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Systematic review

Fragility Index as a Measure of Randomized Clinical Trial Quality in Adult Reconstruction: A Systematic Review

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ABSTRACT

Background: The Fragility Index (FI) and Reverse Fragility Index are powerful tools to supplement the *P* value in evaluation of randomized clinical trial (RCT) outcomes. These metrics are defined as the number of patients needed to change the significance level of an outcome. The purpose of this study was to calculate these metrics for published RCTs in total joint arthroplasty (TJA).

Methods: We performed a systematic review of RCTs in TJA over the last decade. For each study, we calculated the FI (for statistically significant outcomes) or Reverse Fragility Index (for nonstatistically significant outcomes) for all dichotomous, categorical outcomes. We also used the Pearson correlation coefficient to evaluate publication-level variables.

Results: We included 104 studies with 473 outcomes; 92 were significant, and 381 were nonstatistically significant. The median FI was 6 overall and 4 and 7 for significant and nonsignificant outcomes, respectively. There was a positive correlation between FI and sample size ($R = 0.14$, $P = .002$) and between FI and *P* values ($R = 0.197$, $P = .000012$).

Conclusions: This study is the largest evaluation of FI in orthopedics literature to date. We found a median FI that was comparable to or higher than FIs calculated in other orthopedic subspecialties. Although the mean and median FIs were greater than the 2 recommended by the American Academy of Orthopaedic Surgeons Clinical Practice Guidelines to demonstrate strong evidence, a large percentage of studies have an FI < 2. This suggests that the TJA literature is on par or slightly better than other subspecialties, but improvements must be made.

Level of Evidence: Level I; Systematic Review.

Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are 2 of the most commonly performed orthopedic surgeries in the world [1-4]. Current data suggest an increase by 143% in TKAs performed annually in the United States by 2050, [4] with similar numbers for THA [2]. Given this scenario, researchers are constantly looking for ways to evaluate and improve techniques and outcomes in these patient populations, often in the form of randomized controlled trials (RCTs). Analyzing RCTs can, thus, facilitate establishing a standard for both clinical practice guidelines and future research.

In evaluating these studies, the *P* value is the most used tool. However, the *P* value provides information solely relevant to an outcome's relation to the null hypothesis. It is unable to comment on sample size or strength of association. Thus, the Fragility Index (FI) and Reverse Fragility Index (RFI) have emerged as supplemental tools to assess clinical trial results. The FI and RFI are defined as the number of patients (or events) that would need to have an alternative outcome to convert an outcome from significant to nonsignificant or vice versa. A large FI suggests a robust outcome, as it

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would require many changed events to have a different outcome. Alternatively, a small FI suggests less confidence in an outcome, as very few events would be required to change its *P* value. The FI, thus, provides information on effect size, demonstrating how each event impacts the *P* value.

The FI has increasingly been used to evaluate orthopedic surgery clinical trials. The American Academy of Orthopaedic Surgeons (AAOS) published clinical practice guidelines for evaluating research, stating that an article with a median FI of 2 would be considered "strong research" [5]. The FI for orthopedic subspecialties is generally low, with reported FIs ranging from 2 to 5, with sports literature thus far being the most robust with an FI of 5 [6-10].

A recent study by Ekhtiari et al. described the FI of statistically significant outcomes in 34 RCTs in total joint arthroplasty (TJA) [11]. However, their sample was small, and this article seeks to expand that search. Research by Kahn et al. and McCormick et al. recently described the "reverse fragility index," which determines FI in nonstatistically significant outcomes in general and orthopedic research, respectively [12,13]. This allows the FI to be applied to a much larger body of research. The aim of our study was to evaluate the quality of RCTs in the orthopedic subspecialty of adult reconstruction using FI and RFI as metrics.

Material and methods

Study design and eligibility

The authors performed a systematic review of all RCTs using methods akin to those described in previous analyses of statistical fragility [5-10,14]. The top 25 highest impact orthopedic surgery and arthroplasty journals were determined via Incites Journal Citation Reports. These journals were queried for all RCTs in knee or hip arthroplasty published in the last 10 years in English.

Inclusion criteria were articles written in English between January 1, 2010, and September 1, 2020, that investigated surgical interventions for primary TJA and required the use of a 1:1 parallel, 2-arm randomization procedure, with at least 1 dichotomous outcome. Articles were excluded if they did not meet any of these criteria. Titles and abstracts were screened independently by 2 different authors (K.L.M. and A.G.) to ensure studies met inclusion criteria. If there was disagreement, a third author (C.L.H.) read the article as well. All articles were reviewed in their entirety to record all dichotomous, categorical outcomes for further analysis. The following study characteristics were collected for analysis: study size, number of patients lost to follow-up, outcome type, reported *P* values, and journal of publication. We used PubMed, Embase, and Medline to search, and the specific search criteria are summarized in Table 1.

Calculation of FI

The FI is defined as the lowest number of outcomes that must be changed to reverse the statistical significance of a *P* value. FI scores were calculated for each categorical, dichotomous outcome using Fisher's exact test as described by Walsh et al. [14]. For statistically significant outcomes, discrete outcome events were switched from the larger outcome group to the smaller group in a stepwise fashion until the *P* value was greater than 0.05. For statistically insignificant *P* values, events in the smaller outcome group were changed in a similar manner, until the *P* value was less than .05 and, thus, statistically significant.

Table 1
Search terms used for systematic review.

Search category	Terms used
Keywords	"Arthroplasty" OR "knee arthroplasty" OR "hip arthroplasty" AND "orthopedics" OR "Orthopedic Surgery" OR "surgery" OR "surgical procedure"
Article type	"Randomized controlled trial"
Publication date	"2010/01/01" [PDAT]: "2020/09/01" [PDAT]
Language	"English"

Statistical analysis

As stated previously, all *P* values were recalculated using Fisher's exact test. A Student's t-test was used to calculate the difference between the aforesaid study variables. Finally, the Pearson Correlation Coefficient was used to evaluate associations between FI and *P* values of included studies, as well as the associations between publication-level variables. All statistical analyses were performed using Microsoft Excel 2016 (Microsoft, Redmond, WA) and SPSS Version 23 (IBM, Armonk, NY).

Results

Characteristics

A total of 1069 articles were identified. After abstract review, 459 studies were excluded because they did not evaluate surgical interventions (eg, postoperative pain management, rehabilitation protocols). An additional 502 studies were excluded because they lacked dichotomous, categorical outcomes, and 5 studies for being focused on hemiarthroplasty and unicompartmental surgery. Ultimately, 104 studies were included for analysis with a total of 473 outcomes (Fig. 1). A full list of the included articles can be found in the appendices. The top 3 referenced journals were the *Journal of Arthroplasty* with 37 studies (35.6% of total articles), *Clinical Orthopaedics and Related Research* with 23 studies (22.1%), and *Bone & Joint Journal* with 14 articles (13.5%) (Table 2). The most often reported outcome type was postoperative complications (154 outcomes, 33%), as shown in Table 3.

Fragility index

Among the 473 outcomes assessed, the median FI was 6 (mean 6.7, range 1-40). Of the 91 statistically significant outcomes, the median FI was 4 (mean 5.6, range 1-26) (Fig. 2). The median FI for the 382 nonstatistically significant outcomes was 7 (mean 7.0, range 1-40) (Fig. 3). The FI was less than or equal to 3 in 98 outcomes (Fig. 4). There was a statistically significant difference between statistically significant and statistically insignificant outcomes ($P = .0007$). The number of subjects lost to follow up can be seen in Appendices Tables 1-3. Number of patients lost to follow-up was found to be greater than FI for 181 outcomes (38.3%). There was a positive correlation between FI and sample size ($R = 0.14$, $P = .002$), and between FI and *P* values ($R = 0.197$, $P = .000012$). There was no, however, correlation between FI and number of patients lost to follow-up ($R = 0.022$, $P = .62$) (Table 4).

Discussion

We identified 104 studies and 473 outcomes in our systematic analysis. This is the largest study to date examining FI for surgical clinical trials in TJA and, moreover, in any orthopedic subspecialty, as well as the first study to evaluate nonstatistically significant outcomes in TJA literature through the use of the RFI. We found a median FI of 6 for all 473 outcomes assessed, with a median FI of 4 and RFI of 7 for statistically significant and nonstatistically significant

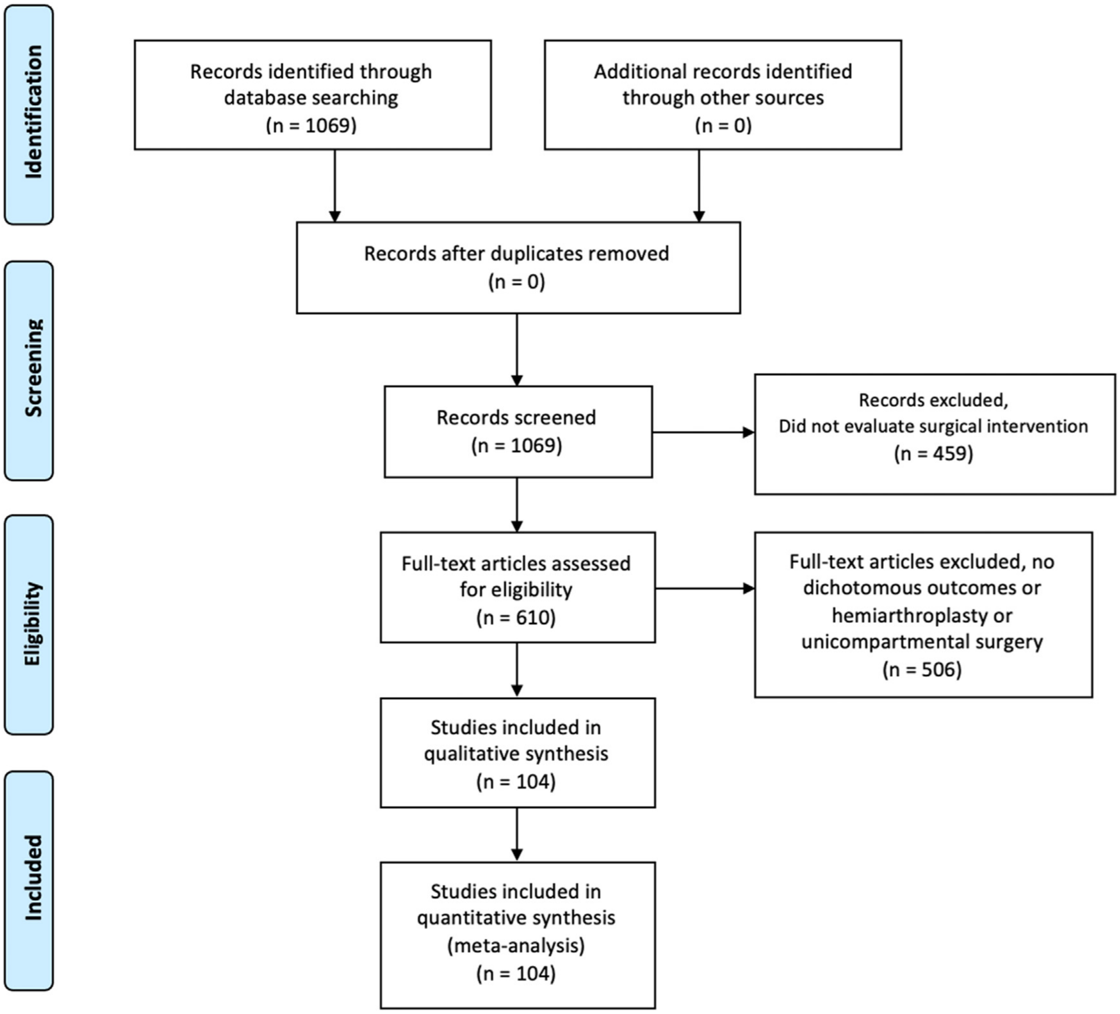

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

outcomes, respectively. These median FIs are comparable to or greater than those reported for other orthopedic subspecialties, which ranged from 2 to 5 [6-10]. As stated previously, the AAOS released guidelines which consider an FI above 2 as “strong evidence” [5]. According to that guidance, the FI and RFI calculated here demonstrate strong evidence and robust *P* values. In this investigation, FI/RFI ranged from 1 to 40. The largest value was an RFI of 40, assigned to an RCT investigating the effect of triclosan-coated sutures on surgical site infection after TKA and THA [15].

In addition, there were positive correlations between FI and sample size ($R = 0.14$, $P = .002$), and between FI and *P* values ($R = 0.197$, $P = .000012$). We would expect to see these results, as it suggests that the larger a sample size is, the more confident one can be in the *P* value. The further the *P* value moves from the null hypothesis in either direction, the more changes in event are needed to change the significance level and the stronger the result.

This study contradicts that of Ekhtiari et al. that was recently published [11]. In it, the authors performed a literature search to identify RCTs performed for primary or revision surgery and ultimately included 34 RCTs from the past decade in TJA literature and found that the median FI was 1, meaning that reversing the outcome of just one subject would change any statistically significant outcome to not statistically significant. Furthermore, they found that the FI was lower than that in any other reported orthopedic subspecialty. In their discussion, they argue that as TJA is such a common procedure and has widely accepted indications and

Table 2
Number of included publications by journal.

Journal	Number of publications
Journal of Arthroplasty	37
Clinical Orthopaedics and Related Research	23
Bone & Joint Journal	14
Journal of Bone and Joint Surgery	12
Knee Surgery Sports Traumatology Arthroscopy	9
Acta Orthopaedica	6
International Orthopedics	3

Table 3
Categorization of dichotomous recorded outcomes.

Outcome	Count, N (%)
Postoperative complication	154 (32.6)
Alignment: radiographic findings	114 (24.1)
Patient pain/function	86 (18.2)
Failure of surgery/required reoperation	49 (10.4)
Other radiological findings	44 (9.3)
Transfusion	19 (4.0)
Patient satisfaction	7 (1.5)

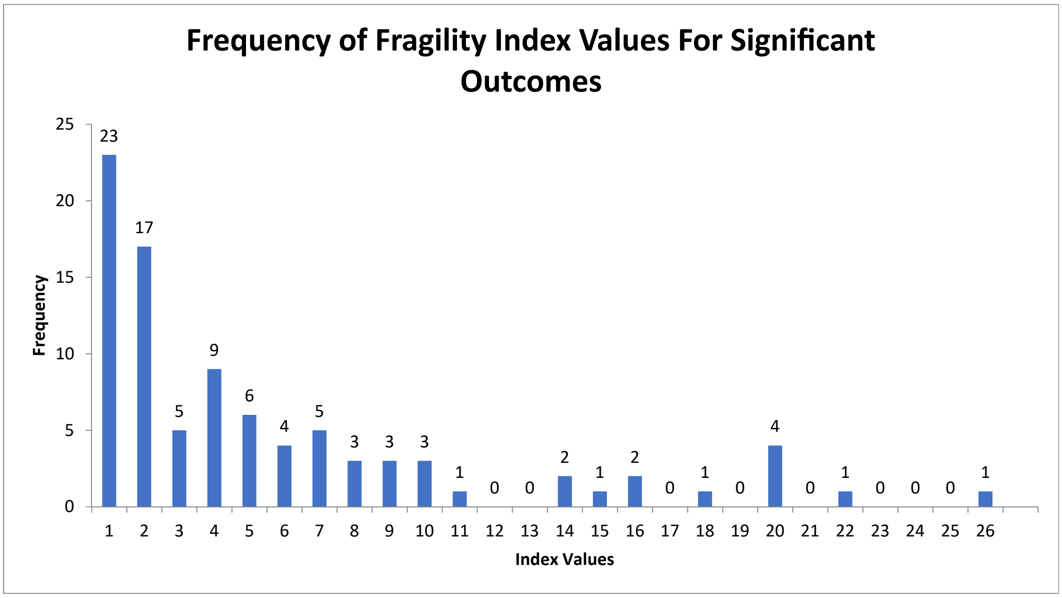

Figure 2. Frequency of fragility index values of significant outcomes histogram.

techniques, future trials should not be hampered by small sample sizes. Our data do corroborate their last point. Based on our calculations, FI does correlate strongly with increasing sample size. In evaluating the FI of both significant and nonsignificant outcomes, however, we found a much higher median FI of 6 overall, and 4 and 7 for significant and nonsignificant outcomes, respectively. Both these values are greater than what their study reported [11]. Our research evaluated different studies—we chose to evaluate solely primary TJA RCTs describing surgical interventions in the top 25 highest impact orthopedic journals, with manuscripts in English. However, we included more than triple the number of studies (104 rather than 34) by including insignificant outcomes and calculating the RFI, the number of patients needed to change outcomes in a study, to change a nonstatistically significant variable into one that is statistically significant. It is possible that this increased FI/RFI is in part due to using higher impact journals.

However, these data should be interpreted with caution. One hundred and eighty-one (38.3%) of the outcomes analyzed in this review had FIs greater than the number of patients lost to follow-up. Combining both FI and RFI, there are 65 outcomes with an FI or RFI $\leq$ 2, which represents 14% of the outcomes studied here (Fig. 4). We attempted to control for this by using median values rather than means, and by including more studies, we were able to show a strong overall median FI; but there is certainly still room for improvement. For comparison, a recent review of RCTs in cardiology showed that the median FI of 123 manuscripts was 13 [16].

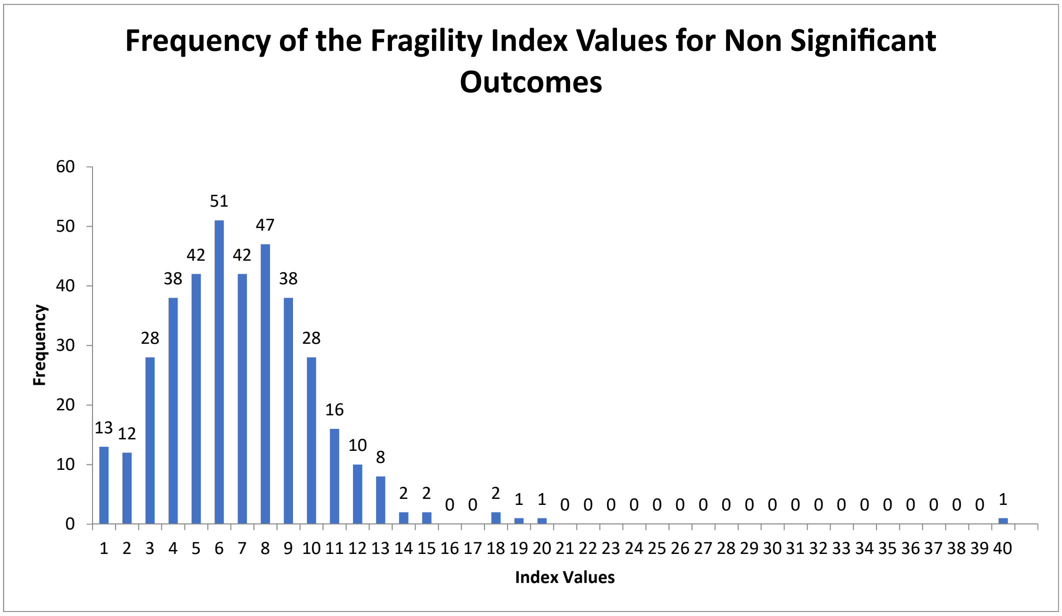

Figure 3. Frequency of fragility index values of nonsignificant outcomes histogram.

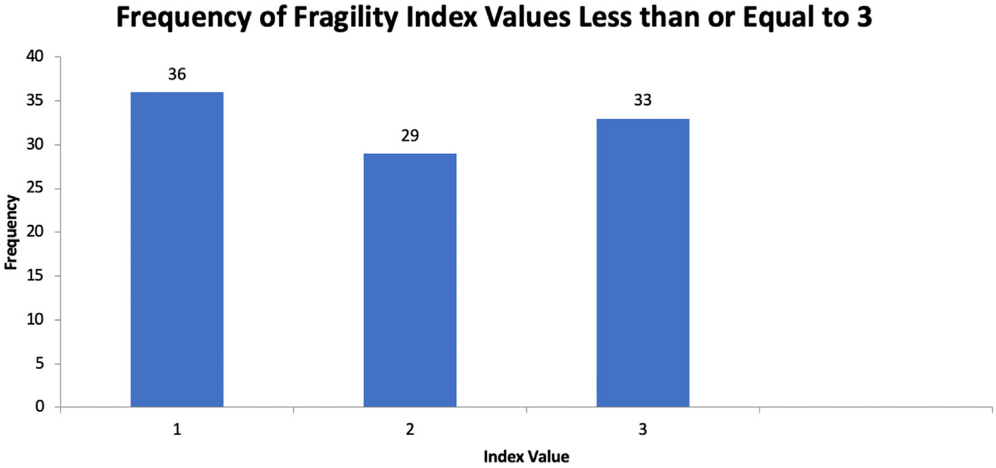

Figure 4. Frequency of fragility index values less than or equal to 3 histogram.

The FI has inherent limitations. A major limitation of this metric is its inability to evaluate nondichotomous outcome variables. Many outcomes in TJA research are reported with continuous metrics including radiographic angles and patient-reported outcomes, which the FI is unable to assess. As a result, a significant portion of studies had to be excluded (Seventy-eight percent of studies evaluated were excluded for not having dichotomous outcomes.). Because of this the FI, while useful in the appropriate setting, has a relatively limited application. Previously, the FI was even more limited, only applicable to significant outcomes. By adding the RFI, we were able to include nonstatistically significant outcomes and expand the FI's usefulness, but it is still limited by design as a statistical tool. Further work needs to be carried out to expand its use or to determine complementary tools.

TJAs remain some of the most common procedures in the world today [1-4]. As of 2010, 0.83% of the population and 1.52% of the population have undergone THA and TKA, respectively. This number is growing, with estimations that THAs will grow by 71% by 2030 to 635,000 procedures annually and that TKAs will grow by 85% to 1.26 million procedures [1]. Given this, research is extremely important to ensure safe and accessible TJAs as demand increases. With RCTs being one of the strongest forms of clinical research, analyzing the robustness of their outcomes is of upmost importance in determining which treatment is safe and efficacious for our patients.

Despite its limitations, we believe the FI and RFI provide value in assessing outcomes in clinical research and holding our field accountable for the research we perform. Given the evidence shown here, although mean and median FI/RFI values were greater than the AAOS benchmark of 2, there are still a wide number of studies with numbers below that, and we must continue to be diligent in how we design trials evaluating TJA.

Table 4
Publication-level associations between fragility index and study variables.

