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EDITORIAL

Are we doing the right surgical trials?

THE DIFFICULT NATURE OF 'TRUE' EQUIPOISE

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There are a number of barriers to recruitment of patients into surgical trials, but a fundamental factor remains the ability to achieve true equipoise.

In early randomized controlled trials (RCTs), the individual physician treating a patient decided whether or not they met the inclusion criteria for a trial. However, Freedman[1] indicated that this judgement was subject to 'individual equipoise' which introduced an element of bias, and led to the concept of 'clinical equipoise'. Whereas 'individual equipoise' pertains to the individual being impartial in their beliefs regarding the merits of one intervention versus another, clinical equipoise is the genuine uncertainty in the practice community over the benefit of a particular intervention.[1]

In pharmaceutical trials, it is potentially easier to achieve clinical equipoise than in surgical trials. For instance, if the surgeon excludes patients who would in their view be best treated by one of the interventions, then we have reverted to individual rather than clinical equipoise. Clinical equipoise assumes that a clinician's own perceptions and opinions regarding a treatment would be mitigated by the assurance that there is a collective uncertainty from peers and the 'expert' community regarding the optimal intervention. As such, clinical equipoise in the context of surgical trials relies on the clinician putting aside personal opinions in order to accept the collective uncertainty of the medical community.

There are several issues with this. Prior evidence has shown that the clinician's pre-existing experience, knowledge, and skills influence their preferences towards treatments and thus affect their position of equipoise.[2] Surgeons, like all clinicians, may struggle to separate clinical care (shaped by their personal values, skills, knowledge, and experience) from their duties as a researcher in delivering two arms of a trial in an unbiased manner.[2]

A surgeon participating in recruitment for a trial of two different interventions with which they have differential expertise is likely to have a biased opinion regarding the more effective intervention based on their own personal experience, training, and mentorship. If the trial permits the surgeon to exclude a given patient based on their own personal view of whether a patient would be best served by one intervention or another, then the trial has reverted to 'individual equipoise'. The same patient, seen by another clinician who does not have experience in either intervention, may have been recruited and randomized. In this way, fundamentally eligible participants may be excluded from a pragmatic trial reliant on clinical equipoise by a lack of individual equipoise.

There is also the question of patient equipoise. Although traditionally clinical equipoise puts the onus on the clinician to set aside individual opinions in preference of community equipoise, there is an additional duty to ensure the patient is in a position of equipoise when being recruited to a trial. The literature suggests that this is a challenge.[2,3] The patient's views regarding interventions can be shaped by their prior experiences, but clinicians often find it difficult to reconcile a patient's existing views so that they would consider trial participation, despite being eligible.[3] Indeed, challenging patients' preferences for treatment, whether those preferences are based on fact or personal experience, may be viewed by some clinicians as potentially prioritizing

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their role as researcher at the expense of their role as patient advocate.[4]

How do we mitigate for these concerns in equipoise, while maximizing the ability to recruit eligible patients?

Firstly, prior studies have emphasized the importance of targeted training for clinicians, which can increase their levels of comfort with equipoise and awareness of potential prejudices.[5] Qualitative analysis of participating clinicians' perspectives at a pre-trial stage could identify issues with equipoise and help formulate this targeted training.

Secondly, the concept of 'expertise-based' clinical trials has recently emerged as a potential solution to the pitfalls of differential expertise within trials comparing surgical interventions.[6] Differential expertise can also affect equipoise in recruitment, as well as outcomes from the surgical procedure. Surgeons who are familiar with or considered 'expert' in one intervention may be more likely to consider that a particular injury would be best served by this procedure 'in their hands', and therefore may find it ethically inappropriate to include this patient in a trial where they may be randomized to a 'less appropriate' procedure. If, overall, there are a greater number of surgeons with expertise in procedure A compared with procedure B participating in the trial, then there may be a greater number of patients from a specific subgroup who are excluded, despite being eligible for recruitment from the perspective of clinical equipoise.

The expertise-based clinical trial requires that surgeons with expertise in a given intervention deliver that respective intervention. For example, those participating surgeons who have expertise in intervention 'A' deliver only that intervention, whereas participating surgeons with expertise in intervention 'B' deliver this intervention. Ideally, the number of cases performed on average by the surgeons delivering intervention A will be similar to those performing intervention B, with a minimum number (to complete the learning curve and separately to be considered an 'expert') being essential for participation in either arm.[7,8] Using this concept, three concerns of pragmatic trials are tackled. First, the problem of differential expertise bias is addressed. Second, there is an increased likelihood of achieving clinical equipoise, as surgeons who have expertise in the delivery of a particular intervention are likely to favour that intervention in preference of others they are not as familiar with.[6] Third, it tackles the potential challenge of comparing procedures of differing technical difficulty, with surgeons required to develop experience with either one or both procedures, potentially developing differing levels of proficiency in each.[7] This remains true in the real-world setting, where surgical procedures are required to be delivered by those who have completed the learning curve for that procedure, and preferably by surgeons who are considered 'expert' in the procedure delivery.

