

Makaram NS, Lamb SE, Simpson AHRW. Are we doing the right surgical trials? *Bone Joint Res.* 2023;12(6):372-374.

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Harnessing Practice Variation: A Crucial Indicator of Clinical Equipoise and a Catalyst for Natural Experiments in Orthopaedic Trauma Care

Sir,

In reference to your recently published editorial discussing the difficulties in achieving true clinical equipoise in surgical trials, I propose a complementary approach.¹ This uses practice variation as an indicator of clinical equipoise and as a vehicle for natural experiments, particularly in orthopaedic trauma care. This approach could be a practical and cost-effective alternative to conventional randomized controlled trials (RCTs) when comparing existing treatments.

Variation in clinical practice for a specific condition is a sign of clinical equipoise and reflects the existence of genuine uncertainty or differing viewpoints within the medical community about the best treatment for that condition.

Randomized controlled trials are rightfully the gold standard in medical research. They provide rigorous and controlled conditions under which to evaluate the efficacy of novel interventions. However, RCTs may not always be the most pragmatic or cost-effective choice when evaluating existing treatment strategies, where real-world variation and clinical practice significantly influence outcomes.²

In trauma care, patients are typically allocated to hospitals and their subsequent treatment is based on geographical factors, which essentially randomizes the allocation process. When coupled with practice variation across hospitals and clinicians, these circumstances form a "natural experiment". Such experiments can provide real-world comparisons of existing treatment strategies and offer meaningful insights, which may not be so readily achieved by conventional RCTs.

Natural experiments have distinct advantages.² First, they are generally more cost-effective than RCTs, using data from existing clinical practice rather than needing a different and often expensive experimental framework. Second, natural experiments inherently encompass all patients, thereby offering a more diverse sample that enhances the generalizability of findings. Lastly, these experiments yield real-world evidence, reflecting the impact of treatment strategies in actual practice settings, including the influence of individual clinician judgment and system-level factors.

The validity of natural experiments relies on meticulous design, appropriate statistical methods, and stringent control for potential confounding factors. These requirements are achievable within our current research infrastructure.⁴

The presence of practice variation signifies clinical equipoise and presents opportunities for comparing existing treatments.

While RCTs remain essential to compare novel interventions with standard treatments, it is valuable to recognize and harness the potential of natural experiments when comparing existing treatments. By using the opportunities presented by practice variation and real-world settings, we can generate valuable, cost-effective, and representative evidence that may better inform clinical practice and ultimately enhance patient outcomes.

I appreciate your consideration of this perspective.

R. W. Poolman

Professor of Orthopaedic Surgery, in particular health care evaluation,
Jointresearch, OLVG Amsterdam,
Department of Orthopaedic Surgery, LUMC Leiden,
The Netherlands.

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