

# Clinical equipoise and personal equipoise: two necessary ingredients for reducing bias in manual therapy trials

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Clinical and personal equipoise exists when a clinician has no good basis for a choice between two or more care options or when one is truly uncertain about the overall benefit or harm offered by the treatment to his/her patient. For most manual therapy trials, equipoise does not likely exist. Because of the nature of the intervention a lack of equipoise can lead to bias and may account for a portion of the 'effect' that has traditionally been assigned to the intervention. Although there are methodological mechanisms to reduce the risk of bias associated with a lack of equipoise, most of the manual therapy trials to date are likely guilty of this form of bias.

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## Background

Clinical equipoise is the assumption that there is not one 'better' intervention present (for either the control or experimental group) during the design of a randomized controlled trial (RCT). A true state of equipoise exists when one has no good basis for a choice between two or more care options.<sup>1</sup> Clinical equipoise has also been called an honest null hypothesis and/or a state of uncertainty.<sup>2</sup> Similar to clinical equipoise, personal equipoise exists when the clinical service provider (or clinician) involved in the research study has no preference or is truly uncertain about the overall benefit or harm offered by the treatment to his/her patient.<sup>3</sup> In other words, the clinician has no personal preconceived preferences toward the ability of one or more of the interventions to have a better outcome than another.

Clinical equipoise provides the principled basis for medical research involving patients randomly assigned to different treatment arms of a clinical trial,<sup>4</sup> and is considered a necessary feature for clinical service practitioners to ethically enroll patients into clinical trials.<sup>4</sup> This assumption of a state of uncertainty has been identified as the central ethical principle for human experimentation.<sup>5</sup> In fact, the majority of the literature and discussion on clinical equipoise is grounded in its theoretical value toward reducing an ethical dilemma of trial design.<sup>6-11</sup>

In truth, it is somewhat naive to assume that all RCTs were and are investigated in a state of equipoise, regardless of whether ethics are the driving force behind the assumption.<sup>12</sup> The foundational notion of equipoise requires that there is insufficient evidence available for the clinician to presuppose that one arm of a randomized trial is any better (even minutely better) than a comparative arm.<sup>13</sup> Given that 'clinician experience' is a form of 'evidence',<sup>14</sup> preconceived personal preferences associated with an intervention, whether wrong or right, are likely always present. Consequently, it is arguable whether an environment can exist in a complete state of equipoise, especially when manual therapy is the treatment intervention.<sup>15</sup>

On the other hand, it is also naive to assume that the results of all manual therapy interventions reported in comparative trials are purely associated with the effects of an intervention and are not influenced by an absence of clinical and personal equipoise. Manual therapy interventions are personalized techniques, which often require careful, long-term study and skill acquisition. The assimilation of these skills, as well as the required interaction between clinicians and patients, means that the majority of manual therapy RCTs have a very high risk of violating personal and clinical equipoise.

## Randomized Controlled Trials

RCTs have traditionally involved the use of a null hypothesis, whereby the researcher assumes that there

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will be no statistical difference between groups. More recently, however, most RCTs have migrated toward directional hypotheses, intended to demonstrate the effectiveness of one intervention over another.

One of the reasons for this change is publication bias, which is the tendency for journals to accept papers for publication based on the direction or strength of the study findings; studies have a higher likelihood of being published if they show a significant difference between groups.<sup>16</sup> Additionally, a factor in designing a comparative trial is the performance of an *a priori* power analysis, intended to determine the number of subjects needed to find a difference between groups. This number depends largely on the estimated effect size.<sup>17</sup> The performance of the intervention can be affected by the expected effect size, particularly risky if the clinicians providing the intervention are the ones who have designed the study. Despite, and perhaps, due to the challenges of meeting statistical significance with a directional hypothesis, the risks associated with experimenter and patient biases are compelling.

These risks manifest themselves through healthcare practitioners' conscious or unconscious placement of importance, enthusiasm, or confidence in one specific intervention versus another.<sup>18–20</sup> These findings have been identified previously in clinical trials that did not involve intimate interventions such as those associated with manual therapy.<sup>21,22</sup>

### Manual Therapy and Equipoise

Within manual therapy, two types of interventions are generally compared. The first involves selected techniques (such as manipulation, mobilization, selected neurodynamics, or any procedure that is specific to a particular manual therapy philosophy) paired against one another, while the second involves comparison of particular systems (such as McKenzie versus orthopaedic manipulative therapy).<sup>23</sup> In most cases the clinicians are experts at one (or in some occasions, both) of the interventions. It is fair to assume that some placement of importance, enthusiasm, or confidence associated to one's expertise in an intervention will play some role in the outcome. This is likely an unconscious bias in the majority of cases, but when the results of a study support a clear pre-study directional hypothesis, (particularly one that supports the authors' previous line of research) interpretation of the results should include analysis about a potential conscious lack of equipoise.

