Evaluation of language analysis to summarize the literature: a comparison to traditional meta-analysis in primary hip and knee surgery

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ABSTRACT

Introduction Sentiment analysis, by evaluating written wording and its context, is a growing tool used in computer science that can determine the level of support expressed in a body of text using artificial intelligence methodologies. The application of sentiment analysis to biomedical literature is a growing field and offers the potential to rapidly and economically explore large amounts of published research and characterize treatment efficacy.

Methods We compared the results of sentiment analysis of 115 article abstracts analyzed in a recently published meta-analysis of peripheral nerve block usage in primary hip and knee arthroplasty to the conclusions drawn by the authors of the original meta-analysis.

Results A moderately positive outlook supporting the utilization of regional anesthesia for hip and knee arthroplasty was found in the 115 articles that were included for analysis, with 46% expressing positive sentiment, 35% expressing neutral sentiment, and 19% of abstracts expressing negative sentiment. This was well aligned with the conclusions reached by a previous meta-analysis of the same articles.

Discussion Sentiment analysis applied to the medical literature can rapidly evaluate large collections of published data and generate an impression of overall findings that are aligned with the findings of a traditional meta-analysis.

INTRODUCTION

As the volume of medical literature continues to grow, meta-analysis studies represent an increasingly used and important mechanism to distil the available published data and make conclusions based on larger patient sample sizes. The clinical utility of these analyses results is derived from strengthened supportive conclusions in those settings where study findings are congruent and in dismissal of findings that fail to be replicated across published studies. While meta-analyses represent a powerful mechanism to evaluate published study data, their conduct can be limited by the time required to locate and evaluate appropriate published studies, export data that are to be included, and perform a statistical analysis. As the number of questions and scenarios explored by clinicians expands, the time constraints associated with traditional meta-analysis studies may render these types of analyses unwieldy and impractical for practicing clinicians.

One potential option to address the growing size of literature on any topic is the utilization of artificial intelligence as an alternative or complement to traditional systematic review and meta-analysis. More specifically, a method such as sentiment analysis or other natural language processing methods could be used to quickly assess the findings of large groups of published studies and serve as a mechanism to generate further hypothesis.

Sentiment analysis is a type of artificial intelligence that can classify a body of text based on the qualitative sentiment (ie, the tone expressed) expressed within it and output either a categorical sentiment score (ie, positive, negative, neutral) or a numerical score which is on a spectrum where -1 is very negative and 1 is very positive.[1] This type of analysis has been applied in a variety of fields in the past for assessing large-scale trends such as those in social media[2] or bodies of clinical trial literature.[3] Furthermore, specific algorithms have been developed that facilitate sentiment analysis of clinical trial abstracts.[4] This presents an intriguing avenue for quick assessment of the qualitative statements made by the authors of a study. However, sentiment analysis as an adjunct or complement to other methods of systemic analysis of biomedical literature has not yet been explored.

With this in mind, we performed a sentiment analysis of the clinical trial abstracts used in a recent meta-analysis evaluating peripheral nerve block anesthesia use in primary hip and knee arthroplasty. We then compared the results of this sentiment analysis to what was reported in the meta-analysis. The goal of this study was to compare the results of sentiment analysis with the more exhaustive process of systematic review and explore its application as an adjunct to such methods of literature review.

METHODS

In this study, the sentiment (ie, the tone or level of support) of articles cited in a recent systematic review of the literature evaluating the use of peripheral nerve block analgesia for primary hip and knee arthroplasty was determined using GAN-BioBERT sentiment analysis.[4 5] These findings were then compared with those expressed in a recent meta-analysis evaluating analgesic techniques for total hip and knee arthroplasty.[5] This algorithm is publicly available under open-source license.[6]

Data collection

The abstracts of published manuscripts included in the systematic review by Memtsoudis *et al* that had abstracts available in the PubMed database were

Table 1 Samples of phrases with each sentiment category and value as determined by GAN-BioBERT

Sample phrases	Sentiment classification
The results of this study were promising.	Positive
The results of this study showed that treatment was contraindicated.	Negative
There were no significant differences found between the treatment and control group.	Neutral

collected using the NCBI's Entrez E-Utilities API by identifying the associated PMID for each paper.[5] Manuscripts that either did not have abstracts available or were not indexed in PubMed were excluded.

Subgroup analyses

From the abstracts, several subgroup analyses were also performed. The subgroups included division by anesthesia technique, study type, surgery type (ie, knee vs hip arthroplasty), risk of bias, and number of patients in the study.

For the bias-based subgroups, studies with a bias rating risk of 'high' for any study characteristic as determined by Memtsoudis *et al* using the Cochrane Risk of Bias Tool were included in the high risk of bias subgroup; all other studies were treated as having a low risk of bias.

The specific division for the subgroups divided by patients per study was studies with greater than the median number of patients of all the studies analyzed versus those that did not.

Sentiment analysis

The algorithm used for sentiment analysis in this study, GAN-BioBERT, was written based on a semisupervised version of the previously described bidirectional encoder representations from transformers (BERT) algorithm for natural language processing by Devlin *et al*.[7 8] GAN-BioBERT was built by Myszewski *et al* specifically for categorically classifying the tone expressed in clinical abstracts as either positive, negative, or neutral. Examples of text classified into each of these categories are shown in table 1.

To understand the utility of GAN-BioBERT as it relates to this study, we first need to discuss its precursors, BERT and BioBERT. The process by which GAN-BioBERT comes from these previous methods is shown graphically in figure 1.

A detailed description of the original BERT algorithm is available elsewhere,[7] but some discussion of the algorithm and its derivations that led to the algorithm used in this study is important to understanding its applicability to clinical literature.

The original BERT algorithm is currently considered as one of the state-of-the-art methodologies for natural language processing with high levels of accuracy. This algorithm uses a methodology known as transfer learning wherein a pretrained language model for a particular domain (ie, biomedical literature) is first developed with an extremely large sample of text from the language domain being studied. The original BERT model by Devlin *et al* was trained on a set of 2.5 billion words of text from English Wikipedia as well as 800 million words of text from BooksCorpus, a large collection of English language novels.[7] This original BERT model was designed to be suited for general language tasks, but not to understand the nuances and complicated language frequently used in biomedical literature.

This general model was then refined in a second 'fine-tuning' step with fewer samples for the task of interest, (ie, biomedical literature) in a method that is dependent on the appropriateness of the original general language model.

To make this general language model more applicable to biomedical literature BioBERT was developed in 2020 by Lee *et al*.[9] This was done by further training the original BERT model with an additional 4.5 billion words from PubMed abstracts as well as 13.5 billion words from PubMed Central full-text articles to create the language model known as BioBERT,[9] which is uniquely designed/appropriate for the nuances of the writing style and terminology used in biomedical and academic literature

The algorithm/language model used in this study, GAN-BioBERT, was developed by Myszewski *et al* by further fine-tuning the biomedically oriented language model BioBERT for the specific task of classifying clinical study abstract sentiment.

The term fine-tuning is used to describe the process of refining a pretrained language model, that is, BioBERT, for a particular task such as sentiment classification of clinical trial abstracts by providing a smaller task specific set of examples to the algorithm. Following this fine-tuning step, the algorithm's performance is assessed and can then be applied for the proposed application (ie, sentiment classification of biomedical abstracts).

The sentiment classifications made by the GAN-BioBERT algorithm used for this study coincided with the determination of clinicians 91.3% of the time for classifying the sentiment in clinical trial abstracts as positive, negative, or neutral. This was determined by comparing the sentiment classifications made by the algorithm to the categorical classifications made by a set of clinicians on a set of sample abstracts that contained an equal
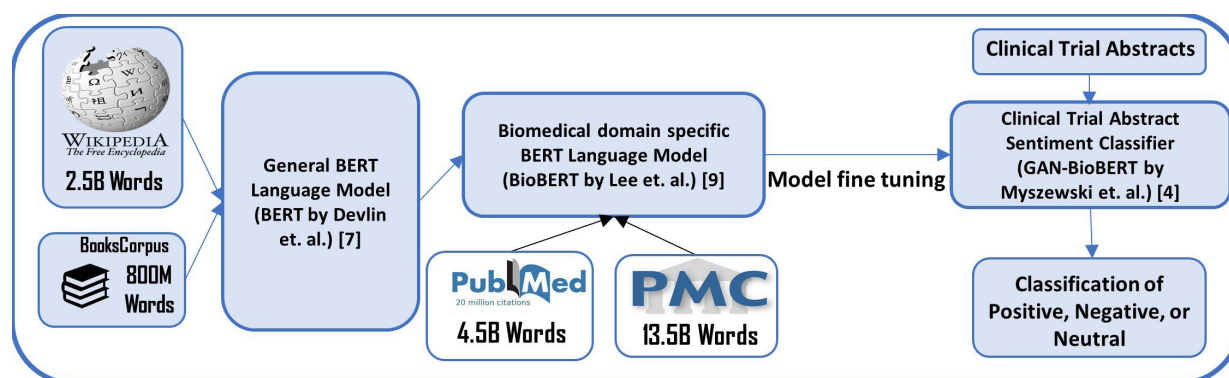
Figure 1 A graphical representation of the development of GAN-BioBERT as it relates to this study. BERT, bidirectional encoder representations from transformers.

amount of positive, negative, and neutral abstracts as determined by the clinicians.[4]

It is important to note that on an individual article level, GAN-BioBERT only categories abstracts as positive, negative, or neutral. This three-category classification scheme was chosen to provide adequate detail without sacrificing an adequate level of accuracy. More finely grained algorithms for sentiment classification are significantly limited by drops in accuracy as the granularity of the sentiment classifications is increased. For example, the original BERT algorithm was correct only 55.5% of the time when used for a sentiment classifier with five categories, as compared with being correct 93.1% of the time for a two-category benchmark dataset.[7] Given this limitation, GAN-BioBERT is only suited to large samples of articles and not for use on individual articles.

RESULTS

Of the 122 study abstracts included in the original meta-analysis, 115 were included for sentiment analysis. One article was excluded due to not having an abstract but was still indexed in PubMed and six other articles were excluded due to not being indexed within the PubMed database. Each study, alongside its corresponding sentiment value determined by the algorithm is provided in online supplemental appendix A1.

Of the 115 articles included for analysis, it was determined that 56 (46.1%) had positive sentiment, 22 (19.1%) had negative sentiment, and 50 (34.8%) were neutral using sentiment analysis. The entire runtime for the analysis program, including data gathering, sentiment classification, and the subgroup analysis, was 8 min and 39 s on a desktop computer.

For comparison, the findings of the meta-analysis by Memtsoudis *et al* expressed a generally positive outlook toward the application of peripheral nerve block analgesia for total hip and knee arthroplasty.[5] This sentiment was determined qualitatively based on the general recommendation made in that study that the use of peripheral nerve block analgesia is recommended for hip and knee arthroplasty as it leads to improved clinical outcomes. This generally positive outlook in the meta-analysis is aligned with the findings determined using sentiment analysis where the greatest proportion of studies had positive sentiment. It is also important to note that a large amount of the studies included expressed neutral sentiment, indicating a more moderate positive outlook.

The results for each of the subgroup analyses are shown in table 2. The median number of patients per study was found to be 80 patients.

DISCUSSION

In this study, a sentiment analysis of the sources used by a recent meta-analysis evaluating the clinical efficacy of regional anesthesia procedures for hip and knee arthroplasty reached a similar conclusion to that of the meta-analysis. In doing so, this current study accomplished two important goals that warrant further discussion. First, this study demonstrated that the GAN-BioBERT sentiment analysis approach yielded results concurrent with the findings of the Memtsoudis *et al* meta-analysis. Second, this study demonstrated that sentiment analysis represents an efficient alternative and/or complement to meta-analysis studies, with the total runtime of the analysis program requiring fewer than 10 min.

This study's (and the GAN-BioBERT algorithm's) major limitation is created by the three-class classification system and manifests as an inability to draw conclusions without an adequate sample size. This limitation restricts the use of the algorithm such that it cannot be used to draw conclusions on an individual level and is most appropriately used on a large aggregative scale to identify publication trends or as a precursor to more in-depth assessment of academic literature. With this in mind, the algorithm's application is limited to assessing larger trends such as topic-specific sentiment, as well as how this sentiment varies across time or specialty. Additional examples of possible applications fitting with this limitation include identifying trends related to publication biases as was shown in the subgroup analysis where the high bias and low bias subgroups had significantly different findings. Ideally, as the technology of sentiment analysis continues to advance, more granular classification schemes will achieve acceptable accuracy levels and the large sample size requirement will be ameliorated.

This study does possess several other limitations that should be considered prior to widespread application of sentiment scoring for guiding clinical decision-making. First, this specific algorithm only examines vocabulary located within abstracts of published studies. This limitation is imposed secondary to a significant loss of classification accuracy when the technology is used to classify sentiment for longer length bodies of text such as those in the body of manuscripts.[1] Therefore, text within the body of the manuscript that may recommend tempered

Table 2	Proportion of positive, negative, and neutral abstracts in each subgroup			
Subgroup	Sample (n)*	Positive	Negative	Neutral
All included studies	115	53 (46.1%)	22 (19.1%)	50 (34.8%)
Both general and neuraxial anesthesia	26	12 (46.2%)	7 (26.9%)	7 (26.9%)
Only general anesthesia	24	12 (50%)	7 (29.2%)	5 (20.8%)
Only neuraxial anesthesia	49	22 (44.9%)	5 (10.2%)	22 (44.9%)
Hip arthroplasty	27	12 (44.4%)	5 (18.5%)	10 (37.1%)
Knee arthroplasty	92	41 (44.6%)	19 (20.6%)	32 (34.8%)
Studies with >80 patients	55	17 (30.9%)	17 (30.9%)	21 (38.2%)
Studies with <80 patients	60	36 (60%)	5 (8%)	19 (32%)
High risk of bias studies	37	23 (62.2%)	3 (8.1%)	11 (29.7%)
Low risk of bias studies	78	30 (38.5%)	19 (24.4%)	29 (37.1%)
Observational studies	40	15 (37.5%)	11 (27.5%)	14 (35%)
Randomized control trials	75	38 (50.7%)	11 (14.7%)	26 (34.6%)

*These subgroups are not all mutually exclusive and there may be overlap between groups.

enthusiasm or shades of optimism would not be subject to evaluation via the reported evaluation method. Second, this study only used sentiment analysis as a mechanism to validate a single meta-analysis study. It is possible that further examination of diverse meta-analysis studies may not result in similar findings or may find that different specialties are more apt to use positive, negative, or neutral terminology within their scientific writing. Third, the use of sentiment analysis in this context is unable to determine the impact of the studied intervention on a variety of clinical outcome domains. For example, the study by Memtsoudis *et al* demonstrated that the use of peripheral nerve blocks in the setting of knee and hip arthroplasty reduced the risk of cognitive dysfunction, respiratory failure, cardiac complications, and surgical site infections. However, in some cases, sentiment analysis may align closer to clinical decision-making where a clinician plans to administer a 'better' option and not necessarily one that offers an improvement in any distinct outcome domain.

Finally, performing a sentiment analysis may be beyond the technology limitations of an individual and therefore may not represent a feasible mechanism of literature review for all providers. Furthermore, while this study showed that sentiment analysis could accelerate the process of assessing literature, the application of sentiment analysis will still require the same careful consideration of the sources used for a particular research question or topic as is currently used in the process of systematic analyses and meta-analyses. However, it is important to consider that meta-analysis and expert opinion are imperfect and potentially subject to biases as rules are variably applied to which manuscripts are included in the final analysis or opinion is based on local experience and training.

Briefly, this study successfully used sentiment analysis as a rapid and efficacious mechanism to reach the same conclusion as a previously published meta-analysis study. With this in mind, sentiment analysis shows promise as a clinical literature evaluation tool that can be added to the repertoire of methods researchers and clinicians use to perform their work, verify study findings, and generate novel hypotheses.

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The majority of this data was retrieved from supplemental 1 provided by Memtsoudis et. al.,[1] with the addition of the sentiment scores from this study. As a reminder, a score of 1 is positive, -1 is negative, and 0 is neutral. n/a is provided for studies that were excluded from sentiment analysis due to either not having an abstract available on PubMed or for not being indexed in the PubMed database.

Randomized Control Trials

A: Allocation concealment B: Blinding of outcome assessors C: Blinding of participants and personnel D: Incomplete outcome data E: Other sources of bias F: Selective outcome reporting G: Sequence Generation

