – 209	Medicare National Payment Amount for CPT codes 99204-99205 (*49*)
Set of radiographs / CT scans			
Number per year	1	-	Assumption (5 radiographs and 1 CT scan)
Cost per set	$155	1 ≥	2017 Physician Fee Schedule CPT Code 73564 (*49*)
Physiotherapy			
Number per year	12	-	Assumption
Cost per visit	$116	-	2017 Physician Fee Schedule CPT Code 73564 (*49*)
Steroid injection			
Probability	30%	0 – 100%	(*75*)
Number per year	5	-	(*75*)
Cost per visit	$76	$57 – 95	(*76*)

CPT: Current Procedural Terminology; CT: computed tomography; GI: gastrointestinal; MI: myocardial infarction;

PE/DVD: pulmonary embolism/deep venous thrombosis; RF: renal failure; UTI: urinary tract infection

Table 3. Medical Management BaseCase Model Parameters

Parameter	Basecase	Range	References
Occasional analgesics: acetaminophen, opioids	$117	$87 - 146	(53)
Nonsurgical regimen 1 annual costs: office visits, devices, physical therapy, NSAIDs, and/or acetaminophen			
Initial Year	$1,249	$587 - 1,715	(53,74)
Subsequent Years	$949	$446 - 1,304	(53,74)
Adverse Events			
Probability of general toxicity (Year 1)	2.76%	2.1 - 3.5%	(53)
Probability of general toxicity (Year 2+)	2.11%	1.6 - 2.6%	(53)
General toxicity cost	$57	$43 - 71	(53)
Probability of cardiovascular toxicity	0.12%	0.1 - 1.5%	(53)
Risk of death due to cardiovascular toxicity	5.29%	4.0 - 6.6%	(53)
Cardiovascular toxicity cost	$21,308	$14,317 - 23,861	(53)
Probability of GI toxicity	0.23%	0.2 - 0.3%	(53)
Risk of death due to GI toxicity	2.68%	2.1 - 3.4%	(53)
GI toxicity cost	$11,145	$8,564 - 14,274	(53)
Nonsurgical regimen 2 annual costs: office visits, Injections	$1,240	$424 - 1915	(53,74)

Parameter	Basecase	Range	References
Adverse Events			(53)
Probability of skin flares	24.00%	18 - 30%	(53)
Cost of skin flares	-	$0 - 25	(53)
Probability of sepsis	0.0013%	0.001 - 0.002%	(53)
Risk of death due to sepsis	8.35%	6.3 - 10.4%	(53)
Sepsis cost	$15,700	$12,065 - 20,108	(53)
Probability of nonsurgical regimen 1 (vs regimen 2)	70%	0-100%	(75)

GI: gastrointestinal; NSAIDs: nonsteroidal anti-inflammatory drugs

Table 4. Utilities (Time) - BaseCase Model Parameters

Parameter	Basecase	Range	References
Wait time for identifying cause / treatment decision (years)	2	-	Assumption
Pre-revision	0.51	0.31 - 0.76	(*33,42,47,73,76,77*)
Surgery/post-op recovery disutility (3 months)	0.19	0.1 - 0.35	(*42,46-48,73*)
Minor complications disutility (3 months)	0.04	0.02 - 0.05	(*78*)
Major complications disutility (3 months)	0.06	0.04 - 0.08	(*78*)
Post–successful revision surgery	0.86	0.78 - 0.9	(*46,47,73*)
Post–failed revision surgery	0.47	0.51 - 0.55	(*48,73,78*)
Medical management disutility	0.08	-	(*76*)

Cost-Effectiveness of Bone SPECT/CT in Painful Total Knee Arthroplasty

Tim Van den Wyngaert, Swetha R Palli, Ryan J Imhoff and Michael T Hirschmann

This article and updated information are available at:
http://jnm.snmjournals.org/content/early/2018/03/29/jnumed.117.205567

Information about reproducing figures, tables, or other portions of this article can be found online at:
http://jnm.snmjournals.org/site/misc/permission.xhtml

Information about subscriptions to JNM can be found at:
http://jnm.snmjournals.org/site/subscriptions/online.xhtml

JNM ahead of print articles have been peer reviewed and accepted for publication in *JNM*. They have not been copyedited, nor have they appeared in a print or online issue of the journal. Once the accepted manuscripts appear in the *JNM* ahead of print area, they will be prepared for print and online publication, which includes copyediting, typesetting, proofreading, and author review. This process may lead to differences between the accepted version of the manuscript and the final, published version.

SNMMI | SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING