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Modelling the cost-effectiveness of total knee arthroplasty: A systematic review

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ABSTRACT

Objective: Osteoarthritis causes a significant healthcare burden and the number of total knee arthroplasty (TKA) procedures is predicted to increase significantly in the coming years. We conducted a systematic review to assess the scope and quality of all current TKA cost-effectiveness analysis (CEA) studies, identify trends, and identify areas for improvement.

Methods: An electronic database search of MEDLINE, Embase, the CEA registry and Scopus was used to identify all CEA studies where TKA was used with a comparator. Studies were included from January 1, 1997 to February 2, 2020. The Quality of Health Economic Analysis Studies (QHES) instrument was used to assess their quality. Thirty-three studies were included that offered both a QALY and cost calculation. The main findings, incremental-cost effectiveness ratios and other important study characteristics were then ascertained, and trends identified.

Results: Certain surgical interventions were suggested to be more cost-effective than TKA. This included unicompartmental knee arthroplasty for unicompartmental osteoarthritis, computer-assisted TKA compared to conventional TKA, and resurfacing the patella compared to no resurfacing. TKA was more cost-effective compared to non-operative management regardless of specific patient variables.

Conclusions: The analyses of the CEAs included in the study have to be interpreted with caution. Overall, certain surgical methods within TKA and alternative methods to TKA appear to be favoured for treating particular knee osteoarthritic conditions due to their suggested greater cost-effectiveness but this should be interpreted within local contexts. Our results should help guide future policy-making as healthcare associated costs continue to rise.

1. Introduction

Osteoarthritis is a common cause of morbidity globally and causes a significant financial burden to healthcare systems.[1] Symptomatic knee osteoarthritis occurs in around 10% of men and 13% of women aged 60 or older,[1] and this percentage is likely to increase with an ageing population and increasing obesity rates. The age standardised prevalence of knee osteoarthritis for adults aged 45 and older was 19.2% in 1990, and increased to 27.8% in 2008.[2] The incidence rate of total knee arthroplasties (TKA) in the USA is the highest globally and even with conservative projection approaches, this is projected to increase up to six-fold by 2030.[3,4] There are various published systematic reviews focusing on areas such as sports,[5] trauma,[6] upper limb[7] and foot and ankle surgery[8] but despite the high economic impact of arthroplasty surgery, there has been no recent systematic review of the cost-effectiveness of TKA.

This systematic review will assess the scope and quality of all current TKA CEA studies. This review will also identify trends, areas where further CEAs must be performed and where improvement is needed for greater quality. We used the Quality of Health Economic Studies (QHES) instrument[9] to measure the quality of the studies and the significance of the findings for clinical practice decision-making. No funding was received for this systematic review.

2. Methods/literature search

2.1. Search strategy

A systematic search was performed to identify all CEA studies that offered an economic evaluation of TKA procedures in MEDLINE, EMBASE, the Cost-Effectiveness Analysis (CEA) Registry (by the Centre for the Evaluation of Value and Risk in Health at Tufts University)[10] and Scopus. The First Panel on Cost-Effectiveness in Health and Medicine

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published their first-consensus-based guidelines for the conduct of CEAs on October 16, 1996 which formed the basis of the rationale for the time limit in our search.[11] Search results were therefore restricted from January 1997 (to allow for sufficient time for studies to reflect these guidelines) to February 2020 (date of the search). This systematic review adheres to the checklist reported by PRISMA.[12] A detailed description of the search terms used for the electronic databases is included in the supplementary file.

2.2. Study inclusion

All titles and abstracts obtained from the initial search were screened for duplicate articles prior to checking for relevance in terms of economic analysis in TKA. This was carried out by 2 independent reviewers in order to ensure consistency. Full-text articles were retrieved and reviewed for further selection by applying the following inclusion/exclusion criteria.

2.2.1. Inclusion criteria

1. Total knee arthroplasty/replacement as a comparator
2. Other comparator is a non-operative management option, or a different surgical procedure performed on the knee.
3. CEAs of different knee implant/prostheses for TKA
4. Clinical studies only
5. Studies adhering to methodology consistent with CEAs

2.2.2. Exclusion criteria

1. Editorials reviews and conference abstracts
2. Not in English language
3. Studies without a comparator
4. Studies that do not offer both a primary quality metric (e.g. quality-adjusted life-years, QALY) and cost calculation
5. Studies comparing non-surgical factors, management options, or venous thromboprophylaxis
6. Studies published before January 1, 1997

As the included studies list quality-adjusted life-years (QALYs) which require subjective valuations of health states by the patients, this review therefore focuses on cost-utility analyses.[5,13] These studies use an incremental cost-effectiveness ratio (ICER), which is calculated by dividing the differences in costs by the differences in QALYs between two management options.[11] ICERs are then evaluated against a willingness-to-pay (WTP) threshold, which indicates the maximum a healthcare consumer is willing to pay to obtain an additional QALY.[14] Hence, if a management option's ICER falls below the WTP threshold relative to its comparator, it can be considered a cost-effective alternative.

2.3. PRISMA flowchart

Fig. 1 shows a PRISMA flowchart demonstrating the search process used to identify the 33 studies from the electronic databases.

2.4. Quality assessment

Quality assessment of each study was performed using the QHES instrument.[9] This score ranges from 0 to 100. Any score from 75 to 90 reflects a study of being good quality and above 90 as excellent quality. The QHES is designed to evaluate the use of suitable methods, valid, transparent results and their comprehensive reporting in each CEA.[9] Each of the 33 studies were reviewed by the secondary author (KT) and the primary author (AK) for a 50% random sample using a random number generator to ensure at least a 90% inter-assessor agreement.

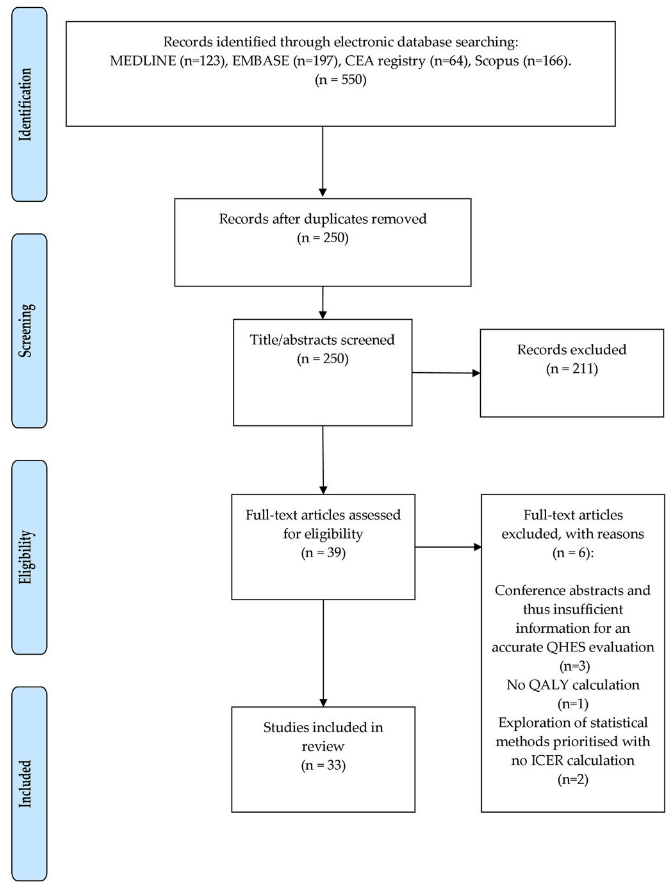

Fig. 1. Shows a PRISMA flowchart demonstrating the search process involved in identifying the 33 studies from the electronic databases.

3. Results

3.1. Overall summary

An overview of the 33 CEAs is presented in Table 1. The ICER values have been adjusted to the 2020 US Dollar using the Consumer Price Index (CPI),[15] 2020 United Kingdom Pound using the Office for National Statistics CPI,[16] and 2020 Euro from the European Commission and the European Central Bank's Harmonised Index of Consumer prices (HICP).[17]

3.2. Main study characteristics

The main study characteristics are summarised in Table 2 and include (i) comparison of unicompartmental knee arthroplasty with total knee arthroplasty; (ii) analysis of patella resurfacing; (iii) analysis of computer-assisted arthroplasty; (iv) comparison of arthroplasty with non-operative management and other surgical alternatives; and (v) analysis of various knee arthroplasty implants.

The study design of choice is the Markov model which was used in 17 of the 33 studies. All studies that originated from the USA were model-based, with nine out of 12 studies using the Markov model. However, those from the UK, Canada and other European countries (denoted as "other" in Table 2) used either model-based or real-life clinical studies indiscriminately. Three of the seven studies from the UK were RCTs.

Interestingly, the most common level of evidence in the studies was Level-I (n = 36.4%). The percentage of studies above Level-II reporting was 63.6% (n = 21) indicating that CEAs tend towards higher levels of evidence. This is important as higher levels of evidence are more convincing to surgeons when tackling clinical dilemmas[18] such as the

Table 1
Summary of the ICERs and key findings of all 33 CEA studies included in this review, stratified by comparator type.

