

Utilising the Fragility Index to Evaluate the Robustness of Randomised Controlled Trial Outcomes in Minimally Invasive Glaucoma Surgery (MIGS)

Ansari, Daniyal M.¹; Ansari, Abdus S.^{2, 3}; Jung, Minsu⁴; Hamdan, Amar⁵; Hayre, Amrit²; Tan, Jeremy⁶; Khaw, Peng T.^{2, 7}; Gazzard, Gus^{2, 7}

1. Maidstone and Tunbridge Wells NHS Trust, Maidstone, England, United Kingdom.
2. Moorfields Eye Hospital NHS Foundation Trust, London, England, United Kingdom.
3. Section of Academic Ophthalmology, King's College London School of Life Course & Population Sciences, London, England, United Kingdom.
4. University of New South Wales, Sydney, NSW, Australia.
5. Universitätsklinikum Hamburg-Eppendorf, Hamburg, HH, Germany.
6. Sydney Hospital and Sydney Eye Hospital, Sydney, NSW, Australia.
7. University College London Institute of Ophthalmology, London, England, United Kingdom.

Introduction

For glaucoma surgeons, decision-making relies on the strength and reliability of published evidence. Minimally invasive glaucoma surgery (MIGS) has rapidly transformed clinical practice, offering faster and less invasive alternatives to traditional filtration procedures (1). However, despite its widespread adoption, many MIGS trials report “statistically significant” outcomes often based on a few events. While such results may seem convincing, they might not reflect true robustness or reproducibility. The Fragility Index (FI) created by Walsh et al (2014) offers an intuitive way to assess this by quantifying how many patients would need to experience a different outcome to overturn statistical significance (2). By applying this concept to MIGS randomised controlled trials (RCTs), we can better understand how stable current evidence truly is and where methodological rigour could be strengthened in future studies.

Aim

The aim of this study was to systematically evaluate the robustness of statistically significant outcomes in MIGS RCTs using the Fragility Index (FI) and Fragility Quotient (FQ). By quantifying how easily significance could be lost with small changes in event counts, the review aimed to assess the reliability of current MIGS evidence and highlight areas for methodological improvement in future glaucoma surgical research.

Methods

A systematic review was conducted in accordance with PRISMA guidelines and registered on [PROSPERO \(CRD420251166050\)](#). Comprehensive searches of MEDLINE, Embase, PubMed, and Cochrane CENTRAL were performed to July 2025.

Inclusion criteria: RCTs enrolling patients with any form of glaucoma, evaluating any MIGS procedure against any comparator (medical therapy, other MIGS, or conventional glaucoma surgery), and reporting at least one statistically significant binary outcome.

Exclusion criteria: Non-RCTs, observational studies, trials without statistically significant binary outcomes, or those reporting only continuous or non-clinical endpoints.

Outcomes assessed: The primary outcomes were the FI and FQ for statistically significant results. Additional data extracted included study characteristics (year, design, sample size, follow-up duration, funding source), intervention and comparator type, definitions of success and failure, number of events, attrition rate, and p-values. Risk of bias was assessed using the Cochrane RoB 2 tool, and analyses was performed using R (v4.3.2) and Stata (v18).

Results

Sixteen eligible RCTs were included, evaluating trabecular bypass (Hydrus, iStent), canaloplasty-based, subconjunctival microshunt (Preserflo), and goniotomy-based procedures (KDB, GATT, BANG).

The median sample size was 236 eyes (IQR: 88–511) with a median follow-up of 24 months (range: 6–36 months). The average FI was 9.4 (IQR: 1–15) and the mean FQ was 0.031 (IQR: 0.012–0.047), indicating that approximately 3% of participants would need a different outcome to overturn statistical significance.

Three trials (19%) had an FI of 0 and 69% of RCTs would lose statistical significance if fewer than 10 participants had a different outcome.

In six studies (38%), the FI was equal to or lower than the number of participants lost to follow-up, suggesting that attrition alone could have reversed the reported significance (Figure 1). Larger studies tended to have higher FI values but similar FQ, reflecting proportional scaling with sample size (Figure 2).

Risk of bias was generally low to moderate across studies. Fourteen trials (88%) had low risk in the randomisation domain, while incomplete handling of missing data was the most frequent source of bias. Overall, eight trials (50%) were rated low risk and eight (50%) as having some concerns. No consistent associations were observed between FI and device type, comparator, study design, or funding source.

