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## **Sham Surgery and Genuine Standards of Care: Can the Two be Reconciled?1**

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because more preliminary laboratory work or animal studies have to be done or whether holding back is being overly cautious. Where the standard therapy is unsatisfactory and the physician has an idea tied to a theory (e.g., related to physiology or pharmacology) about another treatment that might be more advantageous, fiduciary responsibility might have to serve as the arbiter between cautious hesitation and brave intervention. This is sometimes an ineluctable dilemma for clinical medicine and clinical research, and the difference between them is far less significant than is often presumed.

The literature on error provides a useful framework for summarizing the several points of my discussion above (Chassin 1991; Becher and Chassin 2001). As Miller has explained, standard thinking about clinical research rests on significant conceptual mistakes. As I see it, those mistakes, in turn, result in serious underuse of a research approach to clinical innovation. Although the bioethicists and policy makers who consider the ethics of human-subjects research have instituted important policies to address the overuse and misuse of human subjects, their zealous efforts have left us to confront the serious hazards that flow from the underuse of clinical research methodologies. Their conceptual mistakes have resulted in a failure to engage in research not only in contexts where it would have been ethically permissible to do so but also in contexts where not having done so would have been unethical. The failure to engage in research is wrong because of the potential harm to future patients, and it is intrinsically wrong because it wastes a valuable and, sometimes rare, opportunity. The longer an unstudied intervention continues to be

used in clinical practice, the more indefensible it becomes.<sup>3</sup> If conceptual mistakes are the source of the problem of underuse of a research approach to clinical innovation, the solution lies in a reexamination and redesign of our standards for the ethical conduct of human-subjects research. ■

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3. This point was made by J. Azzouni in conversation.

## ***Sham Surgery and Genuine Standards of Care: Can the Two be Reconciled?***<sup>1</sup>

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Important ethical issues are raised by the use of sham surgery controls in clinical trials, and we agree with Franklin G. Miller (2003) that care must be taken not to obscure significant and morally relevant differences between different uses of sham surgery controls. Because the ethical is-

ssues that arise in this context are so fundamental, however, great care must also be taken to understand the diversity that exists among the *arguments* that have been used to evaluate previous uses of sham surgery controls. In particular, there are at least two views about foundational issues in the ethics of human-subjects research that differ precisely in their *standards for determining which differences between sham surgery controls are the morally relevant ones* (London and Kadane 2002). To be clear, Miller adopts and articulates one of these standards, and the novel aspect of

1. This paper draws on material that A. J. L. presented at Harvard Medical School in December 2002. A. J. L. thanks Baruch Brody and the members of that audience for their feedback and critical remarks.

its analysis lies in the fact that it applies this standard to three different sham surgery-controlled clinical trials. However, Miller's claims about leading arguments against the use of sham surgery controls lump together views that, though they might argue for similar conclusions, do so from very different premises. This creates unnecessary confusion about the state of the debate. The confusion is exacerbated by an apparent conflation of the claim that there are "strong prima facie reasons for rejecting the use of sham surgical controls" (London and Kadane 2002, 414) with the much stronger claim that there should be an absolute prohibition on the use of such controls. In what follows, therefore, we briefly examine the moral presuppositions of Miller's favored standard, the moral presuppositions of an important alternative, and what it takes to override one set of prima facie reasons for rejecting the use of sham surgery controls in clinical research.

#### *Miller's View: Weighing Harms to Individuals against Benefits to Science*

Miller correctly notes that in the context of standard medical practice, patients and their care providers must decide whether the risks to the patient from a proposed treatment plan are reasonable in light of the corresponding benefits to the same patient. In the therapeutic context the various burdens associated with an invasive surgical procedure, for example, are justified only to the extent that they are offset or outweighed by the various potential benefits they promise to the same individual. Presumably the same must be true of the various tools or modalities that are used for diagnostic and monitoring purposes.

Here, and elsewhere (Miller 2002), however, Miller argues that "it is erroneous to hold that clinical research should be governed by the same ethical standards as apply to the practice of medicine" (Miller 2003). Two claims in particular are used to support this conclusion. First, Miller argues that in clinical research a variety of invasive and painful procedures is routinely employed in clinical trials and that

these studies, which pose risks to participants without compensating benefits, are generally considered ethically acceptable, provided that the risks have been minimized, are not excessive, and are justified by the value of the knowledge to be gained from the research.

Second, Miller claims that clinical research would be "impossible if it were held to the ethical standard of promoting the medical best interests of patients that governs therapeutic medicine."

