

# Equipoise in Clinical Nursing Research

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La notion d'équilibre clinique, qui désigne un certain état d'incertitude face aux mérites relatifs de deux traitements ou approches thérapeutiques ou plus, est un élément fondamental de l'éthique en recherche clinique. Le degré d'incertitude nécessaire pour qu'un essai clinique respecte les principes éthiques fait l'objet d'un débat soutenu. Ce concept d'équilibre clinique n'a pas reçu suffisamment d'attention de la part des auteures en sciences infirmières. Le présent article s'y attarde en s'appuyant sur l'expérience de l'auteure relativement à trois essais cliniques portant sur des interventions psychosociales en santé mentale. Il résume les arguments en faveur et à l'encontre de l'équilibre clinique dans l'évaluation éthique de la recherche clinique. L'équilibre clinique peut s'avérer impossible à atteindre dans le cas des essais qui portent sur des traitements psychosociaux présentant des résultats multiples pour les patients et leurs proches. En outre, la nécessité d'atteindre l'équilibre clinique pourrait placer les infirmières qui fournissent ces traitements dans une position conflictuelle, puisque pour être en mesure de donner le meilleur traitement possible, elles doivent croire que ce qu'elles font est dans le meilleur intérêt du client. Or, pour accepter la randomisation, elles doivent, dans une certaine mesure, renoncer à cette attitude. L'article présente des exemples dans le but de voir comment les écarts relatifs à l'équilibre clinique dans la position des chercheurs, des cliniciens et des participants peuvent entraîner des difficultés dans la poursuite, en sciences infirmières, d'objectifs de recherche valides sur le plan méthodologique et conformes à l'éthique.

Equipoise, a state of uncertainty about the relative merits of 2 or more treatments or therapeutic approaches, is fundamental to the ethical conduct of clinical research. The degree of uncertainty necessary for ethical conduct of a clinical trial is the subject of ongoing debate. The concept of equipoise has not received sufficient attention from nurse authors. This paper examines the concept of equipoise by drawing on the author's experience with 3 trials of psychosocial interventions in mental health. Arguments for and against using equipoise in the evaluation of ethics of clinical research are summarized. Equipoise may be impossible to achieve in trials of psychosocial treatments with multiple outcomes for patients and relatives. In addition, the need to achieve equipoise may put nurses who provide psychosocial treatments in clinical trials in conflict. In order to provide the best treatment possible, they must believe that what they are doing is in the best interests of their client. Yet, in order to accept randomization, they must, to some extent, relinquish that belief. Case examples are used to examine how discrepancies with respect to the "equipoise status" of researchers, clinicians, and research participants may be problematic in achieving methodologically sound, ethical clinical nursing research.

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## Background

Equipoise is a state of uncertainty about the relative merits of two or more treatments. It is the reason we do clinical research — to resolve the uncertainty, to find out which treatment or practice is best. At first glance equipoise appears to be a simple concept, but on close examination one realizes that it is a complex phenomenon. This complexity results in controversy within the health-care community about equipoise and clinical research. The concept of equipoise has been discussed primarily with respect to randomized controlled trials. It is, however, more broadly relevant because uncertainty is fundamental to the ethical conduct of all clinical research, not only randomized controlled trials. Furthermore, while the theoretical and practical implications of equipoise in ethical clinical trials have been discussed in the bioethics and medical literature (Edwards, Lilford, Braunholtz, et al., 1998), equipoise has received limited attention from nurse authors (Nield-Anderson, Dixon, & Lee, 1999; Olsen, 2000; Scullion, 2000).

This paper examines the concept of equipoise by drawing on the author's experiences with three trials of psychosocial interventions in mental health. Various definitions of equipoise are described. Arguments for and against using equipoise in the evaluation of ethics of clinical research are summarized. Specific cases are used to show how discrepancies with respect to the "equipoise status" of researchers, clinicians, and research participants may impede methodologically sound, ethical clinical nursing research.

