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# The Fragility of Tourniquet Use in Total Knee Arthroplasty: A Systematic Review of Randomized Controlled Trials

John K. Cordero MD<sup>a</sup>, Kyle W. Lawrence BS<sup>b</sup>,  
Ashley Brown BS<sup>a</sup>, Xinning Li MD<sup>b</sup>,  
Brett L. Hayden MD<sup>a</sup>, Robert L. Parisien MD<sup>a</sup>

<sup>a</sup>Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Pl, New York, NY 10029

<sup>b</sup>Boston University School of Medicine, 72 E Concord St, Boston, MA 02118





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# Disclosures:

**John K. Cordero, MD**

Nothing to Disclose

**Kyle W. Lawrence, BS**

Nothing to Disclose

**Ashley Brown, BS**

Nothing to Disclose

**Xinning Li, MD, FAAOS**

AAOS: Board or committee member

AAOS Now: Editorial or governing board

American Journal of Sports Medicine: Editorial or governing board

American Orthopaedic Association: Board or committee member

American Shoulder and Elbow Surgeons: Board or committee member

Arthroscopy Association of North America: Board or committee member

BMC Musculoskeletal Disorders: Editorial or governing board

DePuy, A Johnson & Johnson Company: Paid consultant

FH Ortho: IP royalties; Paid consultant

Journal of Bone and Joint Surgery - American: Editorial or governing board

Journal of Medical Insight (JOMI): Editorial or governing board

Orthopedic Reviews: Editorial or governing board

World Journal of Orthopaedics: Editorial or governing board

**Brett Hayden, MD**

Bristol-Myers Squibb: Stock or stock Options

Johnson & Johnson: Stock or stock Options

Pfizer: Stock or stock Options

**Robert L. Parisien, MD**

American Orthopaedic Society for Sports Medicine: Board or committee member

Arthroscopy: Editorial or governing board

Arthroscopy Association of North America: Board or committee member

Journal of Cartilage & Joint Preservation: Editorial or governing board

Journal of Sport Rehabilitation: Editorial or governing board

New England Orthopaedic Society: Board or committee member

Society of Military Orthopaedic Surgeons: Board or committee member



# Background

- Physicians rely on P-values when interpreting clinical trial data. However, this metric neglects loss to follow-up, sample size, and power<sup>1-3</sup>
- Statistical fragility assesses the robustness of clinical data based on the number of outcome event reversals required to reverse statistical findings, and may address the limitations of the P-value<sup>4</sup>
  - **Fragility index (FI)** represents the number of outcome reversals required to switch a statistically significant result into a non-significant result
  - **Reverse fragility index (reverse FI)** represents the number of outcome reversals required to switch a statistically significant result into a non-significant result
  - **Fragility Quotient (FQ)** accounts for sample size by dividing FI or reverse FI by sample size
- The utility of tourniquet use in total knee arthroplasty (TKA) remains controversial, with current clinical trials relying on limited data and producing heterogeneous results<sup>5</sup>



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# Study Aim & Hypothesis

- This study aims to assess the statistical fragility of recently published, randomized controlled trials (RCTs) on tourniquet use in TKA
- We hypothesized that a fragility analysis of RCTs investigating tourniquet use in TKA would demonstrate fragility, with few outcome event changes required to reverse statistical significance



