



Review

Different clinical outcomes on the second side after staged total knee replacement. A systematic review☆☆☆



Michael-Alexander Malahias<sup>a,\*</sup>, Alex Gu<sup>a</sup>, Jacqueline Addona<sup>a</sup>, Allina A. Nocon<sup>a</sup>, Alberto V. Carli<sup>b</sup>, Peter K. Sculco<sup>a</sup>

<sup>a</sup> The Stavros Niarchos Foundation Complex Joint Reconstruction Center, Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, USA

<sup>b</sup> Adult Reconstruction & Joint Replacement, Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, USA

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ABSTRACT

**Background:** The clinical outcomes of the contralateral side in staged bilateral total knee arthroplasty (BTKA) are relatively unknown. The purpose of this study was to answer: 1) Does the second-operated knee in a staged BTKA result in inferior clinical and functional outcomes? 2) Is the duration of time between the first- and the second-operated knee defined in a consistent fashion in the literature? 3) Does the time interval between TKAs influence clinical outcomes?

**Methods:** Two reviewers independently conducted a systematic search of the literature using different databases according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Results:** Five of the seven included studies reported significantly inferior postoperative clinical outcomes for the second-operated knee compared with the first-operated knee. There was no difference in the overall major complication rate between first- and second-operated TKA (2.4% and 1.2% respectively). Based on the literature reviewed, there is no consensus on the optimal time interval between the stages. Most studies, which investigated the impact of different intervals on the outcomes of the second-operated knee, concluded that the differences in outcomes with different intervals were not significant.

**Conclusions:** Current literature suggests that the second-operated knee, in patients undergoing staged BTKAs, might have inferior clinical outcomes when compared with the first-operated knee.

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 \* Corresponding author at: Complex Joint Reconstruction Center, Hospital for Special Surgery, 535 E 70th St, New York, NY 10021, USA.  
 E-mail address: alexandermalahias@yahoo.gr (M.-A. Malahias).

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## 1. Introduction

Total knee arthroplasty (TKA) is an effective procedure in reducing pain and improving function in patients with end-stage osteoarthritis. Patient satisfaction after TKA varies between 80 and 95% with 93% of TKA patients reporting that they would choose to undergo the operative procedure again [1]. The incidence of bilateral knee osteoarthritis is high with 1/3 of patients undergoing TKA presenting with bilateral disease [2,3]. Current surgical management for patients with end-stage bilateral osteoarthritis is either staged bilateral or simultaneous bilateral TKA [3]. Simultaneous bilateral TKA has been associated with an increased risk of venous thromboembolic events, readmission within 90 days, and blood transfusion [4–6]. Staged bilateral total knee arthroplasty (BTKA) is considered as a safe and efficacious treatment alternative to managing bilateral disease [7,8]. According to the Canadian Hospital Morbidity Database, from 2006 to 2013, the ratio of simultaneous to staged BTKA was 1:4 among 238,373 patients [9]. The annual number of simultaneous BTKAs decreased eight percent, while staged BTKAs increased 28% [9].

Recently, concerns have been raised regarding the difference in outcomes between the first knee and the contralateral knee in patients treated with staged BTKA. In addition, although most staged TKAs (94%) are performed with at least three months between stages; the ideal timing between TKAs to reduce perioperative complications has still not been determined [10,11]. We therefore performed a systematic review of the literature to examine the differences between postoperative outcomes between first- and second-operated knee in staged BTKA. Specifically, we aimed to answer: 1) Does the second-operated knee in a staged BTKA result in inferior early clinical and functional outcomes? 2) Is the duration of time between the first- and the second-operated knee defined in a consistent fashion in the literature? 3) Does the time interval between TKAs influence clinical outcomes? Our hypothesis is that there would be no difference in clinical outcomes between the first and second TKA regardless of timing in between stages.

## 2. Materials and methods

A systematic review of the literature was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The US National Library of Medicine (PubMed/MEDLINE), SCOPUS, and the Cochrane Database of Systematic Reviews were queried for publications from January 1980 to July 2018 utilizing keywords pertinent to BTKA, staged TKA, and clinical outcomes. Only abstracts that evaluated the clinical outcomes after staged BTKA were reviewed. The specific search terms are further shown in Table 1. Two reviewers independently screened the title and abstracts of all the retrieved articles. Titles and abstracts that did not pertain to staged bilateral knee replacement were excluded. Full-text articles were retrieved and a second round of article selection was performed by the same two independent reviewers to determine if the articles answered one or more of the review questions described previously.

