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Equipose and the Duty of Care in Clinical Research: A Philosophical Response to Our Critics

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Franklin G. Miller and colleagues have stimulated renewed interest in research ethics through their work criticizing clinical equipose. Over three years and some twenty articles, they have also worked to articulate a positive alternative view on norms governing the conduct of clinical research. Shared presuppositions underlie the positive and critical dimensions of Miller and colleagues' work. However, recognizing that constructive contributions to the field ought to enjoy priority, we presently scrutinize the constructive dimension of their work. We argue that it is wanting in several respects.

Keywords: *duty of care, equipose, harm-benefit evaluation*

I. INTRODUCTION

It strikes us that Dag Hammarskjöld, former Secretary General of the United Nations, got it right when he remarked, "Praise those of your critics for whom nothing is up to standard." F.G. Miller and colleagues, in their sustained criticism of our work, are worthy of our praise. Their criticism is partly responsible for our efforts to improve and further develop our account of the norms governing the conduct of clinical research, including clinical equipose and the duty of care (Miller & Weijer, 2003; Weijer & Miller, 2004; Miller & Weijer, 2006a; Miller & Weijer, 2006b). However, the

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work of Miller and colleagues has not been entirely critical. They have also, over the course of three years and some twenty articles, endeavored to provide an alternative account of the norms governing clinical research. We presently critically evaluate the merits of their proposed alternative. In the very best sense of Hammarskjöld's dictum, we propose to repay the favor they have paid to our work.

To be convincing and comprehensive, an account of the norms governing clinical research must do three things. First, it must clearly identify a set of norms. Second, it must clearly specify these norms in consideration of the circumstances in which they are to govern practical reasoning. Third, it must articulate a clear foundation for the norms in law and/or ethics, and explain their derivation from that foundation. Coherence being an indispensable criterion of sound philosophical argument, we presently evaluate the coherence of Miller and colleagues' alternative on each of these points.

II. IDENTIFICATION OF NORMS

The recent work of Miller and colleagues has a characteristic structure. It typically begins with the negative ambition of undermining clinical equipoise and cognate concepts, (Freeman, 1987) and ends by positing an alternative, usually a framework of norms including requirements for value, validity, favorable risk/benefit ratio, independent review, and informed consent (Miller & Brody, 2003; Litton & Miller, 2005). The presentation of the framework as an alternative is evidence of imprecision for the suggested contrast is false. As a moral concept, clinical equipoise is properly understood as specifying one norm (the duty of care) that may, in turn, fall within the broad ambit of one requirement in the framework — that for a favorable risk/benefit ratio. Proponents of clinical equipoise and cognate concepts have not disputed any of the norms in the framework. Indeed, as recognized elsewhere (Emanuel, Wendler, & Grady, 2000, pp. 2710–2711), they have contributed significantly to the elaboration of many of the requirements in the framework, including and especially that for a favorable risk-benefit ratio. The false contrast distracts from the specific point of debate — namely, whether a particular norm (the duty of care) and its specification (clinical equipoise, or a cognate) governs the relationship between physician-researchers and patient-subjects.

Imprecision is also evident in the conflation of analytically distinct questions concerning consent and the duty of care (Miller & Rosenstein, 2003, p. 1384; Miller & Brody, 2003, p. 20 and pp. 25–26; Litton & Miller, 2005, p. 573). For instance, Miller and Brody state that:

The doctrine of clinical equipoise ... constitutes a "therapeutic misconception" concerning the ethics of clinical trials, analogous to the tendency of patient volunteers to confuse treatment in the context of RCTs with routine medical care. (Miller & Brody, 2003, p. 20)

The suggestion of analogy is false. Therapeutic misconception bears on issues of consent; namely, whether researchers have forthrightly explained salient differences between research and treatment to patient-subjects, and whether the latter evidence comprehension of same. It has no normative purchase on the distinct question whether physician-researchers operate under a duty of care to patient-subjects.

Miller and colleagues are also inconsistent in their identification of norms governing the conduct of clinical research. The authors usually simply endorse a seven-point framework articulated by Emanuel and colleagues (hereafter: the seven-point framework) (Emanuel, Wendler, & Grady, 2000), departing only in their insistence that clinical equipoise be expunged (Miller & Brody, 2003, p. 26; Litton & Miller, 2005, p. 569). However, they have without explanation endorsed distinct frameworks for particular forms and areas of clinical research (Horng & Miller, 2002; Horng & Miller, 2003; Miller, 2003a; Silverman & Miller, 2004). For example, in respect of sham surgical trials, Horng and F.G. Miller argue that:

[a] placebo-controlled trial of an invasive procedure can be ethically justified if:

1. there is a valuable, clinically relevant question to be answered by the research,
2. the placebo control is methodologically necessary to test the hypothesis,
3. the risk of the placebo control itself has been minimized,
4. the risk of a placebo control does not exceed a threshold of acceptable research risk,
5. the risk of the placebo control is justified by valuable knowledge to be gained, and
6. the misleading involved in the administration of a placebo control is adequately disclosed and authorized during the informed consent process. (2003, p. S126)

This framework differs substantially from the seven-point framework. Subtracted are requirements for fair subject selection, independent review and respect for enrolled subjects. The general requirement for validity is transformed into a requirement of methodological necessity. Further, most of the requirements are not general in nature. Rather, they are directed at moral evaluation of a particular kind of control (placebo). Norms identified for the selection of control groups for critical care research represent an even more marked departure (Silverman & Miller, 2004, p. 854).