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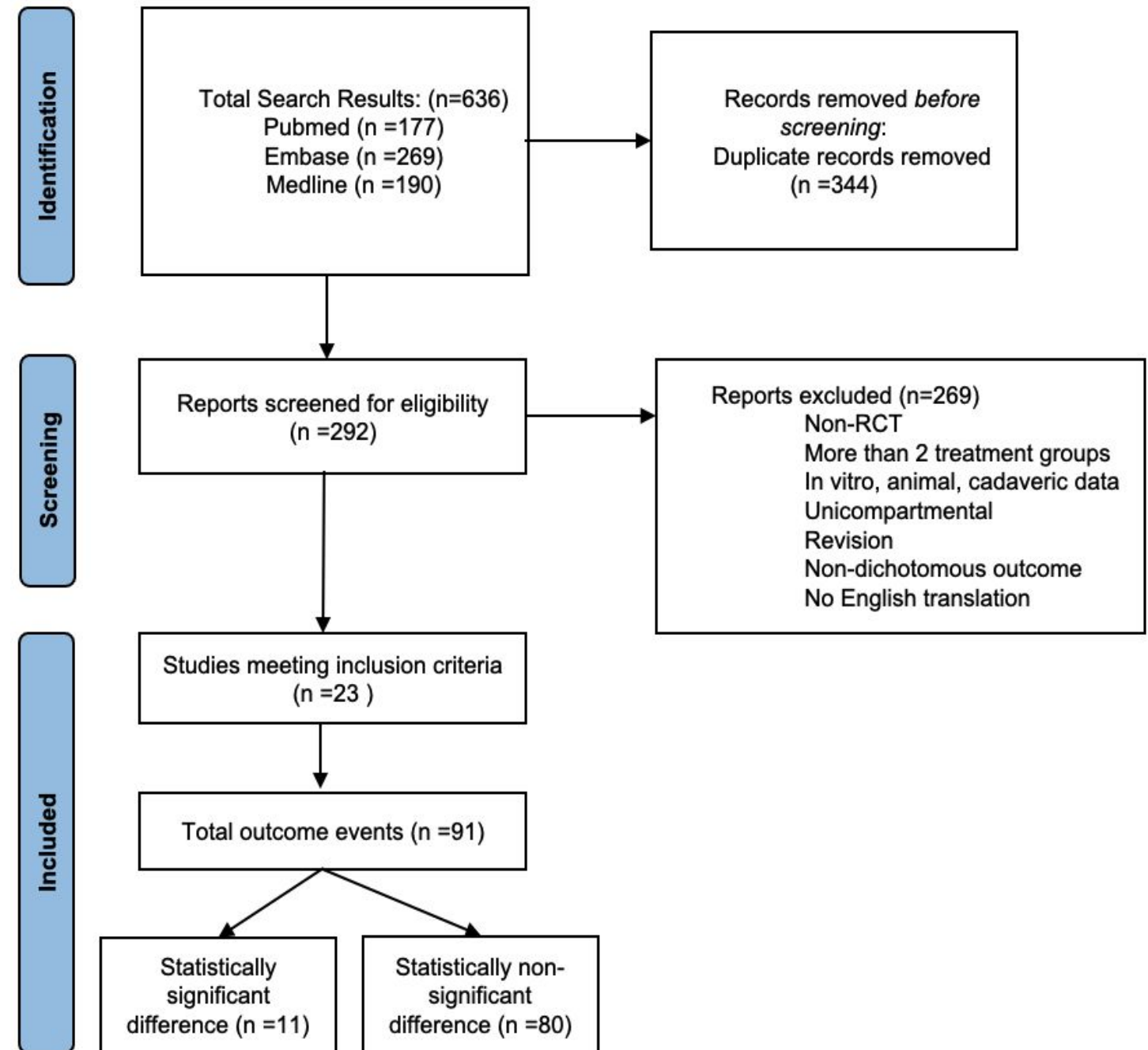
# Methods

- Retrospective review querying PubMed/MEDLINE/EMBASE for articles from 1/2010 to 2/2021
  - Included studies: RCTs reporting categorical, dichotomous data on tourniquet use in TKA
  - Excluded studies: non-English language, non-RCTs, more than two treatment groups, *in vitro* or animal studies, assessing unicompartmental or revision arthroplasty
- Extracted data included sample size, number of outcomes from each intervention group, loss to follow-up, and P-values. Bias was assessed using Cochrane Risk Assessment Tool<sup>6</sup>
- FI and reverse FI were calculated using a 2 x 2 contingency table, by manipulating the outcome events until reversal of significance was achieved
- FQ was calculated by dividing the FI or reverse FI by sample size