### 2.1. Inclusion and exclusion criteria

The inclusion criteria were: 1) studies describing human subjects of any age and gender, 2) studies that include a population of at least 10 patients who underwent staged BTKA and compared the clinical outcomes of the second-operated knee with the first-operated knee, and 3) studies that follow patients for a minimum of 10 days after the second surgical intervention in a staged BTKA. The exclusion criteria were: 1) review articles, 2) case studies, 3) editorial comments, 4) studies stratifying patients based on perioperative management (anesthesia protocol, limitation of blood loss, surgical technique, prosthesis type, etc.) in which allocation of patients who previously underwent a second staged TKA is not specified, 5) studies in which no stratification

**Table 1**  
Search strategy.

Database	PubMed, Cochrane, Embase
Date	July 2018
Strategy	#1 AND #2 AND #3
Limit	Human AND English
#1	("Arthroplasty, Replacement, Knee"[Mesh] AND bilateral[tw]) OR (total knee arthroplasty[tw] AND bilateral[tw]) OR (tka[tw] AND bilateral[tw]) OR (Total knee replacement[tw] AND bilateral[tw]) OR (TKR[tw] AND bilateral[tw])
#2	Staged[tw] OR non-simultaneous[tw]
#3	Treatment outcome[tw] OR Clinical outcome[tw] OR Pain[tw] OR "Treatment Outcome"[Mesh] OR "Pain"[Mesh] OR "Pain Measurement"[Mesh] OR "Patient Reported Outcome Measures"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR Pain, Postoperative[mesh] OR Pain Threshold[tw]

between patients receiving a TKA for their first or second knee, and 6) non-English language publications. For articles that met these criteria, the reference lists were screened for additional studies not captured using the initial search terms.

## 2.2. Data collection

Two authors independently conducted the described search. Both authors compiled a list of articles not excluded after application of the inclusion and exclusion criteria. Discrepancies between the two authors were resolved by discussion. During initial review of the data, the following information was collected for each study: title, author, study design, number of patients, number of knees, time between first and second surgery, gender, change in range of motion (ROM) after first and second surgeries, and pre- and post-TKA clinical outcome scores, such as the Oxford Knee Score (OKS), visual analogue scale for pain (VAS), 12-Item Short Form Health Survey (SF-12), 36-Item Short Form Health Survey (SF-36), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Knee Society Score. Corresponding authors from each qualifying study were contacted by email on two separate occasions and asked to provide raw data on the above patient outcomes to perform cohort-based comparisons. Two authors failed to respond to written requests and the remaining authors replied stating that they did keep the raw data from their studies.

Descriptive statistics were calculated for each study and parameters analyzed. The quality of the evidence was classified using the US Preventive Services Task Force system for ranking level of evidence [19]. The methodological quality of each study and the different types of detected bias were assessed independently by each reviewer with the use of modified Coleman methodology score (0–100 scale) [20]. In addition, the overall quality of the studies was graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group guidelines [21]. Selective reporting bias, like publication bias, was not included in the assessment.

## 3. Results

The search criteria evaluating staged BTKA resulted in 217 abstracts (Figure 1). Following elimination of duplicate articles and predetermined exclusion criteria, seven articles were included for analysis [12–18] (Table 2).