Miller thus thinks that recent critics of the use of sham surgery controls make the fundamental error of not recognizing that medical research and clinical medicine are governed by different moral norms. This leads them to err in

treating sham surgery controls as exceptional or as qualitatively different from other aspects of clinical research that "expose patients to risks that are not compensated by medical benefits."

On Miller's view, what these critics have failed to see is that within medical research the risks to an individual, whether associated with the use of a sham surgery control or otherwise, are ultimately justified by the benefits in scientific knowledge to be gained from the research. To be sure, Miller argues that these risks cannot be gratuitous. They must emanate from or be associated with a necessary component of a rigorous clinical trial design, and they must be minimized as far as is consistent with the integrity of that design. Within these constraints, however, all we have to do is make sure that there exists a favorable ratio between two very different kinds of utility—disutility to individual participants versus potential gains in utility to science.

Before addressing the accuracy of Miller's claims about his critics, it should be noted that Miller's favored framework itself suffers from some important limitations. It is not at all clear how to make an interpersonal-utility comparison of the sort Miller embraces, where harms to individuals are to be "weighed" against gains to science. Keep in mind that in the therapeutic context, patients and their caregivers must decide how to balance the risks to the patient against the potential benefits to the same patient. In the research context, however, Miller claims that risks to a particular participant are to be justified by their benefits to science, and he admits that there are no objective tools for measuring this kind of risk-benefit ratio. So we are left with a view that asks us to carry out a kind of moral accounting but that provides no independent standards to guide our respective judgments.

Now, any normative framework will ultimately rest on the ability of persons of good will to apply it sensibly and in the light of relevant experience. But we can legitimately evaluate different normative frameworks on how far they take us before we are left to our individual judgments. We are concerned, however, that Miller's standard provides almost no guidance for dealing with hard cases where intuitions conflict. We are also concerned that it provides almost no guidance on how to deal with conflicts between different views about how such "tradeoffs" should be made.

Consider, for example, that in order to facilitate meaningful deliberation and prevent widespread equivocation we need to know how to understand or operationalize the concept of potential benefits and burdens to science. Additionally, we also need to know how to determine when these benefits are sufficient to offset risks to the welfare interests of present persons. For example, is the value of the knowledge to be gained in the study to be measured by the

likelihood of publication or the likelihood of producing benefits to future patients, by likely cost savings or by some more complex index? Would even fairly major harms to individuals in a sham-surgery control group be outweighed by a trial that might improve the care of potentially millions of patients over the next five (ten, one hundred) years?

Given the likelihood of disagreement about these substantive issues, whose judgments about these relative values are the most appropriate? Researchers, who might have a variety of reasons to see gains in science as paramount? Clinicians who are advising individual patients about whether to become research subjects? Members of the public who know that they will not be involved in the trial (and therefore not subject to its burdens) but who also know that they might be future patients (and therefore potential recipients of the benefits)? Institutions that have a financial stake in promoting research?

The clearest aspect of Miller's proposed framework is that it permits the knowing compromise of the welfare of trial participants as ethically acceptable so long as such compromises are necessary components of a trial whose potential benefits to science are sufficiently large and important. When it comes to setting substantive limits on potential trades in individual welfare for scientific knowledge, however, Miller's framework offers little guidance for decision making. At best, a great deal of additional, substantive work will be needed to give real content to key elements of the framework. At worst, Miller's proposal provides the appearance of a common framework for deliberation while obscuring the more substantive moral judgments that operate behind the scenes, isolated from public scrutiny.

### *Sham Surgery Controls and Conflict over Treatment Options*

Unlike Miller, we do not believe that basic obligations to safeguard the welfare of persons and to protect them from preventable harms are suspended in the context of medical research. We do recognize, however, that there might be substantive differences about how to operationalize this obligation in the research context. In our evaluation of the trial conducted by Freeman and colleagues (1999), of fetal nigral cell transplants for Parkinson's disease, we asked whether the sham surgery control could be justified as part of a well-designed clinical trial in which there is credible doubt about the relative net therapeutic advantage of the interventions in each arm of the trial *and* where there is no third intervention that is preferable to or that dominates those that are used in the trial (London and Kadane 2002). The rationale behind this question is to ensure that the fact of someone's participation in medical research is not taken as a license to provide that person with care that falls be-

low the standards for treatment that obtain in the expert medical community (London 2000; Lemmens and Miller 2002; Weijer 2002). Put another way, the goal is to ensure that the welfare interests of each trial participant are given the same moral consideration within the context of medical research as they would be if the individual were receiving advice about care from various expert clinicians (Kadane 1996).