Study variables	Pearson correlation coefficient	*P* value
Patient sample size	0.140	.002[a]
Journal impact factor	-0.0263	.56
Number of journal citations	-0.096	.035[a]
Patients lost to follow-up	0.022	.62
All *P* values	0.197	.000012[a]
Significant *P* values	-0.028	.78
Nonsignificant *P* values	0.177	.000045[a]

[a] Statistically significant.

Conclusions

This study is the largest evaluation of FI in orthopedics literature to date. We found a median FI/RFI of 4 for recently published TJA literature, which is comparable to or higher than FIs calculated in other orthopedic subspecialties. Although, overall, these numbers suggest strong evidence, there is still a large minority of studies with poor methodology. These data should be interpreted with caution, and we must continue to demand more sound research designs from our subspecialty.

Conflicts of interest

C. L. Herndon is a board member in AAOS.

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Appendix

Appendix Table 1
Analyzed total hip arthroplasty articles.

Journal	Author	Year	Comparison	Patients enrolled	Lost to follow-up	Outcomes (no.)	FI*
ACTA	Gustafson et al. [1]	2014	Metal-on-metal hip resurfacing vs metal-on-polyethylene THA	54	10	14	6
	Flatøy et al. [2]	2016	Electrochemically deposited vs conventional plasma-sprayed hydroxyapatite femoral stem	55	30	2	9
BJJ	Vendittoli et al. [3]	2013	Hybrid hip resurfacing vs metal-on-metal uncemented THA	219	55	6	5
	Lee et al. [4]	2014	28-mm vs 32-mm Ceramic heads	120	107	1	13
	van der Veen et al. [5]	2015	Metal-on-metal vs metal-on-polyethylene THA	104	6	1	9
	Schilcher et al. [6]	2017	Bisphosphonate solution vs saline	60	2	3	5
	Ando et al. [7]	2018	Large vs conventional femoral head	185	69	1	2
	Sköldenberg et al. [8]	2019	Argon-gas gamma-sterilized vs vitamin E-doped, highly crosslinked polyethylene	42	4	1	2
CORR	Della Valle et al. [9]	2010	Mini-incision vs two-incision THA	72	0	3	8
	Goosen et al. [10]	2011	Minimally invasive vs classic posterolateral approach	120	0	10	7
	Corten et al. [11]	2011	Cemented vs cementless	250	0	5	6
	Weber et al. [12]	2014	Fluoroscopy vs imageless navigation	125	9	4	7
	Engh et al. [13]	2016	Ceramic-on-metal vs metal-on-metal	72	9	2	5
	Parratte et al. [14]	2016	Computer-assisted vs conventional	60	0	1	10
	Kim et al. [15]	2016	Ultrashort vs conventional anatomic cementless femoral stem	212	12	3	16
	Hopper et al. [16]	2018	Crosslinked vs conventional polyethylene	230	0	4	4
	Nakamura et al. [17]	2018	Robot-assisted vs hand-rasped stem	130	15	1	4
	Taunton et al. [18]	2018	Direct anterior vs mini posterior THA	116	15	1	4
	Mjaaland et al. [19]	2019	Direct anterior vs direct lateral THA	164	11	2	9
Int. Orthop.	Bascarevic et al. [20]	2010	Alumina-on-alumina ceramic vs metal on highly cross-linked polyethylene	150	0	23	6
JOA	Amanatullah et al. [21]	2011	Ceramic-ceramic vs ceramic-polyethylene	357	45	19	6
	Beaupre et al. [22]	2013	Ceramic-on-ceramic vs ceramic-on-crossfire polyethylene	92	14	1	3
	Barrett et al. [23]	2013	Direct anterior vs posterolateral THA	87	0	20	7
	Gurgel et al. [24]	2014	Computer-assisted vs conventional THA	40	0	1	9
	Lass et al. [25]	2014	Imageless navigation system vs conventional THA	130	5	1	7
	Hamilton et al. [26]	2015	28-mm vs 36-mm Femoral heads	345	113	1	3
	Wegrzyn et al. [27]	2015	Tantalum vs titanium cup	111	25	2	4
	Gao et al. [28]	2015	Tranexamic acid with epinephrine vs tranexamic acid alone	110	3	11	7
	Suarez et al. [29]	2015	Bipolar sealer vs standard electrocautery	118	0	1	1
	Sculco et al. [30]	2016	Perioperative corticosteroids vs placebo	40	13	7	7

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Appendix Table 1 (*continued*)