The authors have identified yet other norms. The first is a general duty of non-exploitation:

Physician-investigators do have an obligation to each research participant ... it is an obligation not to exploit participants for the sake of scientific investigation. (Brody & Miller, 2002)

The second is a general duty of protection:

... both the attending physician and the investigator have a general duty to protect the patient-subject from harm. (Brody & Miller, 2003, p. 336)

The relationship between these duties is as unclear as is that between the two collectively and the seven-point framework. At times, the duty of non-exploitation is presented as a sort of super norm, as where Brody and Miller assert that “the harm-avoidance duty ...is best understood as one of a number of duties that can be viewed collectively as [sic] non-exploitation” (2003, p. 336). At other times, the duties are presented as interchangeable and therefore presumably indistinguishable (Miller & Silverman, 2004, p. 562). At yet other times they are presented as independent and therefore presumably distinguishable (Buchanan & Miller, 2005, p. 171).

Furthermore Miller and colleagues’ account is contradictory on the central question—whether the duty of care is properly identified as a norm governing the conduct of clinical research. The authors repeatedly reject both clinical equipoise and the underlying duty of care (Miller & Brody, 2002; p. 5; Miller & Rosenstein, 2003, p. 1384; Brody & Miller, 2003, p. 334; Miller & Silverman, 2004, p. 562; Miller, 2004, p. 115; Buchanan & Miller, 2005, p. 162; Litton & Miller, 2005, p. 566). However, they contradict themselves in two ways.

First, they endorse component analysis. The endorsement comes in the context of their warning against the exploitive potential of “whole protocol” evaluations of the net harms and benefits of research (Miller, Wendler, & Wilfond, 2003, pp. 103–104). The authors recognize that component analysis is consistent with the language of federal regulation, and cite approvingly the National Bioethics Advisory Commission’s recognition that “[a] major advantage of this approach is that it avoids justifying the risks of procedures that are designed solely to answer the research questions based on the likelihood that another procedure in the protocol is likely to provide a benefit” (2003, p. 103). According to Miller and colleagues, “The components approach to risk-benefit assessment is not only consistent with the regulations governing research with children; it follows from the ethical and regulatory requirement of minimizing risks” (Miller, Wendler, & Wilfond, 2003, p. 103).

The core structural feature of component analysis is the demarcation of procedures in accord with the presence or absence of therapeutic warrant (Freedman, Fuks, & Weijer, 1992; Weijer 2000; Weijer & Miller, 2004). Demarcation reflects patient-subjects' distinguishable entitlements to competent care and to protection from exposure to undue harm. The former entitlement is secured by the standard for evaluating therapeutic procedures — clinical equipoise. Miller and colleagues' endorsement of component analysis undermines their rejection of the duty of care elsewhere because its structure (demarcation) and norms (clinical equipoise) are premised on recognition of the patient-subject's entitlement to competent care, an entitlement correlative to the duty of care.

Second, Miller and colleagues repeatedly endorse the duty of care. For example, Miller and Rosenstein say:

Especially in the context of research with severely ill patients, physician-investigators have a responsibility to provide appropriate medical attention and care at the same time that they engage in scientific investigation. (Miller & Rosenstein, 2003, p. 1385)

No attempt is made to justify this marked departure from Miller and colleagues' repeated rejection of the duty of care. Further, the terms of the endorsement are problematic. The authors suggest the duty applies “especially” in respect of “severely ill patients,” but are silent on what counts as severe illness, and why recognition of the duty should turn on it.

Further evidence to similar effect is found in the following statement by Brody and Miller:

Is it sufficient for the clinician-investigator *merely* to prevent harm to the subject? ... If the protocol allows for such flexibility, then the clinician has a special obligation to try to secure whatever additional benefit for the patient that might be achieved, *within* the parameters of maintaining the integrity of the research design. (Brody & Miller, 2003, pp. 340–341, emphasis in original)

This statement obviously conflicts with Miller and colleagues' rejection of the duty of care. It further belies their claim elsewhere that physician-researchers are obliged only to “prevent harm and exploitation” (Buchanan & Miller, 2005, p. 171). As above, the terms of the endorsement are problematic. Why is observance of the duty made contingent on flexibility in the protocol? How is it “special”? What kind and how much “additional benefit” is the physician-researcher obliged to provide? What is the standard for assessing fulfillment of an obligation to “try”?