Author (year, country)	Study Design	ICER[a]	WTP[a]	Key findings
UKA vs TKA				
Soohoo et al. (2006, USA)[33]	Decision Tree	Implant survival: 12 y vs 15 y: $440, 11 y vs 15 y: TKA dominant, 17 y vs 20 y: $59,556^	$50,000	UKA is a cost-effective alternative for unicompartmental OA when the durability and function of the UKA implant is similar to the TKA one and with appropriate patient selection. However, when adjusted for 2020, UKA is no longer cost-effective to TKA for the 17 y vs 20 y category.
Slover et al. (2006, USA)[51]	Markov	Base case: UKA dominant	$50,000	Although UKA was dominant, the average differences in costs and QALYs with TKA were $200 and 0.05 respectively. Thus, both have similar cost-effectiveness in the elderly low-demand population.
Peersman et al. (2014, Belgium)[52]	Markov	UKA dominant	€10,000, €25,000, €50,000	UKA offers a clear increase in health outcomes for a smaller cost than TKA for unicompartmental OA.
Ghomrawi et al. (2015, USA)[34]	Markov	Age at surgery (TKA vs. UKA): 45 y: $34,011 55 y: $71,425 65 y,75 y,85 y: UKA Dominant	$100,000	UKA is cost effective compared to TKA in patients over 65 years of age for end-stage unicompartmental OA. However, modest improvements in implant survival could make it cost-effective in younger patients.
Chawla et al. (2017, USA)[35]	Markov	PFA vs TKA: 50 y - $3445 60 y - $ 3405	$50,000	Improvements in implant survival have resulted in PFA being a more cost-effective joint preserving procedure in younger patients.
Burn et al. (2018, UK)[53]	Markov	UKA Dominant	£20,000	UKA is expected to provide better health outcomes and lower lifetime costs than TKR. However, surgeon usage of UKA has a significant impact on cost-effectiveness.
Xie et al. (2010, Canada)[54]	Prospective cohort	Perspective (TKA vs. UKA): Societal - $79,430 Patient - $73,510 Government - $5917	$10,000 and $50,000	There is a 0.4 probability of TKA being cost-effective from the societal or patient's perspective at a $50,000 WTP and 0.7 from the government's at a WTP of $10,000 for unicompartmental OA (without inflation adjustment). Longer study needed.
Beard et al. (2019, UK)[55]	RCT	PKR dominant	n/a	During the 5-year study period, PKR offers slightly better outcomes, lower surgical costs and lower follow-up health-care costs compared to TKR for treatment of late-stage isolated medial compartment OA. Hence, it should be first choice for it.
Resurfacing vs No Resurfacing in TKA				
Weeks et al. (2018, Canada)[36]	Decision Tree	Resurfacing Dominant	n/a	Resurfacing the patella is cost-effective due to higher revision rates for non-resurfaced TKA.
Zmistowski et al. (2019, USA)[37]	Decision Tree	Overall: $3,032[b], Nonarthritic patellae only: $183,584[b]	n/a	It is not cost effective to routinely resurface nonarthritic patella during primary TKA. Selective resurfacing for arthritic patients is vital for cost-effectiveness.
Computer-Assisted TKA vs Non-Assisted TKA				
Novak et al. (2007, USA)[31]	Decision Tree	$59,033^	$50,000/ $100,000	Computer-assisted implant alignment systems increase the precision of component alignment enough to reduce failure rates and revisions to justify the extra cost vs. mechanical alignment systems during TKA (not true following 2020 ICER adjustment).
Dong et al. (2006, UK)[30]	Markov	CAS dominant vs. Conventional TKA	£30,000	Computer-assisted TKA is cost effective in the long-term through reducing revision rates and complications via more precise component alignment.
Gothesen et al. (2013, Norway)[29]	Markov	Conventional TKA dominant vs CAS	500,000 kr (NOK)	At high operation volume hospitals, CAS needs to improve implant survival in 60 and 75-year-old cohorts just marginally for cost-effectiveness. A more significant increase is needed for low volume hospitals.
TKA vs Non-Operative Management				
Losina et al. (2009, USA)[39]	Markov	Overall: $21,123 High-risk patients only: $36.415	$50,000/$100,000	TKA is cost-effective across all risk groups for perioperative complications.
Ponnusamy et al. (2018, Canada)[40]	Markov	Non-obese: $3510, Overweight: $3,002, Obese: $3,118, Severely obese: $3,742, Morbidly obese: $5,853, Super obese: $12,569	$50,000	Not opting for TKA care based on BMI is not justified, even in the super obese cohort.
Elmallah et al. (2017, USA)[56]	Prospective	$47,357	$50,000	Following an OA diagnosis, TKA is cost-effective.
Dakin et al. (2012, UK)[38]	RCT	Baseline patient OKS: <9: £5,768, 9-11: £5,577, 12-13: £5,032, 14-15: £5,152, 16-17: £6,407, 18-19: £8,068, 20-21: £14,735, 22-24: £11,270, 25-27: £13,655, >27: £14,366,	£20,000 -£30,000	The UK primary trust criteria (2012) restricting TKA to patients with pre-operative OKS <27 is denying a cost-effective treatment to patients above this OKS.
Skou et al. (2020, Denmark)[57]	RCT	TKR plus non-surgical treatment vs. non-surgical treatment only:	€22,655	From a 24-month perspective, in patients with moderate to-severe knee OA in secondary care in Denmark, TKR plus non-surgical (exercise, education, diet, insoles and pain medication).