### Theoretical Versus Clinical Equipoise

In his analysis of the problems of applying the standard of equipoise in the evaluation of the ethics of clinical research, Freedman (1987) differentiates between theoretical and clinical equipoise. Theoretical equipoise, also known as individual equipoise, is the individual researcher's state of uncertainty about the relative merits of two or more therapies. According to Freedman, it exists when "overall, the evidence on behalf of two alternative treatment regimens is exactly balanced" (1987, p. 143). When equipoise exists, a trial of the two treatments is ethical.

As noted by Freedman (1987) and others (Alderson, 1996; Chard & Lilford, 1998; Scullion, 2000), theoretical equipoise is practically untenable. It does not reflect the complexity of clinical decision-making and is disturbed as soon as the clinician or researcher *perceives* a difference — whether or not a difference exists. Clinicians are rarely in a state of

equipoise; they have opinions as to the effects of particular treatments. These opinions may be based on a variety of sources, including research literature, theory, clinical experience, intuition, and ideology. Ethical clinical practice entails providing the care that is most likely to benefit the patient. This means that in ethical nursing practice, recommendations or choices are based on the nurse's opinion. Thus, nurses who enrol patients in research may be in conflict. If a nurse believes one treatment is better than another, how can that nurse enrol a client in research where the client may not receive the preferred treatment?

The author managed a randomized clinical trial that presented this dilemma to some nurses who made referrals to the trial. The trial was a comparison of time-limited psychosocial interventions for schizophrenia. All the research participants received routine outpatient care from their primary clinicians. In addition, they were randomly assigned to either (1) family psychoeducation, (2) psychosocial rehabilitation, or (3) both family psychoeducation and psychosocial rehabilitation. Both programs lasted 4 months and were provided in the community prior to the trial (Munroe-Blum & McCleary, 1995). At the time of the trial, there was good research evidence for positive effects of family psychoeducation for families with specific risk factors. The trial was conducted because there was limited evidence for each of: (1) effects for the trial population, which was not limited to higher-risk families; (2) the effectiveness of time-limited psychosocial rehabilitation; and (3) the effectiveness of the two treatments in combination. Both treatments were accepted by mental health clinicians in the local community and there were usually waiting lists for the programs.

When the trial was introduced in the community, a number of clinicians who usually made referrals to the programs disliked the idea of randomization. The primary criticism was "We know what our clients need and what will work for them; they shouldn't be randomized." The research team's response was to present a critique of the limitations of the evidence and to remind referring clinicians of the potential benefits of the research. These benefits included the potential to avoid repetitions of past mistakes in psychiatric care, where treatments were provided based on ideology and subsequently disproven theories such as the theory of the schizophrenogenic mother. In effect, this response was designed to produce uncertainty among the referring clinicians, to move them closer to equipoise. The clinicians were presented with evidence of the existence of what Freedman (1987) calls "clinical equipoise."

Freedman (1987) proposes a modification of the concept of equipoise, which he calls clinical equipoise. Clinical equipoise is also known as communal equipoise (Alderson, 1996) and collective equipoise (Chard & Lilford, 1998). Freedman suggests that research is ethical "if there [is] honest, professional disagreement among expert clinicians about preferred treatment...[when] there is not consensus within the expert clinical community about the relative merits of the alternatives to be tested" (p. 144). Applying this standard, as long as the nurse accepts that there is disagreement among the expert community about what is best, the nurse can, in good conscience, enrol participants in a clinical trial.

Freedman's (1987) position is not without controversy. The problem is that while clinical equipoise may mean that a trial is ethical, it still may not be ethical for particular clinicians, who are not themselves in equipoise, to recommend the trial to a particular patient. This point has been argued without resolution in the medical literature (e.g., Enkin, 2000; Lilford, 2001; Lilford & Djulbegovic, 2001; Sackett, 2000a, 2000b, 2001; Weijer, Shapiro, Glass, & Enkin, 2000). The arguments apply equally to nursing practice and research. Sackett's position, argued in the Canadian and British medical literature (2000a, 2000b, 2001), is that clinical equipoise in the medical community does not let the individual clinician off the hook. His opinion is that a physician must be in equipoise to enrol a participant in a trial, that the physician cannot ethically ignore clinical judgement about what is best for a particular patient. The counter-argument is that treatment recommendations depend not only on clinical skill, but also on up-to-date knowledge of the best therapeutic strategies available, that knowledge is not developed in isolation and physicians must rely on the collective judgement of the medical community (Shapiro & Glass, 2000).