Study	Ref	Year	Study Type	n	A	B	C	D	E	F	G	Sentiment
Aksoy	2	2014	THA	70	Unclear	Low	High	Low	Low	Low	Low	1
Amundson	3	2017	TKA GA NA	157	Low	Low	Low	Low	Low	Low	Low	-1
Andersen	4	2012	TKA NA	40	Low	Low	Low	Low	Low	Low	Low	0
Angers	5	2019	TKA GA	90	Low	Low	Low	Low	Low	Low	Low	-1
Ashraf	6	2013	TKA NA	40	Low	Low	Low	Low	Low	Low	Unclear	0
Bali	7	2016	TKA GA	68	Low	Low	High	Low	Low	Low	Low	0
Baranovi	8	2011	TKA NA	71	Unclear	Unclear	Unclear	High	Low	Low	Low	1
Barrington	9	2005	TKA NA	108	Low	High	High	Low	Low	Low	Low	0
Beausang	10	2016	TKA NA	96	Unclear	High	High	Low	Low	Low	Unclear	0
Biswas	11	2018	TKA NA	130	Low	Low	Low	Unclear	Low	Low	Low	0
Bogoch	12	2002	THA TKA GA	115	Low	Low	Low	Low	Low	Low	Unclear	-1
Bron	13	2018	THA NA	162	Low	Low	Low	Low	Low	Low	Unclear	0
Campbell	14	2008	TKA NA	56	Unclear	Low	Unclear	High	Low	Low	Low	1
Chan	15	2013	TKA GA NA	135	Low	Low	High	Unclear	Low	Low	Low	1
Chan	16	2014	TKA	135	Unclear	Low	Unclear	Low	Low	Low	Unclear	0
Chaumeron	17	2013	TKA NA	59	Low	Low	Low	Low	Low	Low	Low	1
Chelly	18	2001	TKA GA NA	92	High	Unclear	High	Low	Low	Low	Unclear	1
Chen	19	2017	THA TKA GA	90	Low	Low	Unclear	Low	Low	Low	Low	n/a
Fahs	20	2018	THA GA	99	Low	Low	Unclear	Low	Low	Low	Low	1
Fan	21	2016	TKA GA	157	Low	Low	Low	Low	Low	Low	Low	-1
Fan	22	2017	TKA GA	65	Unclear	Unclear	Unclear	Low	Low	Low	Unclear	n/a
Fenten	23	2018	TKA NA	80	Low	Low	Low	Low	Low	Low	Low	1

Gasanova	24	2019	THA GA	60	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear		1
Gmez	25	2017	TKA NA	574	Unclear	Unclear	Unclear	Low	Low	Low	Unclear		1
Good	26	2007	TKA	42	Low	Low	Low	Low	Low	Low	Unclear		1
Goytizolo	27	2016	THA NA	90	Low	Low	Low	Low	Unclear	Low	Low		0
Goytizolo	28	2020	TKA NA	111	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear		0
Grosso	29	2018	TKA NA	102	Low	Low	Low	Unclear	Low	Low	Low		0
Hua	30	2017	THA GA	60	Unclear	Unclear	Unclear	High	Low	Low	Low	n/a	
Johnson	31	2017	THA GA NA	159	Low	Low	High	Low	Low	Low	Low		0
Kadic	32	2009	TKA NA	53	Low	Low	Unclear	Low	Low	Low	Low		-1
Kampitak	33	2018	TKA NA	57	Low	Low	Low	Low	Low	Low	Low		1
Kardash	34	2007	TKA NA	40	Unclear	Low	Low	Low	Low	Low	Unclear		-1
Kayupov	35	2018	TKA GA NA	91	Low	High	High	High	Unclear	Low	Low		0
Kearns	36	2016	THA NA	108	Low	Low	Low	Low	Low	Low	Low		-1
Kendrii	37	2017	THA GA NA	30	Unclear	Unclear	Unclear	Low	Low	Low	Unclear	n/a	
Kovalak	38	2015	TKA NA	60	Low	Unclear	Unclear	Low	Low	Low	Low		1
Kratz	39	2015	THA GA	52	Low	Low	High	High	Low	Low	Low		1
Kuchlik	40	2017	THA NA	56	Low	Low	Low	Low	Low	Low	Low		0
Kulkarni	41	2019	TKA NA	100	Low	Low	Low	Low	Low	Low	Low		-1
Lee	42	2011	TKA NA	78	Low	Low	Low	Low	Low	Low	Low		0
Lee	43	2012	TKA GA	40	Unclear	Unclear	Unclear	Low	Low	Low	Unclear		-1
Leung	44	2018	TKA NA	70	Low	Low	Low	Low	Low	Low	Low		1
Li	45	2017	TKA	53	Low	Low	Low	Low	Low	Low	Low		1
Long	46	2006	TKA NA	70	Unclear	Unclear	Unclear	High	Low	Unclear	Unclear	n/a	
Lu	47	2017	TKA GA NA	57	Unclear	Low	High	Low	Low	Low	Low	n/a	
Luezner	48	2020	TKA	139	Low	Low	Low	Low	Low	Low	Low		-1
lvarez	49	2017	TKA NA	39	High	High	High	Low	Low	Low	Low		1
Marino	50	2009	THA NA	150	Low	High	Unclear	Low	Low	Low	Low		1
Mei	51	2017	THA GA	132	Low	Low	Unclear	Low	Low	Unclear	Low		1
Moghtadaei	52	2014	TKA NA	36	Low	Low	Low	Unclear	Low	Low	Low		1
Nader	53	2012	TKA NA	62	Low	Unclear	Unclear	Low	Low	Low	Low		1