Conclusion

Many MIGS RCTs are ‘statistically fragile’. Small changes in just a few patient outcomes can overturn the reported significance of the results.

Limitations

- Only RCTs with binary outcomes were eligible — excludes many glaucoma trials.
- Comparison between devices should be done with caution, given the variability in trial designs and outcome measures.
- The Fragility Index does not account for effect size or clinical relevance.

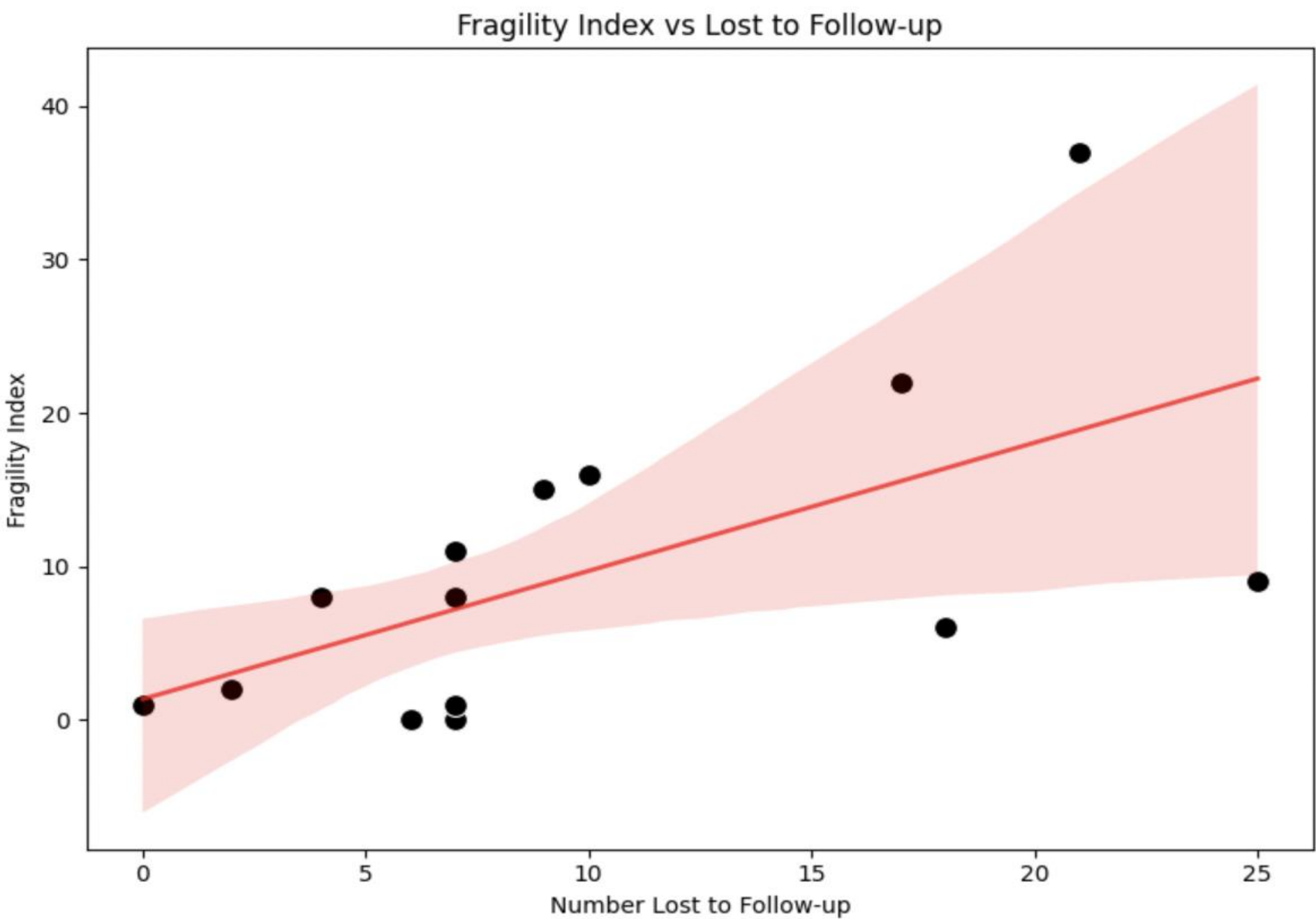


Figure 1: Scatter plot showing the Fragility Index of each trial relative to the number of participants lost to follow-up. The red line represents a fitted linear regression, illustrating the potential impact of patient attrition on trial robustness.