### **Individual Clinician Equipoise and Psychosocial Treatments**

Clinical equipoise about the treatments under investigation may provide sufficient justification for the physician researcher prescribing one or another medication as part of a clinical trial. However, at least one nurse author believes that clinical equipoise is insufficient justification for nursing research because nursing involves the nurse as a therapeutic agent. Olsen (2000) argues that equipoise is reasonable in trials of interventions with a physiologic mechanism of action but not where benefit for the patient depends on the nurse-patient interaction. At the heart of his argument is a position that trials of psychosocial interventions are unethical. He believes that subjective experience cannot be

objectively measured and thus a patient's subjective experience is inaccessible to researchers. Furthermore, when the relative benefits of the intervention rely directly on subjective experience, the expert community's assessment of benefit is less valid than the individual's assessment. Thus, in Olsen's opinion, clinical equipoise is not reason enough to ask a person to forego personal preference and enter a randomized controlled trial of a psychosocial intervention. This argument may apply to trials of existing treatments, where there are sufficient resources to respond to patient choice. There are, however, practical limitations to accommodating patient choice. When resources are limited, new treatments may not be available except as part of their development and testing.

What about the nurse researcher who provides a nursing intervention as part of a clinical trial? What would uncertainty about the effects of a treatment mean for nurses who provide a psychosocial treatment as part of a trial? To some extent, a nurse's motivation and enthusiasm depend on a belief that the treatment or nursing care is beneficial. It would likely be difficult for an enthusiastic nurse to accept a randomized design.

In the trial of psychosocial treatments for schizophrenia described earlier, there was tension between "clinical equipoise" and "individual equipoise" for some of the multidisciplinary staff who provided the treatments. There was initially some discomfort with the idea of randomization. On the one hand, the clinical staff were involved and informed as the research was planned, and they understood the limitations of the empirical evidence for the treatments. They accepted both the notion of clinical equipoise and that the trial was ethical. On the other hand, prior to the introduction of the research, the clinical staff, like the referring clinicians, "knew what was best" and believed in the potential benefits of their work. This meant that there were times when a clinician was not in equipoise about a particular patient. On these occasions, there was discussion about whether the clinical staff's opinion justified making exceptions to the randomized design. The standard of clinical equipoise prevailed.

In this example, entire programs were being evaluated. In this context, if a nurse staff member had disagreed with clinical equipoise as a justification for the randomized controlled trial, or disagreed about whether clinical equipoise existed, the nurse's options would have been limited. The nurse could either work for a program that was being evaluated using an experimental design or work elsewhere. Where research involves evaluation of specific interventions rather than entire pro-

grams, it is possible for nurses to decide whether to participate as treatment providers. As well, there may be choice as to which treatment to provide. For example, ongoing research about family psychoeducation for adolescent depression (Sanford et al., 2000) involved introducing family psychoeducation as a new treatment within outpatient clinics. Nurses were in a position to decide whether to learn how to provide the new treatment and whether to participate in the trial. In a trial of group and individual psychotherapy for borderline personality disorder, the nurses and other clinicians who provided the therapy decided which kind of therapy to participate in (Marziali, Munroe-Blum, & McCleary, 1999; Munroe-Blum & Marziali, 1995).

Consideration of research ethics generally focuses on the effects of the research on patient participants. The potential effects on providers of the experimental treatments are rarely considered. One might question whether it is justifiable to produce uncertainty among nurses who provide nursing care as part of research. Shouldn't the nurses who are providing the care believe in what they are doing? Is it fair to move them towards equipoise? The answer comes down to the issue of the basis of their belief. In this era of evidence-based health care, the evidence underlying belief in the effectiveness of a particular nursing intervention is more important than the belief itself.

In addition to the possible moral implications of producing uncertainty among nurses who provide nursing care as part of research, there are practical implications for research design. Consider, for example, the development and evaluation of a telephone counselling intervention for diabetes control among adolescents. In a recent randomized controlled trial of this nursing intervention, the nurses who provided the counselling were initially very enthused about the potential benefits. As the trial proceeded, that enthusiasm was needed to maintain their motivation for the challenging work. The work required perseverance and creativity in the face of numerous obstacles (C. Richardson, personal communication, June 2001).