Journal	Author	Year	Comparison	Patients enrolled	Lost to follow-up	Outcomes (no.)	FI*
	North et al. [31]	2016	Topical vs intravenous tranexamic acid	139	0	1	1
	Cheng et al. [32]	2017	Direct anterior vs posterior approach THA	75	2	15	5
	Guild et al. [33]	2017	Hybrid plasma scalpel vs bipolar sealer	232	0	1	29
	Abdel et al. [34]	2017	Two-incision vs mini-posterior approach THA	72	1	4	8
	Gielis et al. [35]	2019	Short vs wedge-shaped straight stem	150	10	8	7
	Brun et al. [36]	2019	Direct lateral vs minimal invasive anterior approach THA	164	0	8	5
JBJS	Barsoum et al. [37]	2011	Bipolar sealer vs standard electrocautery	140	0	2	9
	Howie et al. [38]	2012	28-mm vs 36-mm Femoral heads	645	30	1	2
	Devane et al. [39]	2017	Highly cross-linked vs ultra-high-molecular-weight polyethylene	122	31	1	5
	Kayupov et al. [40]	2017	Oral vs intravenous tranexamic acid	89	6	1	10

Acta, *Acta Orthopaedica*; BJJ, *Bone & Joint Journal*; CORR, *Clinical Orthopaedics and Related Research*; Int. Orthop., *International Orthopedics*; JBJS, *Journal of Bone and Joint Surgery*; JOA, *Journal of Arthroplasty*.

* Average for all outcomes rounded to the nearest digit.

Appendix Table 2
Analyzed total knee arthroplasty articles.

Journal	Author	Year	Comparison	Patients enrolled	Lost to follow-up	Outcomes (no.)	FI*
Acta	Meijerink et al. [41]	2011	CKS vs PFC TKA designs	82	0	3	3
	Stilling et al. [42]	2011	High-porosity trabecular metal vs low-porosity titanium-pegged porous fiber-metal polyethylene backing tibial components	50	4	1	6
	Wilson et al. [43]	2012	Trabecular metal vs cemented tibial component	70	25	1	11
	Van Leeuwen et al. [44]	2018	Patient-specific positioning guides vs conventional method	109	15	6	4
BJJ	Breeman et al. [45]	2013	Mobile vs fixed-bearing TKA	539	7	14	8
	van Jonbergen et al. [46]	2014	Circumpatellar electrocautery vs no treatment	300	98	1	1
	Boonen et al. [47]	2016	Patient-matched positioning guides and conventional instruments	180	17	1	2
	Schotanus et al. [48]	2016	MRI vs CT patient-specific guides in TKA	140	3	11	7
	Powell et al. [49]	2018	Mobile vs fixed-bearing TKA	167	82	2	3
	Lachiewicz and O'Dell [50]	2019	Standard vs highly crosslinked polyethylene	265	56	5	8
	MacDessi et al. [51]	2020	Kinematic vs mechanical alignment	128	0	21	9
CORR	Hernández-Vaquero et al. [52]	2011	Navigation vs jig-based TKA	97	24	5	7
	Charoencholvanich et al. [53]	2011	Tranexamic acid vs placebo	100	0	1	9
	Laffosse et al. [54]	2011	Midline vs anterolateral skin incision	64	2	3	5
	Cip et al. [55]	2013	Autotransfusion vs control	151	11	1	12
	Roh et al. [56]	2013	Patient-specific instrumentation vs conventional method	100	10	6	2
	Fernandez-Fairen et al. [57]	2013	Porous tantalum cementless vs cemented tibial component	145	13	3	6
	Pongcharoen et al. [58]	2013	Medial parapatellar vs midvastus approach TKA	59	0	13	8
	Song et al. [59]	2013	Robot-assisted vs conventional TKA	100	0	5	9
	Pinsornsak et al. [60]	2014	Infrapatellar fat pad excision vs no excision	90	13	3	2
	Sah [61]	2015	Bidirectional barbed vs standard sutures	50	0	3	7
	Young et al. [62]	2017	Kinematic vs mechanical alignment	114	0	3	8
	Kim et al. [63]	2018	Navigation vs conventional TKA	296	14	9	11
Int. Orthop.	Chen et al. [64]	2014	Whole vs half course tourniquet use	64	0	1	8
	Ha et al. [65]	2019	Resurfacing vs nonresurfacing of the patella	66	4	2	6
JOA	Hamilton et al. [66]	2011	High flex vs standard rotating platform TKA	142	6	1	2
	Plymale et al. [67]	2012	Unipolar vs bipolar hemostasis in TKA	113	0	1	9
	Georgiadis et al. [68]	2013	Topical tranexamic acid vs placebo	101	0	5	6
	Kusuma et al. [69]	2013	Bovine thrombin vs no treatment	80	0	1	4
	Liow et al. [70]	2014	Robot-assisted vs conventional TKA	60	0	3	4
	Nam et al. [71]	2014	Extramedullary vs accelerometer navigational cutting guides	100	6	4	5
	Randelli et al. [72]	2014	Topical novel fibrin vs no treatment	62	0	1	6
	Patel et al. [73]	2014	Intravenous vs topical tranexamic acid	100	0	1	7
	Gao et al. [74]	2015	Tranexamic acid with epinephrine vs tranexamic acid alone in TKA	103	0	7	7
	Fricka et al. [75]	2015	Cemented vs cementless TKA	100	3	3	5
	Shi et al. [76]	2016	Fixed vs individualized valgus correction	133	0	3	17