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Ng	54	2001	TKA GA	48	Low	Low	Low	Low	Low	Low	Low		-1
Ng	55	2012	TKA GA	32	Low	Low	Low	Low	Low	Low	Low		0
Nishio	56	2014	THA GA NA	19	Low	Unclear	Unclear	Low	Low	Low	Low		1
Niskanen	57	2005	TKA NA	50	Unclear	High	High	Low	Low	Low	Unclear		1
Peng	58	2014	TKA GA	280	Low	Unclear	High	Low	Low	Low	Low		1
Reinhardt	59	2014	TKA NA	94	Low	Low	Low	Low	Low	Low	Low		0
Rizk	60	2017	TKA GA	75	Low	Unclear	Unclear	Low	Low	Low	Low	n/a	
Safa	61	2014	TKA NA	68	Low	Low	Low	Low	Low	Low	Low		0
Sahin	62	2014	TKA NA	104	Low	Low	Low	Low	Low	Low	Low		1
Saine	63	2018	TKA NA	60	Low	Low	Low	Low	Low	Low	Low		0
Seet	64	2006	TKA NA	37	Low	Unclear	Unclear	Low	Low	Low	Unclear		0
Siddiqui	65	2007	THA GA	34	Low	High	High	Low	Low	Low	Low		1
Singelyn	66	1998	TKA GA NA	30	Low	Unclear	Unclear	Low	Low	Low	Low		1
Sites	67	2004	TKA NA	40	Low	Unclear	Unclear	Low	Low	Low	Low		1
Sogbein	68	2017	TKA NA	70	Low	Low	Low	Low	Low	Low	Low		1
Spangehl	69	2015	TKA GA	160	Low	High	High	Low	Low	Low	Low		1
Stathellis	70	2017	TKA GA	50	Low	Unclear	Unclear	Low	Low	Low	Low		1
Stevens	71	2000	THA GA	60	Unclear	Unclear	Low	Low	Low	Low	Unclear		1
Sundarathiti	72	2009	TKA NA	61	Unclear	Unclear	Unclear	Low	Low	Low	Unclear		1
Thybo	73	2016	THA NA	100	Low	Low	Low	Unclear	Low	Low	Low		0
Toftdahl	74	2007	TKA NA	77	Low	Unclear	Unclear	Low	Low	Low	Low		0
Tong	75	2019	TKA NA	40	Low	Low	Low	Low	Low	Low	Low		0
Twyman	76	1990	THA GA	20	Unclear	Unclear	Unclear	Low	High	Low	Unclear		1
Wall	77	2017	TKA GA NA	257	Low	Low	Unclear	Unclear	Low	Unclear	Low		1
Wang	78	2019	TKA	90	Low	Low	Low	Low	Low	Low	Low		0
Widmer	79	2012	TKA GA	55	Low	Low	Low	Low	Low	Low	Low		1
Wu	80	2014	TKA NA	79	Low	High	High	Unclear	Low	Low	Low		1
Yamamoto	81	2019	THA NA	53	Low	Low	Low	Low	Low	Low	Low		0
Zhou	82	2018	TKA GA	40	Low	Low	Low	Low	Low	Low	Low		0
Zinkus	83	2017	TKA NA	54	Low	Low	Low	Low	Low	Low	Low		1

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Observational Studies

A: Failure to adequately control for confounding B: Failure to develop and apply appropriate eligibility criteria C: Flawed measurement of exposure or outcome D: Incomplete follow-up