Medical research is possible under this standard to the extent that different medical experts might recommend different treatment options to the same patient for a particular medical condition. In the case of the Parkinson's disease trial we argued that the relevant experimental question was the clinically relevant question of whether the potential benefits and burdens of fetal nigral cell transplantation *and all that is associated with their implantation* compared favorably to or dominated the benefits and burdens of standard treatment with levodopa. At that point in time this was a question about which there might have been genuine disagreement among clinicians and researchers. As a result, we argued that a trial could be designed in which subjects who enrolled would be assured of receiving a treatment alternative that at least some reputable group of medical experts might recommend as an appropriate treatment option for their condition.

We also argued that the results of such a trial would be necessary in order to determine whether a trial that employed a sham surgery control would be ethically and scientifically warranted. If the transplant procedures and all that is associated with them were dominated by the standard treatment, then there would be no rationale for carrying out another trial with a sham surgery control. If the standard treatment were dominated by an experimental arm, then a subsequent sham surgery-controlled trial might be warranted *if* there were reasonable disagreement among experts about the causal origins of the perceived benefit. That is, there would have to be reasonable disagreement about whether the perceived benefits were caused by the tissue transplants and all that is associated with them or were caused by the experience of surgery and the same follow-up care.

How should this framework be applied to the study conducted by Moseley and colleagues (2002)? For the use of the sham surgery control in this trial to be ethically appropriate, each of the following claims would have to be true:

1. Skepticism exists among reputable experts in the medical community about the nature and cause of the perceived therapeutic merits of arthroscopic surgery for osteoarthritis of the knee.
2. In a rigorously controlled clinical trial comparing actual debridement and lavage against a benign placebo

control, the actual arthroscopic procedures dominated the placebo, and experts disagree about the causal origins of this perceived benefit.

3. This skepticism amounts to a worry that the actual debridement and lavage might not be causally responsible for the perceived benefits of the procedure and that such benefits might, instead, be caused simply by the “experience of surgery” and postoperative care that necessarily accompanies the procedure.
4. The risks in the sham surgery arm have been reduced as far as possible, consistent with the validity of the trial design.
5. There is no alternative therapy that dominates any or all of these trial arms.

If each of these claims were true, potential participants in such a trial could think about participating as follows. Some expert clinicians would recommend arthroscopic surgery for my osteoarthritis of the knee, but others would not. Among those who would not, some doubt the reality of the benefits this procedure is perceived to produce, and some think that the temporary relief of pain might simply be due to a placebo effect. Whose advice should I follow? If I participate in this clinical trial and am randomized to an arm with actual treatment, then I will receive a treatment that some experts would recommend because they believe it offers genuine relief. If I am randomized to the sham surgery arm, then I will have the experience of surgery with fewer risks than if I had the actual procedure. Given the susceptibility of the experience of pain to potential placebo effects, and the belief by some experts that the only therapeutic merits of this intervention are of this type, such experts might reasonably doubt whether the level of care I will receive in this arm of the trial is any better or worse than doing nothing or actually having the real procedure. Clearly, if I participate in the trial I cannot choose which intervention I will receive. But, since I am not confident enough in the conflicting recommendations of the experts in the medical community to have a clear preference, I will let the random allocation procedure of the clinical trial decide for me.

Whether a justification of this sort is available to Moseley and colleagues will hinge on the truth of the premises in the above argument. Here we have important reservations. As Moseley and colleagues (2002) report, the only previous double-blind, randomized, controlled trial of arthroscopy for osteoarthritis of the knee showed no statistically significant difference between subjects who received arthroscopic lavage with 3000 ml of fluid and the controls who received only 250 ml of fluid. In light of this data and the fact that “there is no evidence that arthroscopy cures or arrests the osteoarthritis” (81) we question the use of the sham surgery by Moseley and colleagues on

the grounds that there does not seem to be credible evidence of a therapeutic benefit associated with this procedure whose causal origins might be the subject of dispute.

In this brief commentary we have argued for a framework within which sham surgery controls might be permissible under well-articulated conditions. These conditions are motivated by a fundamental commitment to ensuring that the legitimate health interests of persons are not neglected simply because they have agreed to participate in clinical research. Miller’s proposal is premised on the rejection of such a moral baseline. Additionally, it does not address substantive issues about how to formulate key elements of its favored framework. While this will no doubt generate substantive differences among people of good will, the framework provides little guidance about how to resolve those differences. In contrast, the position that we articulate views clinical trials as morally justified precisely when there is meaningful disagreement among informed people of good will about which medical interventions will adequately serve the individual’s health needs (Freedman 1990). By designing clinical trials whose goal is to resolve such disagreements, research can accommodate both the basic interests of participants and the legitimate interests in medical progress that we all share. ■

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