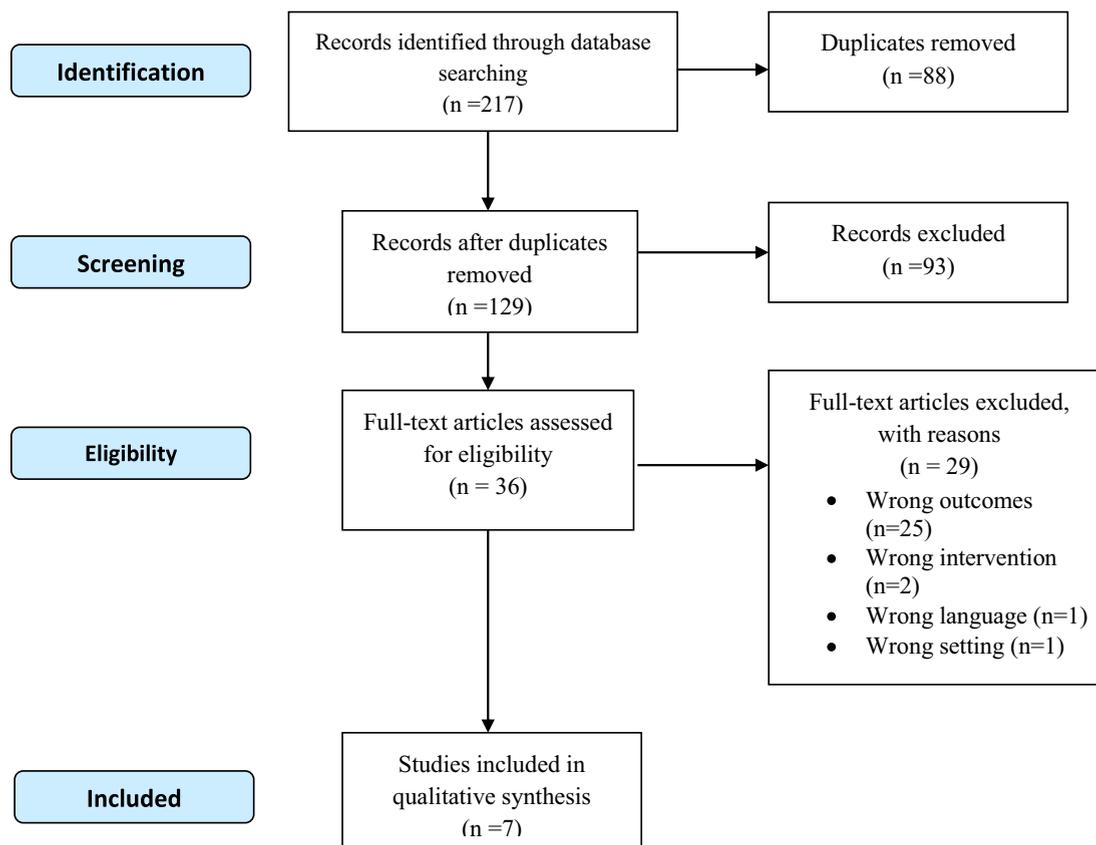


Figure 1. Systematic review PRISMA flow diagram.

**Table 2**

Type of study, level of evidence, follow-up, early clinical evaluation and modified Coleman methodology score (MCMS).

Author(s)	Type of study	Level of evidence	Follow-up period	Early 1st week evaluation	MCMS 0–100
Abram et al. [15]	Retrospective	III	12 months	No	45/100
Kim et al. [13]	Prospective	II	48 h	Yes	87/100
Sun et al. [12]	Retrospective	III	12 months	Yes	56/100
Qutob et al. [33]	Retrospective	III	12 months	No	58/100
Scott et al. [14]	Retrospective	III	6, 12 months	No	53/100
Gabr et al. [17]	Retrospective	III	12 months	No	47/100
Kumar et al. [16]	Retrospective	III	24 months	No	46/100

### 3.1. Type of studies and level of evidence

Qualifying articles included one prospective study [13] and six retrospective studies [12,14–18]. All studies made comparisons between the outcomes of the first- and second-operated knee on the same group of patients [12–18]. One study further compared the outcome of staged and simultaneous BTKA [15]. There was one prospective randomized controlled clinical trial (RCT) [13], one retrospective case–control study [15], and five retrospective cohort comparative studies without control groups [12,14,16–18]. As for the level of evidence, one study was level II [13] and six studies were level III [12,14–18] (Table 2).

### 3.2. What is the quality of evidence of studies that compare clinical outcomes between the first- and the second-operated TKA?

The overall quality of evidence, as assessed by using the GRADE Working Group guidelines [21], was moderate and ranged from moderate [12,14–18] to high [13]. When considering GRADE Working Group guidelines [21], based on the quality of the evidence of the different studies, the balance between desirable/undesirable outcomes and the values of patients, there was moderate evidence that the second-operated knee leads to worse early outcomes in comparison with the first-operated knee. The mean modified Coleman score for methodological deficiencies of the studies was 56/100, and ranged from 45 to 87 indicating a moderate level for overall methodological quality (Table 2).

### 3.3. General characteristics

The studies of this review included 1347 patients in total. Females ( $n = 897$ ; 66.6% of all patients) outnumbered males ( $n = 450$ ; 33.4% of all patients). The mean patient age among studies was 67.6 years (range of the mean age per study: 65 to 71.7 years) (Table 3). The final follow-up evaluation point varied between 48 h postoperatively (perioperative outcomes to two years postoperatively (short-term outcomes)). Two out of the seven studies [12,13] documented an early (first postoperative week) evaluation of the operated knees, while five studies reported a long-term ( $\geq 12$  months) evaluation [14–18] (Table 2).

### 3.4. Implants utilized

Five out of the seven studies included provided information pertaining to specific aspects of the operation [12,13,15,16,18], while two studies did not [14,17]. Three studies (43%) documented whether patellar resurfacing was performed or not [12,13,16]. Two of these studies did not utilize patellar resurfacing in any patient [12,16], whereas one study resurfaced the patella in all patients [13]. TKA implant design varied between studies. One study reported the use of posterior stabilized (PS) knee implants exclusively [13], another reported outcomes on only low contact stress (LCS) mobile bearing knee implants [15], and the third reported on only cruciate retaining (CR) knee implants [12]. The remaining two studies included a mixture of implant designs, with one comprised mostly

**Table 3**

Number of patients per study, sex, mean age and time between the first and the second surgery in the patients with staged bilateral TKA.

Author(s)	Number of patients	Sex	Mean age (years)	Time between first and second TKA
Abram et al. [15]	328	113 males 215 females	65	23 months (2–74)
Kim et al. [13]	30	5 males 25 females	71	1 week
Sun et al. [12]	87	31 males 56 females	68.3	<6 months, 6–12 months, >12 months
Qutob et al. [33]	668	218 males 450 females	68.5	1st subgroup <12 months, 2nd subgroup >12 months
Scott et al. [14]	70	29 males 41 females	71.7	7.8 months (2–25)
Gabr et al. [17]	64	26 males 38 females	N/A	1st subgroup <6 months, 2nd subgroup >12 months
Kumar et al. [16]	100	28 males 72 females	66	6–12 months

of PS knees [18] and the other that had a vast majority (95%) of patients treated with CR implants [14]. Furthermore, two studies reported only on a cemented TKAs [12,13], whereas one study (14%) used only uncemented prostheses [15], and four studies (57%) did not provide any information on the method of implant fixation [14,16–18].

### 3.5. Is the second-operated knee in a staged BTKA associated with inferior clinical and functional outcomes?

None of the seven included studies reported that the first-operated knee had worse preoperative clinical subjective scores compared with the second-operated knee. Five of the seven included studies reported significantly inferior postoperative clinical outcomes for the second-operated knee compared with the first-operated knee [12–15,18]. No studies in this review reported clinically superior outcomes in the second-operated knee versus the first-operated knee.

With regard to outcome measures utilized, four out of the seven trials used the OKS for the preoperative and postoperative follow-up evaluation [14–16,18]. Three of these studies showed that postop OKS of the second-operated knee was significantly inferior compared with the first-operated knee [14,15,18], whereas only one study reported no significant difference in postoperative OKS among knees [16]. Three trials utilized the SF-12 [14,15,17], with two reporting significantly worse outcomes scores [14,15] and one reported no significant difference in the long term [17]. Two trials used the VAS [12,13] for pain and both showed that the second-operated knee had significantly higher pain scores compared with the first knee. Finally, one study made use of the WOMAC [17], while another one applied the Knee Society Score and the SF-36 [16]. Both studies identified no significant differences in their respective outcome measures for the first versus second-operated knees and no difference in postoperative ROM.

Those studies which reported the immediate early postoperative outcomes (<1 week) consistently reported poorer outcomes in the second-operated knee compared with the first-operated knee [12,13]. In contrast, those studies, which used an intermediate (three to 11 months) evaluation, showed conflicting results [14,16]. Scott et al. reported significantly poorer pre- and postsurgical improvements in OKS with the second-operated knee versus the first after six months of follow-up [14]. Kumar et al. identified no differences in six-month postoperative Oxford knee questionnaire scores, and ROM between operated knees [16]. As for the long term (≥12 months) results, three studies noted that the second-operated knee resulted in worse outcomes when compared with the first-operated knee [14,15,18] and two studies illustrated no significant difference [16,17]. The longest follow-up was reported by Kumar et al., at two years after surgery, reporting no differences in OKS and ROM between the first- and second-operated knees.