Study	Year	Ref	Study Type	Study Technique	Patient	A	B	C	D	Sentiment
Akkaya	2014	84	Case-control	TKA NA	27	High	Low	Low	High	-1
Alsheik	2020	85	Retrospective cohort	TKA GA NA	80	Unclear	Low	Low	Low	1
Antoni	2014	86	Retrospective cohort	TKA GA	98	High	High	Low	Low	-1
Asakura	2011	87	Retrospective cohort	TKA GA	40	High	Low	Low	Low	1
Beaupre	2012	88	Prospective cohort	TKA GA NA	39	High	Low	Low	Low	0
Cien	2015	89	Retrospective cohort	TKA	122	Low	Low	Low	Low	0
Danninger	2014	90	Retrospective cohort	THA TKA GA NA	530089	Unclear	Low	Unclear	Low	-1
DeRuyter	2006	91	Prospective cohort	TKA GA NA	50	High	Low	Unclear	Low	1
Duncan	2013	92	Retrospective cohort	TKA GA NA	108	High	Unclear	Low	Low	1
Fetherston	2011	93	Prospective cohort	THA TKA	52	Unclear	Low	Low	Unclear	0
Fukuda	2020	94	Retrospective cohort	TKA GA	5094	Low	Low	Low	Low	-1
Green	2018	95	Retrospective cohort	THA GA	20	Unclear	Low	Low	Low	0
Gwam	2018	96	Retrospective cohort	TKA	110	Unclear	Low	Low	Low	-1
Henson	2019	97	Retrospective cohort	TKA	144	Unclear	Low	Low	Low	0
Horn	2015	98	Retrospective cohort	TKA	32	Unclear	Low	Low	High	1
Jacob	2011	99	Retrospective cohort	TKA GA NA	8590	Unclear	Low	Low	Low	-1
Jacob	2011a	100	Retrospective cohort	THA	9844	Unclear	Unclear	Low	Low	-1
Kim	2012	101	Retrospective cohort	TKA NA	80	High	Low	Low	Low	0
Kinjo	2012	102	Prospective cohort	TKA GA NA	81	Unclear	Low	Low	High	-1
Kirkness	2017	103	Retrospective cohort	TKA GA NA	268	Low	Low	Low	Low	n/a
Kukreja	2019	104	Retrospective cohort	THA NA	71	Low	Low	Low	Low	1

Liu	2015	105	Retrospective cohort	TKA NA	1768	Unclear	Low	Low	Low	0
Lovald	2015	106	Retrospective cohort	TKA GA NA	35642	High	Low	Unclear	Unclear	1
McIsaac	2017	107	Retrospective cohort	TKA GA NA	178214	Low	Low	Low	Low	0
Memtsoudis	2016	107	Retrospective cohort	TKA GA NA	719426	Low	Low	Low	Low	-1
Memtsoudis	2016	108	Retrospective cohort	THA GA NA	342726	Low	Low	Low	Low	-1
Peters	2006	109	Retrospective cohort	THA TKA GA NA	100	High	High	Low	High	0
Pope	2015	110	Retrospective cohort	TKA GA NA	294	High	Low	Low	Low	0
Raimer	2007	111	Prospective cohort	TKA GA NA	42	Unclear	Low	Low	High	0
Rajeev	2016	112	Prospective cohort	TKA GA NA	114	High	High	Low	Low	1
Rames	2019	113	Retrospective cohort	TKA	693	Low	Low	Low	Low	0
Roberts	2019	114	Retrospective cohort	TKA	236	Low	Low	Low	Low	1
Schmidt	2009	115	Retrospective cohort	TKA GA NA	200	Unclear	Unclear	Low	Low	-1
Schwab	2019	116	Retrospective cohort	TKA	224	Unclear	Low	Low	Low	1
Simonsen	2011	117	Prospective cohort	TKA NA	67	Unclear	High	Low	Low	1
Singelyn	1999	118	Prospective cohort	THA GA NA	1274	High	Low	Low	Low	1
Sporer	2016	119	Retrospective cohort	TKA NA	597	Unclear	Low	Low	Low	0
Sugar	2011	120	Prospective cohort	TKA NA	28	Unclear	Low	Low	Low	1
Suthersan	2015	121	Prospective cohort	TKA GA NA	46	Unclear	Low	Low	Low	1
Tetsunaga	2016	122	Retrospective cohort	THA GA	62	High	High	Low	Low	0
Willett	2019	123	Retrospective cohort	TKA	151	High	Low	Low	Low	1

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