

The Statistical Fragility of Outcomes on Breast Reconstruction with Acellular Dermal Matrix: A Systematic Review of Randomized Controlled Trials

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1. BACKGROUND

- **Acellular dermal matrices** (ADMs) are often used in breast reconstruction
- P-value reliance in ADM efficacy Randomized Controlled Trials (RCTs) can lead to misconceptions that affect patient and provider decision-making¹
- The **Fragility Index (FI)** is a metric to assess the statistical strength of RCTs and aid in interpreting P-values^{2,3}
- FI measures the **minimum number of outcome changes needed to affect the study's statistical significance**^{2,3}
- Fragility analysis is common in other medical fields, but application in plastic and reconstructive surgery (PRS) remains understudied

The study analyzed the **statistical fragility** of **ADM outcomes** in breast reconstruction RCTs within PRS literature

2. METHODS

Literature Review

- PubMed, Embase, SCOPUS, Medline, and Cochrane databases were reviewed for breast-related ADM RCTs (2003-present)

Eligibility Criteria

- **Included:** 1:1 two-arm RCTs with a dichotomous, categorical outcome
- **Excluded:** Non-RCTs, studies with more than two treatment groups, in vitro/animal/cadaveric studies, and non-English articles

Data extraction

- Publication details and intervention types were collected
- Outcome frequencies, P-values, and number patients lost to follow-up for each dichotomous outcome were recorded
- Interventions were categorized as ADM vs ADM, ADM vs Other Material, ADM vs Control

Fragility analysis

- **Fragility index** and **reverse fragility index (rFI)** = minimum event reversals necessary to alter statistical significance through a 2x2 contingency table
- **Fragility quotient (FQ)** = the FI or rFI divided by the study sample size
- Fragility analysis was performed on subgroups of outcome significance and intervention type
- Results were reported as **median (IQR)**

3. RESULTS

There were **19 articles** with a total of **204 outcomes** (Figure 3)

- The median FI was **4 (3-5)** for all 204 outcomes
- The 26 **significant** outcomes had a median FI of **3.5 (1-5)**
- The 178 **non-significant** outcomes had a median FI of **4 (3-5)**

Patients Lost to Follow-up

- The number of patients lost to follow up was equal to or greater than the fragility index in **36** out of **204 outcomes (17.6%)**

Subgroup Analysis

- Median Fis were comparable across categories and remained **low**
- The median FI was **4** for each intervention category

A)

	(+)	(-)	Total
Intervention A	5	5	10
Intervention B	0	10	10
P-value			p=0.033

B)

	(+)	(-)	Total
Intervention A	5	5	10
Intervention B	1	9	10
P-value			p=0.141

	(+)	(-)	Total
Intervention A	5	5	10
Intervention B	1	9	10
P-value			p=0.033

	(+)	(-)	Total
Intervention A	5	5	10
Intervention B	0	10	10
P-value			p=0.141

Figure 1. Demonstration of significance reversal with a A) FI of 1 and B) rFI of 1

- The bias risk assessment revealed **“some concern”** of bias in 3 out of the 19 (**15.8%**) reviewed studies

Characteristic	Number (%)
Outcome Category	
Complication	106 (52)
Clinical outcome	41 (20)
Pain	1 (1)
Reoperation	56 (27)
Total	204 (100)
Outcome Type	
Primary	123 (60)
Secondary	81 (40)
Outcome Reported P value	
<0.001	0 (0)
<0.05	12 (6)
>0.05	59 (29)
Not reported	133 (65)

Table 1. Outcome characteristics

	# Outcomes	FI, Median (IQR)	FQ, Median (IQR)
Significance:			
Total Outcomes	204	4 (3 - 5)	0.039 (0.029 - 0.070)
Significant Outcomes (P<0.05)	26	3.5 (1 - 5)	0.033 (0.010 - 0.073)
Nonsignificant Outcomes (P≥0.05)	178	4 (3 - 5)	0.040 (0.030 - 0.070)
Intervention Type:			
ADM vs ADM	55	4 (3 - 5)	0.038 (0.019 - 0.051)
ADM vs Other Material	31	4 (3 - 4)	0.083 (0.048 - 0.102)
ADM vs Control	118	4 (3 - 5)	0.038 (0.030 - 0.066)