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Appendix Table 2 (*continued*)

Journal	Author	Year	Comparison	Patients enrolled	Lost to follow-up	Outcomes (no.)	FI*
	Ahn et al. [77]	2016	Reduction osteotomy vs pie-crusting for medial release	106	0	1	4
	Chan et al. [78]	2017	Bidirectional barbed vs traditional sutures in TKA	117	0	6	5
	Wang et al. [79]	2017	Tranexamic acid vs placebo	200	0	4	4
	Kim et al. [80]	2017	High flex vs standard TKA	994	34	2	11
	Teeter et al. [81]	2017	Measured resection vs gap balancing TKA	23	0	1	3
	Gharaibeh et al. [82]	2017	Navigation vs conventional TKA	190	4	10	6
	Tammachote et al. [83]	2018	Customized cutting block vs conventional TKA	108	2	9	7
	Cip et al. [84]	2018	Navigation vs conventional TKA	200	141	11	5
	Dong et al. [85]	2018	Patellar resurfacing and circumpatellar electrocautery vs circumpatellar electrocautery alone	53	5	2	8
	Thiengwittayaporn et al. [86]	2019	Patellar resurfacing vs nonresurfacing	84	4	1	10
JBJS	Hui et al. [87]	2011	Oxidized zirconium vs cobalt-chromium femoral component	40	6	1	9
	Huang et al. [88]	2011	Computer-assisted navigation vs conventional TKA	113	0	4	2
	Hinarejos et al. [89]	2013	Erythromycin and colistin cement vs standard cement	3000	52	3	8
	Schimmel et al. [90]	2014	Bicruciate substituting vs conventional posterior stabilizing implant	124	0	1	4
	Verburg et al. [91]	2016	Mini-midvastus vs conventional TKA	100	0	3	5
	Petursson et al. [92]	2018	Computer assisted vs conventional TKA	190	23	11	4
	Abdel et al. [93]	2018	Intravenous vs topical tranexamic acid	664	24	2	13
	Nam et al. [94]	2019	Cemented vs cementless TKA	147	6	2	14
KSSTA	Demey et al. [95]	2011	Cemented vs uncemented femoral component	130	9	5	6
	Pang et al. [96]	2011	Computer-assisted gap balancing vs conventional measures	140	0	4	6
	Jung et al. [97]	2013	Intramedullary vs extramedullary alignment	91	0	3	6
	Lee et al. [98]	2013	Tranexamic acid + indirect factor Xa inhibitor vs indirect factor Xa inhibitor alone	72	0	4	6
	Breugem et al. [99]	2014	Fixed vs mobile posterior stabilized design	103	3	3	6
	Izumi et al. [100]	2015	Transcutaneous electrical nerve stimulation vs control	90	0	1	1
	Chen et al. [101]	2015	Pin-less navigation vs conventional surgery	100	0	3	1
	Ollivier et al. [102]	2016	MRI-based vs computer-assisted TKA	80	0	5	6
	Collados-Maestre et al. [103]	2017	Single radius vs multiradius TKA	240	3	3	2

Acta, *Acta Orthopaedica*; BJJ, *Bone & Joint Journal*; CORR, *Clinical Orthopedics and Related Research*; Int. Orthop., *International Orthopedics*; JOA, *Journal of Arthroplasty*; JBJS, *Journal of Bone and Joint Surgery*; CKS, continuum knee system; PFC, press fit condylar; MRI, magnetic resonance imaging; CT, computed tomography; KSSTA, knee surgery, sports traumatology, arthroscopy.

[*] Average for all outcomes rounded to the nearest digit.

Appendix Table 3
Analyzed total hip and total knee arthroplasty articles.

Journal	Author	Year	Comparison	Patients enrolled	Lost to follow-up	Outcomes (no.)	FI*
BJJ	Sprowson et al. [104]	2018	Triclosan-coated vs standard sutures	2546	109	20	9

BJJ, *Bone & Joint Journal*.

[*] Average for all outcomes rounded to the nearest digit.