In the case of a hypothetical new nursing intervention, development might proceed from theory and hopefulness about its effectiveness through to pilot testing. When the pilot study has produced promising evidence, a clinical trial would be conducted. Enthusiasm for the intervention and belief in its effectiveness would build among participating nurses, perhaps even contributing to the intervention's effectiveness and intensifying the effort they put into their work. Given this scenario, what happens when the intervention is tested in a randomized controlled trial? It may be impossible to test the new intervention

fairly using a randomized design, as introducing uncertainty about the effectiveness of the intervention might compromise the nurses' ability to provide the intervention. At best, if effectiveness was reduced, then a sample size based on the effect size in the developmental research would be insufficient and the trial would be under-powered. At worst, the effect would disappear and the research results would incorrectly indicate that there was no benefit.

### **Equipose in the Context of Shared Decision-Making in Nursing Practice**

Another objection to randomization, one that was raised by referring clinicians in the trial of psychosocial treatments for schizophrenia described earlier, is that randomization is incongruent with the philosophies of client-centred care and shared decision-making espoused in the field of psychosocial rehabilitation and in the nursing profession. Does randomization detract from efforts to have clients involved in their own care? Similar issues have been raised by nurses (Nielsen-Anderson et al., 1999; Scullion, 2000) and other authors (Karlavish & Lantos, 1997). One solution to this dilemma is already in place in clinical research. The informed-consent process ensures that the decision to participate in research is freely made. In the trial of psychosocial treatments described earlier, research participants provided informed consent. In response to their concerns about randomization versus shared decision-making, the referring clinicians were told about the process of informed consent.

Informed consent does not, however, mean that research participants can choose between treatments in a trial, based on their wishes. Another solution to the tension between randomized design and the shared decision-making model is to modify the research design to allow for patient choice within the study. For example, in a randomized controlled trial of relaxation training as an adjunctive therapy for pain management in sickle cell anemia, a research participant who had been assigned to the control condition asked to receive the relaxation training. The nurse investigators adopted a modified cross-over design to accommodate participant feedback (Nielsen-Anderson et al., 1999).

Theoretically, consenting to enter a clinical trial implies that the research participant/patient is in equipose. However, there is evidence that a significant proportion of people who consent to participate in clinical trials may not fully understand what they are consenting to (Edwards, Lilford, & Hewison, 1998) and may assume that they will receive whatever treatment is deemed best for them (Alderson, 1996).

This indicates that some research participants do not understand the randomization process and do not understand that the researchers do not know what is best.

Research participants' understanding of consent for nursing research has not been investigated. However, it seems reasonable that the patient's process of arriving at equipoise and consenting to participate in research may be equally difficult regardless of whether the research is about nursing or medical practice. The challenge of ensuring that research participants are really in equipoise could be met by improving the process of informed consent. For example, Chard and Lilford (1998) suggest that decision analysis can be used to help patients make decisions about participation in clinical trials by trading off potential outcomes, their probabilities, and associated patient-specific utilities. This approach would give patient values primacy and would be consistent with a shared decision-making model of nursing.

### **Community Equipoise**

The case for the primacy of patient equipoise in determining whether a trial is ethical is taken further with the argument that patient values must be formally considered earlier in the research process than at trial entry (Chard & Lilford, 1998; Karlawish & Lantos, 1997; Lilford & Jackson, 1995). Theoretically, community members on research ethics boards represent patient and community values in the judgement of whether equipoise exists; they ensure that "community" equipoise exists. However, depending on how community is defined, it may be that research ethics boards are insufficient and that, in order to ensure community equipoise, it is necessary and desirable to consider patient values by involving patients in study design (Karlawish, 1997; Karlawish & Lantos). To ensure that community equipoise is representative of patient values, it may be necessary to involve patients, patient advocacy groups, or patient representatives in decisions about which research questions to pursue and which research methods to use. This kind of process has been used in AIDS research, with activist groups influencing the US Food and Drug Administration to modify the process of clinical research (Epstein, 1996). Nurse researchers could (and do) involve patient organizations in discussions on research questions and design. For example, nurses planning interventions for families of people with Alzheimer's disease could collaborate with members of an Alzheimer society. Inasmuch as such members are the "community" of users of services for families of people with Alzheimer's

disease, this collaboration could produce research questions and designs that reflect community equipoise.