(continued on next page)

Table 1 (*continued*)

Author (year, country)	Study Design	ICER[a]	WTP[a]	Key findings
		Unadjusted base-case: €19,579, Adjusted base-case: €34,519, Adjusted base-case including deaths: €48,984 to 67,964		treatment is not cost-effective compared with non-surgical treatment with the potential for later TKR if needed when adjusted for the covariates: age, sex and baseline values.
TKA Implant Type				
Fennema et al. (2014, Germany)[46]	Markov	TKA with advanced low-wear bearings vs standard polyethylene bearing: overall: €18,198, patients <55 y: €722 and 75: €91,687[b]	€0, €10,000, €25,000, €50,000	Low-wear articulations may be considered cost-effective overall but it is age-dependent, with the ICER being significantly lower for younger people than for older people, where it no longer becomes cost-effective.
Pennington et al. (2016, UK)[48]	Markov	AGC Biomet dominated Genesis 2 and Triathlon. PFC Sigma dominated by Nexgen. For 70 y men and women, Nexgen vs. AGC Biomet, £2715 and £2667 respectively	£20,000 - £30,000	AGC Biomet prostheses are the least costly cemented unconstrained fixed brand for TKR but Nexgen prostheses lead to improved patient outcomes, at low additional cost and so should be first choice as they are the most cost-effective.
Suter et al. (2013, USA)[47]	Markov	Innovative vs standard TKA implants: $\geq$ 50% decrease in long-term TKA failure at $\leq$ 50% increased cost: < $100,000. A 20% decrease in long-term failure at 50% increased cost: < $150,000 (only in healthy 50,59 y)	$150,000	Innovative implants must decrease TKA failure by 50–55% or more compared to standard implants to be broadly cost-effective.
Hamilton et al. (2013, UK)[58]	RCT	Over a lifetime and at 1 year, Triathlon TKA dominated Kinemax TKA	£20,000	The values for money saved per QALY were statistically insignificant and so both implants were of similar value using the SF-6D and QALY methodology.
Multiple Surgical Comparator studies				
Konopka et al. (2015, USA)[59]	Markov	50-60 y: TKA vs HTO - $262,908, TKA vs UKA - $14,058[c]	$50,000/$100,000/ $150,000	In a 50-60 y with unicompartmental medial knee OA, HTO is the most cost-effective management option. TKA is also more cost effective than UKA in the same cohort.
Kazarian et al. (2018, USA)[60]	Markov	TKA dominates NST from 40 to 69 years and just over $16,494 at 80 y, UKA dominates TKA for all ages at time of treatment	$50,000	In unicompartmental OA, using surgical treatments is cost-effective in all age groups. UKA should be prioritised over TKA.
Stan et al. (2015, Romania)[45]	Prospective	TKA to unoperated knee dominates both TKA after HTO and CM	n/a	Careful patient selection could help optimise the cost-effectiveness of TKA as unoperated knee TKA is dominant to operated knee TKA.
Murray et al. (2014, UK)[61]	RCT	Patellar resurfacing vs. no resurfacing: >95% probability of being cost-effective at WTP, Mobile bearing vs fixed bearing: £2044 Metal-backed tibial components vs all-polyethylene ones: £43	£20,000	Patellar resurfacing is cost-effective, mobile bearings highly cost-effective (however there was considerable uncertainty), all-polyethylene components are poor value for money and should not be used in place of metal-backed components.
Hak et al. (2013, UK)[44]	n/a	Lifetime + 10-year durability: UKA, HTO and KineSpring system dominated TKA, TKA dominated CM. TKA vs no treatment: £1,303[b] (lifetime) €4,153[b] (10 year)	£20,000–£30,000	In the NHS, the KineSpring System is the most cost-effective strategy to treat knee OA.
Marcacci et al. (2013, Italy)[41]	n/a	Lifetime + 10 year durability: UKA, HTO and KineSpring system dominated TKA, TKA dominated CM, TKA vs no treatment: €2348[b] (lifetime) €4,884[b] (10 year)	€25,000–€30,000	In the Italian Healthcare system, the KineSpring system offers the lowest cost/QALY and so is the most cost effective option.
Li et al. (2013, Germany)[42]	n/a	KineSpring System dominated surgical treatments (TKA, UKA and HTO) and conservative management. Surgical treatments vs. no treatment: €10,722	€ 39,742	The KineSpring System is the most cost-effective option for knee OA patients in Germany.
Strain et al. (2015, Spain)[43]	n/a	Lifetime + 10-year durability: UKA, HTO and KineSpring system dominated TKA, TKA dominated CM. TKA vs no treatment: €2530 (lifetime) €5264 (10 year)	€20,000 to €30,000	Same results achieved in the Spanish Healthcare system as Italian.[41] The KineSpring System is the most cost-effective treatment for knee OA.
Other:				
Odum et al. (2013, USA)[20]	Markov	Simultaneous bilateral TKA dominated staged bilateral TKA	$328,874	Simultaneous bilateral total knee arthroplasty is more cost-effective with lower costs and greater health outcomes for the average patient.
Van der Woude et al. (2016, Netherlands)[62]	Markov	KJD dominant vs. TKA	€ 20,000	Treating knee OA with KJD over TKA has a high potential to be cost-effective, which is most likely in the younger population.
Clement et al. (2019, UK)[63]	Markov	Robot-assisted UKA vs TKA by annual patient case volume (patients/year): 10: £7170[b], 100: £1395[b], 200 (with a 2 day stay): £648[b], 200 (with a 1 day stay): £364[b]	£20,000	Robot-assisted UKA is cost-effective compared with manual TKA for patients with isolated medial compartment knee OA. Increasing the annual patient case volume and reducing the length of hospital stay decreased the ICER of using rUKA over manual TKA.