### 3.6. Complications

Two studies documented postoperative complication rates after staged BTKA [14,16]. Both studies reported no significant differences in complication rates between the first- and the second-operated knee [14,16]. The overall major complications' rate for the treated patients was estimated at 4.1% (seven out of 170 patients) [14,16]. Two patients (1.2%) experienced a major complication after their first operation and five patients (2.9%) after the second operation [14,16].

### 3.7. Time interval

There was substantial heterogeneity among studies regarding the time interval used between surgeries, ranging from one week [13] to 24 months [15,16]. For this reason, an optimal time interval could not be identified (Table 3).

### 3.8. Are outcomes influenced by the interval between TKAs?

Four studies investigated the impact of different intervals on the outcomes of the second-operated knee [12,15,17,33]. Three out of four studies concluded that the differences in outcomes with different intervals were not significant [15,17,33]. Of these three, Sun et al. reported deteriorated outcomes when the interval was less than six months [12], Gabr et al. reported that there were not any differences when the cut-off time point was less than six months [17], and Qutob et al. found that there were no differences in outcomes either when the interval was less or more than 12 months [33]. The fourth article written by Abram et al. could not associate time interval with changes in clinical outcomes after the second-operated knee [15].

## 4. Discussion

Given that the number of TKAs performed annually in the United States is projected to increase by 85% from 2014 to 2030 [22], identifying the functional benefits of performing unilateral versus staged bilateral procedures has important societal cost-effectiveness implications when considering that a third of knee arthritis patients present with bilateral disease [2,3]. A consistent finding among five of the studies analyzed in this review was that functional and patient-reported outcomes associated with the second-operated knee within bilateral staged TKAs had inferior outcomes. Although reported inferior outcomes were often observed within the first year after surgery, findings across different knee designs and methods of fixation suggest that factors outside of the operative technique could be responsible. Based on the consolidated literature, clinicians might consider counseling patients on the elevated risks associated with the second-operated knee in staged bilateral procedures. Additionally, surgeons might also consider employing a more aggressive analgesic strategy when performing the second TKA in the staged procedure to potentially offset poor short-term outcomes. Lastly, surgeons themselves should also consider the findings of this review in the decision-making process when considering which procedure, staged versus simultaneous, would best suit the patient, since patient experiences can differ considerably.

Surgeons and patients are faced with the option of performing both knee replacement procedures simultaneously under one anesthetic (simultaneous BTKA) or staging the procedures over a specific time interval (staged BTKA) [23]. Supporters of simultaneous BTKA suggest many advantages, including limiting surgery and anesthesia to a single event, promoting symmetrical rehabilitation among both knees and a reduced length of stay at hospitals, which also translates to lower hospital costs [23–25]. However, different studies have linked an increased number of complications and mortality events with simultaneous BTKA [26–28]. For example, a clear disadvantage associated with simultaneous BTKA is greater blood loss than that which occurs in the staged procedure [27,29]. In a single-center comparative clinical trial, the mean transfusion rate was higher for the simultaneous BTKA group than for the staged BTKA group [30].

Compared with the staged BTKA, several trials have reported that simultaneous BTKA increased gastrointestinal events, deep-vein thrombosis, pulmonary embolism, fat embolism and cardiovascular events [31–33]. A recent systematic review by Fu et al. confirmed these results [7]. Finally, Huang et al. found that there was improved patients' satisfaction with the second knee in the early stage after simultaneous BTKA, which provide some considerations for surgeons choosing simultaneous BTKA for patients with bilateral osteoarthritis [34].

Most of the literature concerning BTKA tended to compare simultaneous and staged procedures. However, though the evidence points towards staged procedures being the safer option, there have been limited studies comparing the functional and clinical outcomes between the first-operated and second-operated TKA in a staged procedure. To our knowledge, this is the first systematic and comprehensive review of comparative trials assessing the different outcomes of the first- and the second-operated knee in staged BTKA. Five out of seven trials, which were included in this review, supported that the second knee had worse postoperative clinical outcomes when compared with the first [12–15,18].