### **Family Research**

In addition to the practice context of shared decision-making, nursing differs from biomedical research in that much of nursing involves work with families. Application of the concept of equipoise in research where the risks and effects differ for each family member has not been well examined. When evaluating the ethical basis of interventions that involve more than one family member, it may be difficult to weigh competing risks and benefits in order to determine which family member's interests are most important.

Consider, for example, a family education intervention for adolescent depression that is designed primarily as an adjunctive treatment. Adolescent patients, their parents, and their siblings may participate. For the adolescent, the intended benefits are reduced duration of their depression and reduced risk of recurrence. For the parents and siblings, the possible benefits include improved knowledge about depression and enhanced ability to cope with the adolescent's depression. There are potential risks. For example, among parents, increased knowledge about depression and risk of recurrence may result in prolonged anxiety for their child. Among siblings, learning about familial risk for depression may produce anxiety about their own risk for depression.

As with other kinds of psychoeducation, family education interventions for adolescent depression have been tested (e.g., Brent et al., 1997; Sanford et al., 2000). Such trials are ethical if there is equipoise about the benefits. In trials of family education for depression, there are unique risks and benefits for the adolescent patients, their parents, and their siblings. As long as the potential risks and benefits for individual family members are balanced, then equipoise is present. But what about instances where benefit to one family member is associated with risk to another family member? Does a potential benefit to, say, the depressed sibling outweigh the potential risk to the well sibling? These questions are not unique to research in this field. They are just as important in clinical decision-making on family interventions.

### **Conclusion**

We conduct clinical trials because we are uncertain about the relative merits of one treatment over another. The degree of uncertainty necessary for the ethical conduct of a clinical trial is the subject of ongoing

debate. The British bioethicist Richard Ashcroft writes about the epistemological problems of equipoise (1999). In his discussion of the relationship among equipoise, knowledge, ignorance, and belief, he hits the nail on the head when he states that the debate about equipoise in research ethics turns on the role of belief. Differences of opinion with respect to what constitutes evidence are present in much of the debate about using equipoise as a standard for ethical evaluation of clinical research. There may be conflicting degrees of uncertainty at the level of the clinical community, the individual clinician-researcher, and the patient. This can make some research impractical, even if it is ethical.

The standard of clinical equipoise may be impossible to achieve in trials of psychosocial treatments with multiple outcomes for patients and relatives. In addition, the need to achieve equipoise may put nurses who provide psychosocial treatments in clinical trials in conflict. In order to provide the best treatment possible, they must believe that what they are doing is effective, in the best interests of their client. Yet, in order to accept randomization, they must, to some extent, relinquish that belief.

In debates about equipoise and clinical research, there are strong opinions but no easy answers. It behoves nurses to enter into these debates. We must think carefully about uncertainty and equipoise as we plan and conduct clinical research. We need to think about the implications of our choices for patients and nurses who participate in research and those who may benefit from the research.

### References

- Alderson, P. (1996). Equipoise as a means of managing uncertainty, personal, communal and proxy. *Journal of Medical Ethics*, 22(3), 135–139.
- Ashcroft, R. (1999). Equipoise, knowledge and ethics in clinical research and practice. *Bioethics*, 13(3–4), 314–326.
- Brent, D. A., Holder, D., Kolko, D., Birmaher, B., Baugher, M., Roth, C., Iyengar, S., & Johnson, B. A. (1997). A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. *Archives of General Psychiatry*, 54(9), 877–885.
- Chard, J. A., & Lilford, R. J. (1998). The use of equipoise in clinical trials. *Social Science and Medicine*, 47(7), 891–898.
- Edwards, S. J. L., Lilford, R. J., Braunholtz, D. A., Jackson, J. C., Hewison, J., & Thornton, J. (1998). Ethical issues in the design and conduct of randomised controlled trials. *Health Technol Assessment*, 2(15).

- Edwards, S. J. L., Lilford, R. J., & Hewison, J. (1998). The ethics of randomised controlled trials from the perspectives of patients, the public, and health-care professionals. *British Medical Journal*, 317(7167), 1209–1212.
- Enkin, M. W. (2000). Clinical equipose and not the uncertainty principle is the moral underpinning of the randomised controlled trial: Against. *British Medical Journal*, 321, 757–758.
- Epstein, S. (1996). *Impure science: AIDS, activism, and the politics of knowledge*. Berkeley: University of California Press. Retrieved January 9, 2002, from the World Wide Web: NetLibrary, Inc. [http://emedialibrary.com/reader/reader.asp?product\\_id=4620](http://emedialibrary.com/reader/reader.asp?product_id=4620)
- Freedman, B. (1987). Equipose and the ethics of clinical research. *New England Journal of Medicine*, 317(3), 141–145.
- Karlawish, J. H. T. (1997). Permissible risk and acceptable benefit: The ethics of research involving the cognitively impaired. *FORUM Trends in Experimental and Clinical Medicine*, 7(3), 277–285.
- Karlawish, J. H. T., & Lantos, J. (1997). Community equipose and the architecture of clinical research. *Cambridge Quarterly of Healthcare Ethics*, 6(4), 385–396.
- Lilford, R. J. (2001). Uncertainty about clinical equipose: Clinical equipose and the uncertainty principles both require further scrutiny. *British Medical Journal*, 322(7289), 795.
- Lilford, R. J., & Djulbegovic, B. (2001). Declaration of Helsinki should be strengthened: Equipose is essential principle of human experimentation. *British Medical Journal*, 322(7281), 299–300.
- Lilford, R. J., & Jackson, J. (1995). Equipose and the ethics of randomization. *Journal of the Royal Society of Medicine*, 88(10), 552–559.
- Marziali, E., Munroe-Blum, H., & McCleary, L. (1999). The effects of the therapeutic alliance on the outcomes of individual and group psychotherapy with borderline personality disorder. *Psychotherapy Research*, 9(4), 424–436.
- Munroe-Blum, H., & Marziali, E. (1995). A controlled trial of short-term group therapy for borderline personality disorder. *Journal of Personality Disorders*, 9, 190–198.
- Munroe-Blum, H., & McCleary, L. (1995). Social treatment for schizophrenia: 12-month findings. [Abstract]. *Schizophrenia Research*, 15(1–2), 221.
- Nield-Anderson, L., Dixon, J. K., & Lee, K. (1999). Issues in clinical nursing research: Random assignment and patient choice in a study of alternative pain relief for sickle cell disease. *Western Journal of Nursing Research*, 21(2), 266–274.
- Olsen, D. P. (2000). Equipose: An appropriate standard for ethical review of nursing research? *Journal of Advanced Nursing*, 31(2), 267–273.
- Sackett, D. L. (2000a). Equipose, a term whose time (if it ever came) has surely gone. *Canadian Medical Association Journal*, 163(7), 835–836.

- Sackett, D. L. (2000b). Why randomized controlled trials fail but needn't: 1. Failure to gain "coal-face" commitment and to use the uncertainty principle. *Canadian Medical Association Journal*, 162(9), 1311-1314.
- Sackett, D. L. (2001). Uncertainty about clinical equipoise: There is another exchange on equipoise and uncertainty. *British Medical Journal*, 322(7289), 795-796.
- Sanford, M., Boyle, M., Offord, D., McCleary, L., Fisman, S., & Steele, M. (2000). Family psychoeducation for adolescent major depressive disorder. Unpublished study funded by the Hospital for Sick Children Foundation, Toronto.
- Scullion, P. (2000). Is the research necessary? Equipoise and other fundamental ethical considerations...including commentary by de Raevé L. *Nt Research*, 5(6), 461-469.
- Shapiro, S. H., & Glass, K. C. (2000). Why Sackett's analysis of randomized controlled trials fails, but needn't. *Canadian Medical Association Journal*, 163(7), 834-835.
- Weijer, C., Shapiro, S. H., Glass, K. C., & Enkin, M. W. (2000). For and against: Clinical equipoise and not the uncertainty principle is the moral underpinning of the randomised controlled trial. *British Medical Journal*, 321(7263), 756-758.