Table 2. Fragility data based on outcome significance and intervention type

4. PRISMA DIAGRAM

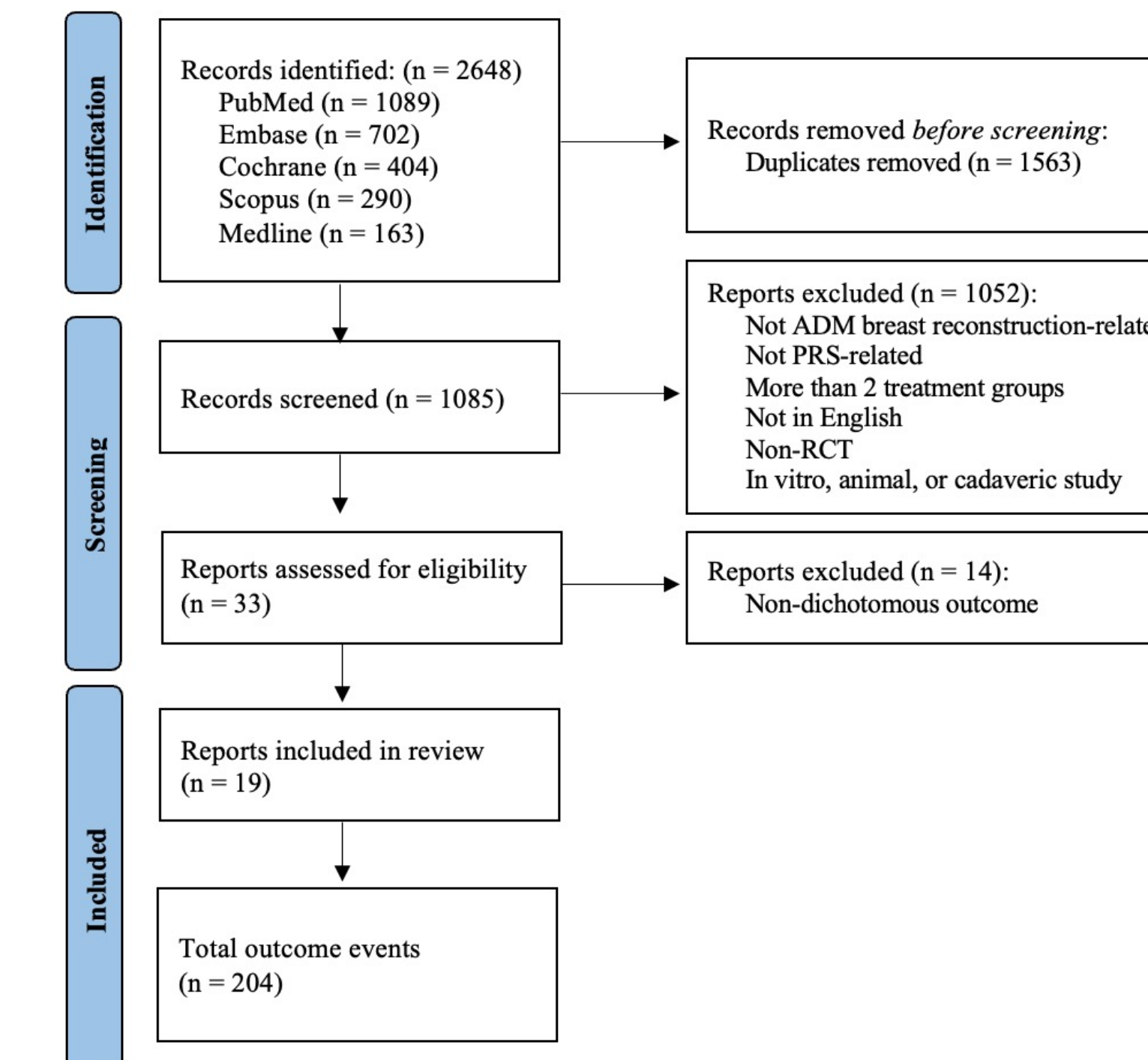


Figure 2. PRISMA diagram on identification and screening of eligible articles

5. CONCLUSIONS

- ADM-related breast reconstruction RCT outcomes are **statistically fragile**, with minor outcome reversals potentially altering result significance
- **Retaining patients** and **decreasing the number lost to follow up** can impact the significance of outcomes
- Since patient team and insurance providers' decisions for care often revolve around RCT data, researchers are recommended to **report the FI and FQ with P-values** to aid future readers with appropriately assessing outcomes when determining care strategies

6. REFERENCES

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