There have been different explanations cited as the reason behind poor outcomes of the second-operated knee. Poultsides et al. compared preoperative expectation scores between stages in patients with BTKA using intraclass correlation coefficients [35]. In multivariable analyses controlling for first expectation score, second expectation score was associated with better WOMAC stiffness score [35]. Poultsides et al. showed that patients' outcomes could possibly be skewed due to the fact that the expectations of the patients have risen after the success of the first operation. This might be a possible explanation for why patients with staged BTKA usually report worse clinical outcome after the second-operated TKA.

In addition, Scott et al. reported that patients undergoing bilateral staged TKA had higher levels of satisfaction following their first TKA than those reported for the TKA population as a whole [14]. Satisfaction with the first TKA undoubtedly influences the decision to proceed to the second knee's operation, possibly at an earlier stage than might be expected. This population is therefore a pre-selected group and would be predicted to do well following the second TKA. However, satisfaction with the first TKA did not predict satisfaction with the second TKA, and owing to the small numbers of dissatisfied patients, Scott et al. documented that it was not possible to correlate satisfaction with expectation level [14]. According to Qutob et al., those patients suffering from bilateral knee osteoarthritis who have already been operated for the first knee were presented at an earlier stage in the disease process as compared with side-one knee [18]. This article supports the theory that patient expectations regarding surgical outcomes are skewed by the first procedure, resulting in a relatively decreased patient perceived improvement in the second-operated knee outcome [18].

Kim et al. had a different perspective; they assumed that hyperalgesia may be responsible for the deteriorated early outcome of the second-operated knee [13]. Hyperalgesia was induced from the repeated surgical injury, possibly via central sensitization [13]. According to a special commentary regarding the previous article [13], a second possible explanation could be the decreased sensitivity to analgesics administered for the second TKA [36]. The paper suggests that opioid tolerance may be a key factor in the perception of deteriorated outcomes. In this paper, patients were administered fentanyl after the first surgery, which might have led to opioid tolerance resulting in decreased response to perioperative opioids after the second surgery.

On the other hand, there were two trials that did not demonstrate any significant difference between the first- and the second-operated knee [16,17]. Kumar et al. discussed that a limitation of their study was the absence of early patients' assessment after surgery [16]. This fact might be crucial because the second-operated knee has shown worse clinical outcomes mostly when patients were assessed in the short-term [12,15]. It is very likely that any possible differences in the clinical outcomes of the two knees would be lost in a longer follow-up. In addition, Gabr et al. reviewed prospectively collected data of outcomes of knee replacements to show that there were no differences between the first- and the second-operated knee [17]. However, Gabr et al., like Kumar et al. [16], did not use early- to short-term follow-up scores [17].

This systematic review presented conflicting results for the optimal time span between staged procedures. Although Sun et al. argued that a time interval less than six months between the two operations deteriorated the results of the second-operated knee [12], Gabr et al. illustrated that there was not any significant difference with the six-month cut-off interval [17]. There was only one study to illustrate that a second operation very soon after the first one (within a week) should be rather avoided due to the inferior outcomes of the second-operated knee [13]. Overall, the results of this review signified that more clinical trials are required in order to establish the ideal time interval between surgeries.

The modified Coleman methodology score varied widely across studies, from low to high values. The strength of the recommendations provided from this review was weak, in the direction of confirming our initial hypothesis. The studies, which were included in this review, were not without limitations. The time frame for follow-up varied widely, the study designs were limited to retrospective observational studies that are accompanied by smaller sample sizes. Also, there were several variations in the clinical aspects of each study: surgical technique, the type of knee implant, the use of patellar resurfacing as well as the application of drainage differed from study to study. Overall, the quality of the studies, which were included in this review, was moderate. We were not able to identify higher level study designs (level I) such as RCTs. Provided this limitation in currently cited work, further studies of higher quality should be conducted in order to increase to confirm the results of this review.

## 5. Conclusions

Current literature suggests that the second-operated knee, in patients undergoing staged BTKAs, might have inferior clinical outcomes when compared with the first-operated knee. While factors that influence clinical outcomes after staged BTKAs are often multifactorial, patients and providers should be aware of the risk of potential increased likelihood of inferior outcomes in the second-operated knee and use this information to guide and modify patient expectations, accordingly. Further prospective studies are needed to assess optimal timing and how this is associated with clinical outcomes. Additionally, perioperative pain management strategies may be examined as a means to which may improve outcomes for the second-operated knee in staged bilateral procedures.

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