BMI – Body Mass Index, CAS – Computer assisted surgery, CM – Conservative management, HTO – High Tibial Osteotomy, KJD - Knee Joint distraction, NST – Nonsurgical treatment, OA – Osteoarthritis, OKS – Oxford Knee Score, PFA – Patellofemoral arthroplasty, PKR – Partial Knee replacement, QALY – Quality-adjusted life year, RCT – Randomised controlled trial, SF-6D – Short-Form 6-Dimension health index, UKA - Unicompartmental knee arthroplasty, WTP – Willingness to pay threshold, y = Years of age.

ˆ Inflation adjustment resulted in ICER increasing above WTP threshold and so the management option no longer being cost effective. This is reflected in the main findings being altered.
[a] All values are given per QALY.
[b] Inflation year not given in study, so 2020 adjustment not performed.
[c] ICER value has been calculated using provided information in study.

Table 2
Main study characteristics of cost-effectiveness studies of total knee arthroplasty (n = 33).

Study characteristic	Number of studies	Percentage contribution to total (% to 1 decimal point)
Country of study		
United States	12	36.4
United Kingdom	9	27.3
Canada	3	9.1
Other (Europe)	9	27.3
Study design		
Randomised controlled trial	5	15.2
Prospective cohort	3	9.1
Markov	17	51.5
Decision Tree	4	12.1
Not stated	4	12.1
Data mining (health outcomes and costs) explained		
Yes	33	100
No	0	0
Level of evidence[a]		
I	12	36.4
II	9	27.3
III	5	15.2
IV	7	21.2
Perspective		
Healthcare payer	18	54.5
Societal	7	21.2
Both	4	12.1
Not stated	4	12.1
Time Horizon		
≤10 years	9	27.3
>10 years	7	21.2
Lifetime	17	51.5
Not stated	1	3.0
Sufficient Time Horizon and Discounting (both costs and health outcomes) present		
Yes	26	78.8
No	7	21.2
Sensitivity Analysis		
Deterministic only	5	15.2
Probabilistic only	4	12.1
Both	15	45.5
Not stated	8	24.2
Unspecified	1	3.0
Statement of funding		
Yes	19	57.6
No	14	42.4
Discussion of potential bias present		
Yes	8	24.2
No	25	75.8

"Other" countries include: Belgium, Denmark, Germany, Italy, Netherlands, Norway, Romania, and Spain.
[a] Based on recommendations by Wright et al. (2003) for judging the level of evidence for a primary research question [64].

ones in question here. However, it is important to acknowledge that since RCTs are not always possible,[19] Level-I evidence may not be available for all clinical scenarios and Level-III or IV evidence may still be of great value to orthopaedic surgeons.