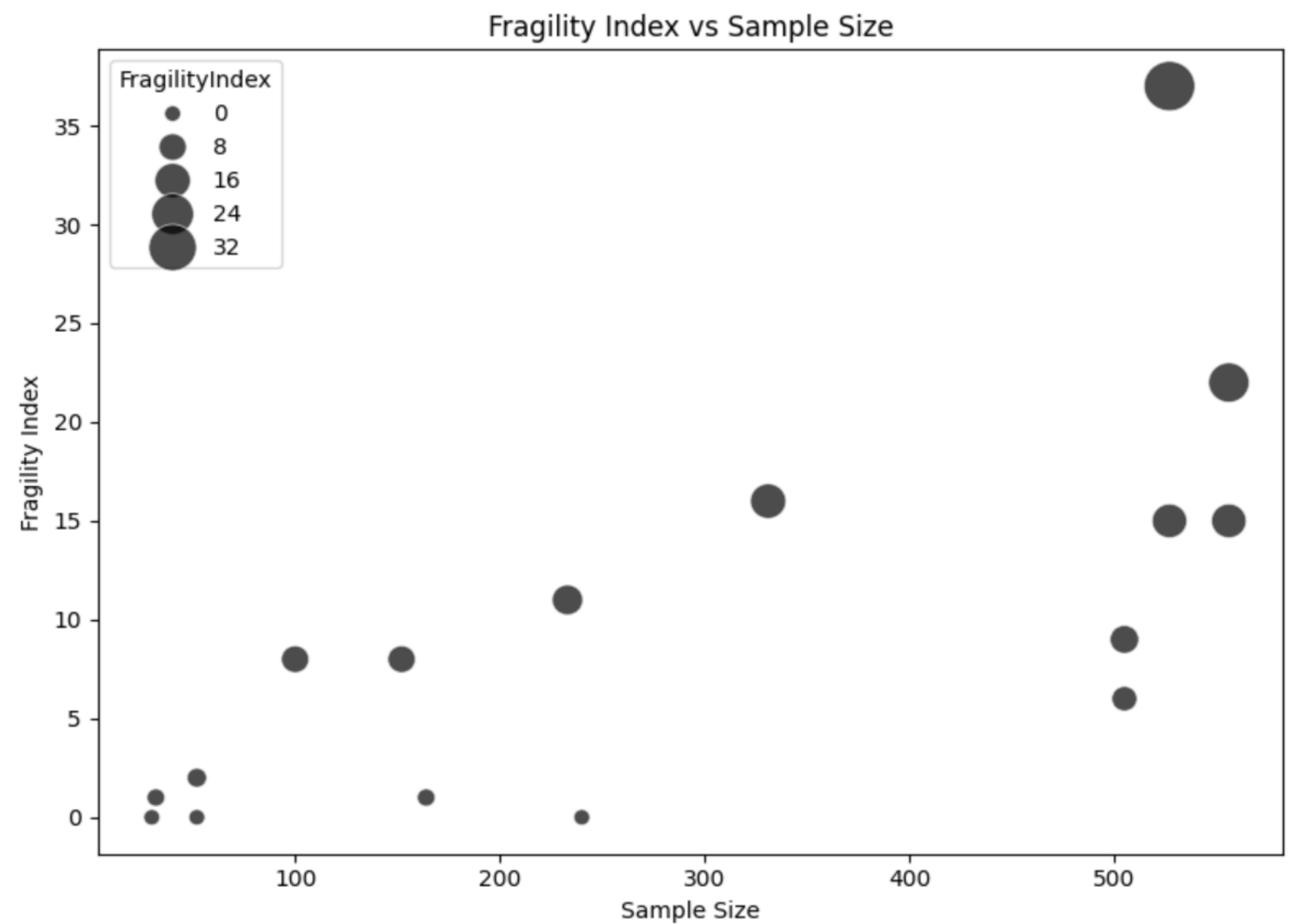


Figure 2: Bubble plot showing the Fragility Index for each trial as a function of the study sample size. The size of each bubble is proportional to the corresponding Fragility Index.

References

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Contact The
Authors:

