Uncertainty about clinical equipoise

It is not surprising that David Sackett[1,2] disagrees with Stanley Shapiro and Kathleen Glass;[3] they are talking about different things.

A clinical trial involves decisions at 3 distinct levels: that of society, the individual physician and the patient.

The decision on whether a proposed trial should be carried out is formally taken by a research ethics board (REB), which, in effect, must decide whether asking patients to consent to participate is consistent with the standards of society as a whole. The concept of clinical equipoise is an essential part of the REB's decision; the REB must be confident that expert clinical opinion regards the trial as valid.

Individual clinicians must decide whether they should enter patients into the trial. The concept of uncertainty addresses this decision.

The consent of the patient is requested by the uncertain physician on a case-by-case basis if he or she believes that the uncertainty for a population of patients applies to the specific case.

The term "clinical equipoise," though perhaps ungainly, effectively captures the valuable concept of collective expert uncertainty and differentiates it from individual uncertainty, which may be insufficient justification for a trial.

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3. Shapiro SH, Glass KC. Why Sackett's analysis of randomized controlled trials fails, but needn't [editorial]. *CMAJ* 2000;163(7):834-5.

In a rebuttal to Stanley Shapiro and Kathleen Glass,[1] David Sackett[2] argues that a term such as "clinical equipoise" is useful only if it has a consistent meaning for everyone, describes something real and is in common currency. With regard to the latter, he states that because "uncertainty" yielded 292 860 hits on a MEDLINE PubMed search whereas "equipoise" yielded only 52, "uncertainty principle" would be a better term to use. However, "uncertainty" has many meanings and a search of "uncertainty principle" using PubMed (1966–present) yielded only 41 articles, of which only 8 were related to Sackett's use of the term. In comparison, a search of "clinical equipoise" yielded 29 articles, all of which were directly relevant to the topic. The term "uncertainty principle" therefore fails the tests of consistent meaning and of frequency of use.

Sackett also argues that bioethicists don't grasp the importance of the trust between individual patients and clinicians, and that the patient and clinician are often reasonably certain of which treatment is needed. This implies, I think inadvertently, that a patient should simply trust his or her clinician and never seek a second opinion. As a clinician and a researcher, I would suggest that in many areas of medicine different expert clinicians often have different opinions as to the most appropriate treatment. Indeed, in life- or limb-threatening conditions, or when a treatment has many side effects, patients should be encouraged to seek a second opinion. In essence, the concept of clinical equipoise as originally articulated by Benjamin Freedman[3] simply suggests that where second opinions are likely to disagree, physicians should be willing to include their patients in a randomized controlled trial. Rather than prohibiting the clinician from informing the patient of his or her personal beliefs,[2] clinical equipoise simply asks the clinician to be honest, letting the patient know that a different but equally competent clinician might decide on a different course. Of course, whether a randomized controlled trial should be done will also depend on the size of the patient population at risk and the cost, but this is an economic argument, not an ethical one. Understood in this light, I cannot agree with Sackett's conclusion that clinical equipoise is inconsistent with the "patient's autonomy and right to refuse to be randomized on the basis of their opinion, bias or certainty."

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[The author responds:]

In conducting, participating in and teaching about randomized clinical trials, I've found it useful to recognize that uncertainty exists at 3 levels. Because the levels each have unique properties, problems and solutions, they must be clearly distinguished.

The first level is community uncertainty, where sufficient numbers of clinicians, methodologists and ethics committees must become sufficiently uncertain whether an intervention is beneficial for a randomized clinical trial of the intervention to be judged both necessary and appropriate; the trial's data safety and monitoring board later resolves this community uncertainty in light of the emerging results.

The second level is the uncertainty of individual clinicians who are deciding whether to join a randomized clinical trial and then, if they join, whether or not to offer trial participation to any of their patients (for example, some clinicians were certain that endarterectomy was beneficial in symptomatic carotid stenosis and refused to join the North American and European trials in