Another important finding is that 54.5% (n = 18) CEAs used exclusively a healthcare perspective in order to derive the costs. Seven studies used societal, four used both and four did not mention such information. Five of the 12 studies (38.5%) from the USA used exclusively a healthcare and another five (38.5%) the societal perspective. This is in contrast to the UK, where studies displayed a slight preference towards the healthcare payer perspective (n = 4, 57.1%). These costs and the associated health outcomes following TKA were calculated across a range of time horizons. There is a trend towards the USA preferring longer time horizons, with 83.3% (n = 10) of their studies declaring either a lifetime or duration greater than 10 years. In contrast, the UK has shown a preference towards time horizons of 10 years and below with 66.7% (n = 6) of their CEAs fitting into this category. No significant trends were observed for the studies from Canada or the European countries.

When the studies were stratified by their country of origin, the USA had the largest range of WTP thresholds between $50,000 per QALY up to $150,000. Furthermore, the study by Odum et al.[20] suggested that the WTP for the USA should be no higher than $328,874 per QALY.[21] This range was to be expected based on previous evidence. Studies performed in the UK had an expected WTP range of between £20,000 to £30,000 per QALY, which is decided by the National Institute for Health and Care Excellence (NICE).[22]

There were a few ill-defined trends when stratifying the type of sensitivity analysis used by country of origin. Eight out of the 12 (66.67%) CEAs from the USA incorporated both a deterministic and probabilistic sensitivity analysis. This indicates a slight preference to using both. Canada, the UK and the other European countries showed no reasonable preference with their choice of sensitivity analysis type.

Only 57.6% (n = 19) of the studies disclosed their source of funding. Of these 19 studies, 47.4% (n = 9) received funding from exclusively public sources, 10.5% (n = 2) from exclusively private sources, 26.3% (n = 3) from both and 15.8% (n = 3) reported having received no funding. The remaining 14 CEAs failed to disclose any funding sources in their reports.

3.3. CEA study quality

The mean summed QHES score for all 33 CEAs studies present was 83.7. According to the thresholds set by Tran et al.,[23] this would mean the studies were on average of good quality. This is perhaps expected considering that the first CEA studies using TKA as a comparator were first published in 2006, ten years after the First Panel on Cost-Effectiveness in Health and Medicine published their first guidelines for the conduct of CEA studies in 1996.[11] The majority of CEAs that failed to achieve higher scores fell short in similar QHES categories including failing to state or justify the perspective used, not discussing the extent of potential biases and not including a statement of funding.

Since 1997, there has been a significant increase in the number of CEAs using TKA as a comparator. Over time, there has been a reduction in the proportion of these CEAs that have scored over 75 in the QHES after an initial increase between 2002-2007 and 2008–2013 (Fig. 2). From 2002 to 2007, 75% (n = 3) of the studies scored greater than 75. This was higher at 88.9% (n = 8) between 2008 and 2013, and 80.0% (n = 16) between 2014–February 2020. However, this result must be acknowledged in the context that there were four, nine and 20 studies in these year groups respectively. This data is illustrated in Fig. 2.

The average QHES scores following stratification of the CEAs via their comparators used are displayed in Table 3.

4. Discussion

Overall, the mean quality of studies as measured by the QHES was high at 83.7. This is comparable to the mean QHES scores observed in the subspecialties of upper-limb orthopaedic surgery,[7] trauma[6] and sports medicine[5] which were 82, 79.25 and 81.8 respectively. This suggests that the findings drawn from such studies are of significant

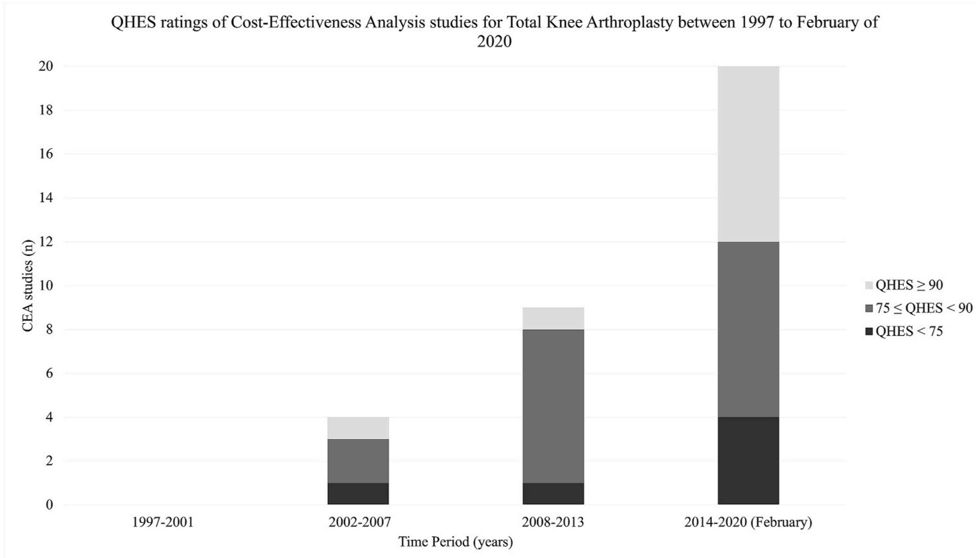

Fig. 2. Bar graph demonstrating the 33 cost-effectiveness analyses (CEAs) studies identified published over time stratified by their QHES scores. Scores of 90 and above are considered excellent quality, between 75 and 90 of high-quality and below 75 of poor quality. [23]