This effect may be observed when the control treatment does not reflect an intervention in a way that it is typically used in clinical practice (e.g., using a posterior–anterior mobilization that does not address the comparable or concordant sign of the individual, or lead to within-session improvements). Nearly all manual therapy interventions, with the

possible exception of thrust manipulation, have been used both as treatments and sham interventions. An intervention that – through intention or training – would have a meaningful effect when applied by one clinician may be no more than a sham control when applied by another.<sup>24</sup>

### Correcting for Biases of Non-equipoise

There are a number of means for correcting for this potentially problematic element. A method called an expertise-based RCT<sup>25</sup> involves randomizing patients to practitioners who specialize in the dedicated intervention within a trial. For example, for a trial comparing manipulation versus soft tissue mobilization, four clinicians who specialize in manipulation of the cervical spine could serve as research participants as could four clinicians who specialize in soft tissue mobilization. Each patient enrolled in the study could be randomized to a specific clinician, versus randomization to a particular treatment. Ideally, this would involve practitioners of similar levels of training, and include multiple therapists in each group. This would increase the likelihood that the variable examined is the technique or method, rather than the skill of a particular clinician.

A similar method to expertise-based RCTs is an equipoise-stratified design. This design<sup>26</sup> involves full pre-randomization recognition of clinician biases toward a specific intervention and balancing of these biases during the study groupings through matching. Equipoise-stratified designs are more appropriate for models, which involve numerous interventions or interventions that are multimodal.

A clinician's choice design<sup>26</sup> model allows the clinician to use their own judgments toward which cluster of interventions, which are selections in the RCT, are most likely to benefit the patient upon receipt. The clinician's choice model is not as useful in a trial that investigates one technique versus another and is also likely to lead to unbalanced numbers in each group. This also results in questionable randomization, which among other concerns will eliminate the ability to assess treatment modifiers. Additionally, this design introduces another variable, as the ability of the clinician to choose the correct treatment is confounded with the effect of the treatment. Consequently the trials would need to involve a large number of subjects for the process to work.

Lastly, statistical adjustment (post-randomization) may include the use of a clinician's recorded conscious or unconscious placement of importance, enthusiasm, or confidence in one specific intervention as a covariate in the final statistical analysis. Post-randomization control for the clinician's expectation is the weakest form of correction, but should be the minimal adjustment made in manual therapy trials.

## Additional Challenges

Even with these attempted corrections, lack of clinical equipoise can be a challenge due to factors out of the researcher's control. Clinician blinding is an important step in maintaining equipoise and should be a goal of clinical trials, yet achieving this goal is so difficult in manual therapy studies that some reviewers have excluded it as a factor in quality assessment.<sup>27</sup> Difficulty with blinding makes assessing the effects of a treatment system that requires progressive clinical reasoning (such as a McKenzie or Maitland-based examination) subject to the effects of equipoise, more so than the immediate effects of an intervention such as spinal manipulative therapy.

A systematic review by Kent *et al.*<sup>28</sup> identified only a single manual therapy subgrouping trial – involving McKenzie (Mechanical Diagnosis and Therapy) trained therapists examining direction-specific exercise – as having a significant treatment effect.<sup>29</sup> They note that this unique finding may be partly due to bias, as the evaluating therapists, who classified the patients, also provided the treatment. Clinicians trained in Mechanical Diagnosis and Therapy may interact differently with patients who received treatment matched to their classification versus movement in the opposite direction, which they expect will increase symptoms. Long *et al.*<sup>29</sup> attempted to control this effect by having only therapists blinded to patients' status provide the treatment, but a large number of patients in their pilot study declined to follow up with a different provider. This study shows the challenges to maintaining equipoise, as patients may not agree to the intended research design. In this case, some of the results were inconsistent with the researchers' hypotheses (a small percentage of patients receiving treatment opposite to their directional preference showed improvement), indicating that the risk of conscious lack of equipoise was minimal.

## Summary

Because of the intimate nature of manual therapy interventions, personal and clinical equipoise are two ingredients necessary for a truly unbiased manual therapy-based RCT. Further work is needed to define the full extent to which a lack of personal and clinical equipoise influences the findings of a manual therapy-based randomized clinical trial. This will require careful evaluation of the presence of clinical and personal equipoise prior to the implementation of the study. Until clinical equipoise is clearly accounted for, studies at risk for violating equipoise should be interpreted with caution.

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