H.M. Evans, "Response to F.G. Miller and J.D. Moreno, 'The State of Research Ethics: A Tribute to John C. Fletcher'," *The Journal of Clinical Ethics* 16, no. 4 (Winter 2005): 372-5.

Response to F.G. Miller and J.D. Moreno, "The State of Research Ethics: A Tribute to John C. Fletcher"

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Miller and Moreno's thoughtful and interesting "secular sermon" praises the work of John Fletcher, partly for its virtues and partly by contrast with the perceived vices of more questionable work on the part of others who, in the matter of consent to clinical research, reach conclusions at odds with his own. Unfortunately, I appear to have a small walk-on part in this villainous role discussed near the end of their engaging article. This is a little frustrating, since, in the article of mine that is discussed,[1] I agree with much of what they say in their wider argument and in their thoughtful reflection on some early influences upon modern bioethics. I also cordially endorse their willingness to consider arguments in favor of uncomfortable resolutions to difficult moral challenges in clinical research (although I am unconvinced by their account of acceptably minimized risk in the case of "sham surgery").

Most pertinently, I strongly share their suspicion that superficially attractive categorical pronouncements are, in the wrong mouths, too easily used as a means for evading moral conflict. So I fervently wish that they might not have me in their sights in such a stricture, but sadly I fear that they may, insofar as their main exemplar of a categorical pronouncement is the notion of clinical equipoise, upon which I conditionally ground my arguments. My defense here is signalled, I hope, by the "modest proposal" reference at the start of my article: *What if* we take clinical equipoise seriously?

Let me elaborate on this a little. Miller and Moreno condemn, reasonably enough, arguments founded uncritically upon a theoretically deficient understanding of clinical research. Readers of my article must judge this aspect for themselves, of course, but my argument is a conditional one that proceeds from taking the idea of clinical equipoise seriously. I do not assert that clinical equipoise applies in any particular case — as a non-scientist and non-clinician I would be in no position to make such an assertion; rather, I explore what follows from its being true, if and when it ever is true. This conditionality is stated and emphatically restated; my challenge is to those who would assert clinical equipoise and yet deny my conclusion.

I will come back to the question of the consequences of equipoise, but first let me deal with what presumably disquiets Miller and Moreno, namely the headline conclusion that I reach, but which I think they rather misportray. It is misleading to suggest, I contend, that we should "dispense entirely with voluntary participation in many RCTs." Under my "modest proposal," participation in all kinds of clinical research

would remain voluntary — but the opportunity to opt-out of *some* very tightly specific kinds of research would come at an unusually high price, that is, the price of being denied free treatment under a publicly funded system, and being asked to obtain treatment elsewhere, not at the public's expense.

This more restricted sense of "voluntary participation" obviously requires some defense, and my article is devoted to that; but one aspect of it is raised distinctly now, and my response here is, I concede, not explicit in my original article.

First, it is not part of the meaning of "voluntary" that the chosen good (be it a process, event, or behavior) be free of cost. I think that I am acting voluntarily when I buy something I want, even though it comes at a monetary cost and monetary costs by definition entail opportunity costs at the price in question.

Second, this surely remains true even if I am buying something that I need, even vitally need, such as food. I definitely have to buy food from time to time; yet on any particular occasion I believe that I do so voluntarily even when I hand over cash for necessary basic foodstuffs, let alone "luxury" foods.

Thus we cannot conclude that my participation in something (be it handing over money or entering into a trial protocol) is nonvoluntary simply because it constitutes the price of getting something that I want, or even need, such as the food on my table or publicly funded healthcare that is otherwise free at the point of use.

Note, also, that my nonparticipation in research effectively comes at a price now, even though officially it does not. The costs are contingent: for example, at a direct and individual level I am sometimes liable to receive somewhat less close medical attention and scrutiny than I would as a research subject; at a general level the overall research effort is delayed to the extent of the recruitment of a replacement participant. (If in practice fewer volunteers are recruited then the price is the statistical security of the data of an additional subject.) This might look like a cost to society in the abstract, but I may well find myself contributing to the price in terms of marginal limitations on the confidence with which my own future treatment is prescribed to me.