Table 3
Mean QHES scores of CEA studies in this review stratified by comparator type (n = 30).

Comparator Type	Mean QHES (n)
UKA vs TKA	84.8 (8)
Resurfacing vs no resurfacing in TKA	90 (2)
Other	87.3 (3)
Computer-assisted TKA vs non-assisted TKA	86.7 (3)
TKA vs non-operative management	84.8 (5)
Multiple surgical comparator studies	79.6 (8)
TKA implant type	80 (4)

value and of greater applicability to clinical decision-making.

However, when stratified into the comparator type categories mentioned earlier, there is a considerable range in both the quantity of studies published and their respective qualities. The mean values for the CEAs following stratification were all still above 75. Between 2014 and 2020 (February), there was a drop in the proportion of high-quality (QHES>75) studies compared to the time period 2008–2013 from 88.9% to 80%. This trend was also observed for CEA studies in upper-limb orthopaedic surgery,[7] where there was a greater proportion of studies demonstrating lower quality (QHES<75) in recent years. This is concerning as it reflects a loss of CEA standards performed across orthopaedics. The Second Panel on Cost-Effectiveness in Health and Medicine has published a new set of guidelines in 2016[24], which should help to re-establish high-quality methodological CEA study practices to maintain standards.

Despite a majority reporting of the perspective used in the CEAs, it is important for indirect societal and direct healthcare costs to be calculated as they are both important. Patient recovery times for the ability to resume normal daily activities following TKA may extend up to 12 weeks or more. This highlights the importance of any unpaid patient costs of lost productivity and unpaid caregiving. This is emphasised by the Second Panel's recommendation to consider both the healthcare payer and societal perspectives when CEAs are performed.[24] This needs to be emphasised so that future CEAs may incorporate both measures and provide a more realistic cost-effective analysis for clinical decision-making.

It is surprising that only five of the 18 studies from the UK and other European countries used RCTs to conduct their CEA. Health-technology assessment (HTA) bodies in Europe emphasise funding for RCT-based research as clinical evidence for CEA studies.[25,26] No RCT CEA studies were identified from the USA. This was also observed by Rajan et al.[7] who looked at CEAs in upper-limb surgery. There has been significant political resistance to the use of CEA studies in Federal coverage decisions for insurance policies, including Medicare.[27] 72.2% (n = 13) CEAs from the UK, Canada and other European countries included at least the healthcare perspective to account for the costs in their analyses. This is in agreement with the formal integration by the HTA bodies of these nations to use CEAs to guide policies of whether to fund a particular management option or not. Hence, third-party payer perspectives are prioritised.[24,28] In contrast, the USA does not show a preference for their payer perspective despite the United States-based First Panel's recommendation to use societal perspectives.[24,28]

A limitation of using model-based papers in a review such as this is made apparent with the recommendation for CAS. Based on the papers selected, TKA with CAS was suggested to be more cost-effective as CAS increases the precision of component alignment during TKA, therefore reducing long-term failure rates and complications sufficiently to justify its extra costs.[29–31] However, in the study by Novak et al.,[31] under a WTP of the $50,000, the ICER for CAS following adjustment to the 2020 inflation value becomes $59,033. This now suggests it to be no longer cost-effective against conventional mechanical alignment systems at the given WTP. In addition, it was shown that hospital operation volume may influence the cost-effectiveness of CAS with low volume hospitals needing a much greater increase in implant survival for it to be deemed cost-effective compared to high operation volume hospitals.[29] However, it must be noted that only three studies looked at TKA with CAS and all of these were model-based.[29–31] CAS may offer theoretical benefit and decrease outliers in some instances, but this conclusion has not been supported in either registry data or smaller prospective studies. The authors of the three papers quoted also recognise this as a shortcoming in their conclusion.