This principle of expertise-based surgical trials can be expanded to recruitment design. An abbreviated clinical record and relevant imaging from potentially eligible patients could be reviewed by an 'expert panel' composed of two surgeons each with expertise in one of the interventions. If both surgeons agree that a patient would be best served with intervention A or with intervention B, then the patient is excluded as there is no question of clinical equipoise. However, when there is disagreement regarding the intervention of choice, and therefore equipoise, these patients are included.

This concept can be further optimized by disclosing the outcome of the expert panel discussion to the eligible patient. The evidence suggests that when eligible patients are informed of the outcomes of their own assessment by 'expert panels', they are much more likely to agree to participate in a trial.[9] Ghogawala et al[9] compared recruitment and randomization acceptance in patients eligible for inclusion in a RCT comparing two forms of decompression for degenerative lumbar spondylolisthesis. Suitability for inclusion was determined by an expert panel of ten spinal surgeons. Importantly, the patient group that was informed of the voting outcome by the expert panel had a significantly higher rate of recruitment and randomization acceptance (80%) compared with those where outcome was not disclosed (40%). This approach of disclosure ensures shared decision-making between clinician and patient, and clarifies the appropriateness of randomization to all parties. If patients know that a group of experts reviewed their specific case and maintained the view that they remain unsure which intervention would provide the greatest benefit, they appear much more likely to accept a position of true equipoise, whatever their preconceived notions of the interventions.

There is greater awareness in society of the pressing need for well-designed surgical RCTs to evaluate new and existing operative procedures; the concept of clinical equipoise is the fundamental basis upon which RCTs are designed. However, clinical equipoise within the surgical community is much more difficult to reflect within a surgical trial, and this can be a driving factor in low recruitment rates. There are multiple sources of bias within surgical trials, including from the clinician, speciality, and the patients themselves, which can disrupt the balance of equipoise. Potential solutions to optimize equipoise and maximize recruitment within a trial include qualitative analysis of potential biases in consultations, a greater consideration of expertise-based trials, the involvement of expert panels to determine eligibility for randomization, and disclosure of outcome from these panels to eligible patients.

References

1. **Freedman B**. Equipoise and the ethics of clinical research. *N Engl J Med*. 1987;317(3):141–145.
2. **Davies L**, **Beard D**, **Cook JA**, **Price A**, **Osbeck I**, **Toye F**. The challenge of equipoise in trials with a surgical and non-surgical comparison: a qualitative synthesis using meta-ethnography. *Trials*. 2021;22(1):678.
3. **Griffin D**, **Wall P**, **Realpe A**, **et al**. UK FASHIoN: feasibility study of a randomised controlled trial of arthroscopic surgery for hip impingement compared with best conservative care. *Health Technol Assess*. 2016;20(32):1–172.

4. **Rooshenas L**, **Elliott D**, **Wade J**, **et al**. Conveying equipoise during recruitment for clinical trials: Qualitative synthesis of clinicians' practices across six randomised controlled trials. *PLoS Med*. 2016;13(10):e1002147.
5. **Donovan JL**, **Paramasivan S**, **de Salis I**, **Toerien M**. Clear obstacles and hidden challenges: understanding recruiter perspectives in six pragmatic randomised controlled trials. *Trials*. 2014;15:5.
6. **Devereaux PJ**, **Bhandari M**, **Clarke M**, **et al**. Need for expertise based randomised controlled trials. *BMJ*. 2005;330(7482):88.
7. **Simpson AHRW**, **Howie CR**, **Norrie J**. Surgical trial design - learning curve and surgeon volume: Determining whether inferior results are due to the procedure itself, or delivery of the procedure by the surgeon. *Bone Joint Res*. 2017;6(4):194–195.
8. **Simpson AHRW**, **Frost H**, **Norrie J**. Pragmatic surgical studies: are they the new gold standard. *Bone Joint J*. 2018;100-B(11):1407–1408.
9. **Ghogawala Z**, **Schwartz JS**, **Benzel EC**, **et al**. Increased patient enrollment to a randomized surgical trial through equipoise polling of an expert surgeon panel. *Ann Surg*. 2016;264(1):81–86.

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