Now let us return to the disputed matter of clinical equipoise. The role of equipoise in my argument is to bring out the force of the "modest proposal," that is, to disclose and, in this case reluctantly, to embrace the logical consequences of a declared position. When clinical research is justified on the basis of a claim of clinical equipoise, we are, I think, entitled to take the claim seriously for its implications as well as its rhetorical force.[2] If I *really am* as likely to receive the best available balance of benefit over harm from treatment P as I am from treatment Q, then I *really don't* have any obviously legitimate grounds for preferring one to the other. This is, it seems to me, a logical consequence of taking equipoise seriously — something the clinical research community generally do, and (presumably) wish us as patients to do.[3]

Once we admit there being no grounds for preferring one treatment to another, then much else follows: as I tried to show in step-wise fashion, a randomizing algorithm is as legitimate a means of allocating presumptively equivalent treatments as is the personal whim or hunch of a doctor, providing the presumption is serious. (If it isn't serious in any given case, we shouldn't be using it as the basis of that research protocol anyway.)

Given all of this, my "even more radical" position is, I think, simply an unfamiliar consequence of the doctrine of clinical equipoise as part of the official basis of much clinical research.

Miller's and Moreno's general opposition to this is grounded on their view that "clinical trials must be understood from an ethical perspective as fundamentally different from medical care." The distinct aims of clinical research and clinical treatment are indeed as they set them out (respectively, generalizable knowledge *versus* individual benefit), and, indeed, I set them out myself in exactly such terms — twice, for good measure — in my own article.

But I dispute that their conclusion follows from such differences in aims. First, different aims are not necessarily *ethically* different as such; helping Smith and helping Jones may constitute obviously different aims, yet they can still be ethically comparable, unless we add in compelling moral differences from somewhere else (such as differences in desert, for instance). Second, it is true that helping Smith as an individual

and helping humanity as a whole may be ethically different — but we most obviously notice this when we cannot do both at the same time. The point about taking equipoise seriously is that we *presume* it is indeed possible to do both at the same time. In helping humanity as a whole (via the generation of new knowledge or the reduction of future uncertainty) we also at the same time help Smith, because if equipoise is true then we have no reason to think that he is receiving anything other than the best treatment via random allocation. The study results may subsequently disclose otherwise — but so may the course of his ordinary clinical treatment which is, after all, an experiment upon a population of $n = 1$. To repeat, if we don't believe equipoise is true in a particular case, we have no business appealing to it in justification of randomizing someone's treatment, and then my own argument no longer applies (as Miller and Moreno accept: they note, correctly, that it is "an explicit background ethical condition for mandatory participation in trials in Evans's argument"). Other difficult questions would arise in such cases, which my article does not aim to cover.

Finally, Miller and Moreno suggest that respecting patients as persons "calls for assuring that research subjects have a minimally adequate understanding of how participation in trials differs from medical therapy." At one level one could hardly disagree with this. The question is what goes into such an understanding, and I'm not sure that analyzing it should, or need, be deferred to "future work in research ethics." I have set out what I think are compelling reasons — *if* we believe that equipoise applies in a particular case — for showing how participation in clinical trials *aligns with* medical therapy in morally important respects, for all that their aims are distinguishable, precisely because those aims can coincide when (and if) clinical equipoise really applies.

Miller and Moreno find this a radical view, but they do not show that it is wrong. They may claim (if it is indeed my article that they have in mind at this point) that there lurks a "theoretically misguided" view of the ethics of clinical trials, contributing to "the erosion of informed consent," but these strictures are, if the authors will forgive me, unsupported by specific demonstration. I would be glad to find common ground with them over the content of a proper understanding of the relation between clinical research and ordinary clinical treatment. It may be that the research community at some stage, quietly or otherwise, lays aside the notion of clinical equipoise as too-often indemonstrable, or as not being held with sufficient conviction by individual researchers, or, in response to the authors' anxieties, as too ready a means for evading moral conflict — but we should not expect this any time soon. Meanwhile, taking seriously clinical equipoise's specific consequence, that at the point of randomization one may truthfully expect to receive the best treatment whatever one receives, requires that a "minimally adequate understanding" of the relation between medical therapy and participation in trials covers not only how they differ, but also how they are the same.

NOTES

1. H.M. Evans, "Should Patients be Allowed to Veto their Participation in Clinical Research?" *Journal of Medical Ethics* 30 (2004): 198-203, pp. 199-200.

2. B. Freeman, "Equipoise and the Ethics of Clinical Research," *New England Journal of Medicine* 317 (1987): 141-5.

3. C. Weijer, S.H. Shapiro, and K.C. Glass, "Clinical Equipoise and Not the Uncertainty Principle is the Moral Underpinning of the Randomised Controlled Trial," *British Medical Journal* 321 (2000): 756-8; D. Machin, S. Day, and S. Green, *Textbook of Clinical Trials* (Chichester, U.K.: John Wiley, 2004). E.g., "It is this [genuine] uncertainty which provides the necessary equipoise . . . to justify random allocation to treatment after due consent is given." (p. 14)