There has been considerable CEA research into the use of UKA over TKA for unicompartmental osteoarthritis (n = 8) and using multiple comparators to TKA such as HTO and UKA (n = 8). However, little research has been undertaken in areas such as the use of patella resurfacing in TKA (n = 2) and computer assisted TKA (n = 3). Modern surgery is more commonly incorporating computer-guidance systems in surgeries such as TKA[32] so there is now an expectation that the number of CEAs exploring this field will increase in the future.

If we consider UKA over TKA for unicompartmental osteoarthritis, UKA was suggested to be the more cost-effective option overall according to the reviewed studies due to the associated improved health outcomes, and lower surgical and follow-up costs. However, the studies included suffer from similar modelling data input issues as previously discussed in the CAS subsection and conclusions need to be interpreted with caution. Following inflation adjustment to 2020 values, UKA appeared to no longer be cost-effective in the 17y vs 20y category.[33] UKA was suggested to not be cost-effective in younger patients below 65y. The studies suggest that the cost-effectiveness of UKA may improve through increasing the surgeon's usage of UKA and the implant's durability and function.[33–35]

Resurfacing the patella was suggested to be cost-effective compared to not resurfacing it during TKA largely due to the associated reduced revision rates.[36,37] However, Zmistowski et al. showed that this was perhaps only true when resurfacing was performed on arthritic patella as routinely resurfacing non-arthritic patella was not shown to be cost-effective.[37] This finding is also supported by national joint registry data.

When comparing TKA to non-operative management options, TKA was proposed to be more cost-effective regardless of patient factors that could potentially influence decision-making policies such as their OKS,[38] risk for perioperative complications[39] and BMI.[40] These findings are important in ensuring a potentially more cost-effective treatment option is not denied to patients based on these aforementioned metrics.

Regarding the eight CEAs that used multiple comparators in their cost-effective analysis, various findings may be drawn. The KineSpring system dominated other surgical treatment methods in Italy,[41] Germany,[42] Spain[43] and the UK.[44] However, the mean QHES score for these studies was the lowest at 79.6 and they failed to disclose their funding source. In addition, careful patient selection can help optimize the cost-effectiveness of TKA; TKA on an unoperated knee is dominant to that after HTO and CM.[45]

Lastly, regarding the TKA implant type, the key factors that influenced whether certain implant types were deemed cost-effective were suggested to be the age of the patient at surgery[46] and the degree to which the given implant reduces the failure rate of TKA. This results in a reduced need for revision surgeries.[47] For example, low-wear bearings were shown to be cost-effective compared to polyethylene bearings, but this was age-dependent, with the ICER being significantly higher in the older population where it was no longer cost-effective.[46] Furthermore, the Nexgen implant was shown to be dominant over the Triathlon, Genesis 2 and PFC Sigma ones.[48] In addition, Nexgen was also indicated as more cost-effective than AGC Biomet by leading to improved patient outcomes at low additional cost.[48] However, it is important to acknowledge that these findings are based on large national joint registries and are therefore vulnerable to all their associated shortcomings. They do not control for all the relevant variables involved, which include: the surgeon's skill, technique, and experience, implant design changes over time, bone cement type and implant alignment.

Any systematic review is limited by the quality of the included studies, and studies were not excluded following the results of quality checks such as the QHES. A potential limitation could be that the CEAs included in this review were conducted across 11 countries in total. This may result in problems associated with the generalisability and so transferability of the CEA study findings to other healthcare settings.[49,50] Using the QHES to measure study quality is also prone to bias due to the subjective nature of reporting by the assessor. However, we ensured at least a 90% inter-assessor agreement between both reviewers. Lastly, the QHES values study design reporting, and gives equal weight to the different methods without consideration of their respective limitations resulting in analytical bias.

5. Conclusions

Overall, CEA studies in TKA have been increasing in number over the past couple of decades. This reflects the increasing interest and importance of this field within resource-limited healthcare environments and with ageing populations. It is reassuring to see a high mean quality of reporting in CEAs whose findings can therefore certainly be considered in clinical decision making. However, there is a clear need for further studies and a greater quality of reporting in the cost-effectiveness literature for total knee arthroplasty in orthopaedic surgery to ensure that high standards of reporting are not lost over time. Results of CEAs should also be interpreted in local healthcare contexts. Therefore, it will be vital to monitor the ongoing quality of these studies in accordance with Second Panel Recommendations.[24]

CRediT authorship contribution statement

Achi Kamaraj: Formal analysis, Writing - original draft, contributed to the design and implementation of the research, to the analysis of the results. **Kendrick To:** Formal analysis, Writing - original draft, contributed to the design and implementation of the research. **KT Matthew Seah:** Formal analysis, Writing - original draft, contributed to the design and implementation of the research. **Wasim S. Khan:** Formal analysis, Writing - original draft, contributed to the design and implementation of the research.

Declaration of competing interest

All authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

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