	+ Outcome	- Outcome		+ Outcome	- Outcome
TKA + Tourniquet	35	57	TKA + Tourniquet	35	57
TKA - Tourniquet	19	65	TKA - Tourniquet	20	64
		P-value 0.033			P-value 0.051

# Results

- Search yielded 636 total articles, with 292 undergoing full-text review
- 23 studies met inclusion criteria
- 91 total dichotomous outcomes:
  - 11 significant ( $P < 0.05$ )
  - 80 non-significant ( $P > 0.05$ )
- 13/23 (56.5%) of studies were at 'some concern' or 'high risk' of bias



# Results

- **91 total outcomes:** median FI 4 (IQR 3 to 6); median FQ 0.0476 (IQR 0.0291 to 0.0867)
- **11 significant outcomes:** median FI 2 (IQR 1.5 to 5); median FQ 0.0200 (IQR 0.0148 to 0.0484)
- **80 non-significant outcomes:** median reverse FI 4 (IQR 3 to 6); median FQ 0.0495 (IQR 0.0310 to 0.0887)
- Substantial statistical fragility observed across outcome categories

	Events	FI (IQR)	FQ (IQR)
<b>All Outcomes</b>	91	4 (3 to 6)	0.0476 (0.0291 to 0.0867)
<b>Reported P-Value</b>			
<0.05 (statistically significant)	11	2 (1.5 to 5)	0.0200 (0.0148 to 0.0484)
>0.05 (not statistically significant)	80	4 (3 to 6)	0.0495 (0.0310 to 0.0887)
<b>Outcome Category</b>			
Skin/Wound Complication	21	4 (3 to 6)	0.0385 (0.0200 to 0.0438)
Transfusion	11	3 (2 to 5)	0.0297 (0.0136 to 0.0508)
Deep Vein Thrombosis	11	4 (4 to 6)	0.0583 (0.0291 to 0.0792)
Postoperative Pain/Pain Management	6	5.5 (5 to 7.5)	0.0455 (0.0348 to 0.0561)
Re-Intervention	6	3 (3 to 4.5)	0.0488 (0.0201 to 0.0625)

# Limitations

- Given narrow topic of investigation, our analysis included a small number of eligible studies and a limited amount of statistically significant outcomes for evaluation
- Fragility analysis is limited to dichotomous, categorical outcomes, and is not generalizable to continuous variables
- Standardized FI/FQ thresholds for evaluating trial data have not been established. It is unclear how these results should impact clinical decision making



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# Conclusions

- RCTs evaluating tourniquet use in TKA demonstrate substantial statistical fragility, as the reversal of a small number of outcomes is sufficient to alter study clinical findings
- Statistical fragility is higher when considering outcomes reported as statistically significant
- We therefore recommend the inclusion of a comprehensive fragility analysis (FI and FQ), in addition to the P-value, to allow for increased reliability in the interpretation of literature on TKA



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# References

1. Sterne JAC, Smith GD. Sifting the evidence-what's wrong with significance tests? *Phys Ther.* 2001;81(8):1464-1469.
2. Ioannidis JPA. Contradicted and initially stronger effects in highly cited clinical research. *JAMA.* 2005;294(2):218-228.
3. Walsh M, Srinathan SK, McAuley DF, et al. The statistical significance of randomized controlled trial results is frequently fragile: a case for a Fragility Index. *J Clin Epidemiol.* 2014;67(6):622-628.
4. Feinstein AR. The unit fragility index: an additional appraisal of “statistical significance” or a contrast of two proportions. *J Clin Epidemiol.* 1990;43(2):201-209.
5. Tarwala R. Tourniquet Versus No Tourniquet in Total Knee Arthroplasty: We Don't Have a Winner Yet: Commentary on article by Rahul Goel, MD, et al.: “Tourniquet Use Does Not Affect Functional Outcomes or Pain After Total Knee Arthroplasty. A Prospective, Double-Blind. *JBJS.* 2019;101(20).
6. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898.