Finally, self-contradiction is also entailed by Miller and colleagues' continuing endorsement of an interesting paper on professional integrity (Brody & Miller, 2003, p. 332; Miller & Rosenstein, 2003, p. 1385; Miller, 2004, p. 115). This paper clearly suggests that the duty of care governs the relationship between physician-researcher and patient-subject. Consider the following selections:

Physician-investigators typically view their guiding moral responsibility as the care of patient volunteers. Although this moral commitment should be paramount, clinical research uses procedures intended not for the benefit of patient volunteers but to generate scientific knowledge. (Miller, Rosenstein, & DeRenzo, 1998, p. 1450)

We need to cultivate a conception of the moral integrity of the physician investigator that integrates the roles of the clinician and scientist without giving predominance to the one or the other ... Investigators must recognize and manage the moral tensions between the norms of patient care and the requirements of scientific investigation. (Miller, Rosenstein, & DeRenzo, 1998, p. 1452)

Miller and colleagues cannot simultaneously endorse this work and retain the central tenets of their more recent work. The recognition that the "care of patient volunteers" is the "paramount" or "guiding moral responsibility" of the physician-researcher is incompatible with their rejection of the duty of care. The same is true of the argument that the physician-researcher must "recognize and manage the moral tensions between the norms of patient care and the requirements of scientific investigation."

Assuming that there are distinctive norms associated with the role of physician, they must include the duty of care. Indeed, Miller and Brody have themselves argued that the "internal morality of medicine" includes obligations to avoid "disproportionate harms that are not balanced by the prospect of compensating benefits" and to maintain "fidelity to the therapeutic relationship with patients in need of care" (Miller & Brody, 2001, p. 583). Tellingly, the authors conclude that the duty of care requires the exercise of clinical judgment:

Clinical research demands the exercise of clinical judgment by physician-investigators ... Pellegrino and Thomasma conclude a detailed analysis of clinical judgments in medicine as follows: "In short, clinical judgments are both medical and inherently moral." This is no less true for clinical judgments in clinical research. (Miller, Rosenstein, & DeRenzo, 1998, p. 1452)

In this one respect, the original position of Miller and colleagues mirrors that of our own (Miller & Weijer, 2003, pp. 110–112; Miller & Weijer, 2006a; Miller & Weijer, 2006b).

III. SPECIFICATION OF NORMS

Likewise problematic are F.G. Miller and colleagues' efforts at specifying norms. Consider first the duty of nonexploitation. The authors specify it in markedly inconsistent ways. At times, they have suggested that it requires the physician-researcher to protect the patient-subject from exposure to "undue harm" (Brody & Miller, 2003, p. 340). At other times, they suggest that the duty requires her to obtain valid consent from the patient-subject and ensure that they are not exposed to "excessive risks" (Miller & Brody, 2002, p. 5). At yet other times, it is suggested that the duty requires her to comply with each of the requirements of the seven-point framework (Horng & Miller, 2002, p. 137).

Miller and colleagues' specification of the duty of protection is equally inconsistent. At one point, they suggest that the duty requires the physician-researcher to ensure that risks to patient-subjects are minimized, and reasonable in relation to the potential benefits to them and to society respectively (Brody & Miller, 2003, p. 336). At another, the authors suggest that the duty requires him to "assiduously protect the patient-subject from harm" (Brody & Miller, 2003, p. 338). No mention is here made of potentially competing interests (e.g., those of society) that might justify the imposition of harm, and thus qualify the duty. Finally, more recently, the authors have said the duty requires the physician-researcher to protect the patient-subject from "unnecessary or unacceptable risks" (Buchanan & Miller, 2005, p. 171). The disjunctive form means that "unacceptable" risks may be imposed if they are "necessary," and vice versa.

Problems also beset Miller and colleagues' specification of the requirement for a favorable risk-benefit ratio,¹ "the pre-eminent ethical requirement of all clinical research" (Miller, 2003b, p. 513). No justification has been provided for these inconsistencies. Miller and colleagues most often suggest that the norms constitutive of this requirement are implemented in an evaluation of the net benefits and harms of a protocol (Miller & Shorr, 2002; Miller, 2003b). Elsewhere, they have criticized whole-protocol analysis and endorsed component analysis, in which distinct norms are implemented in independent evaluation of the harms of therapeutic and non-therapeutic procedures (Miller, Wendler, & Wilfond, 2003). On other occasions, they suggest norms are implemented in evaluation of a single kind of procedure (e.g., placebo) (Emanuel & Miller, 2001, p. 917). These are obviously incommensurable approaches to the moral evaluation of research harms and benefits.

Similarly vexing are Miller and colleagues' efforts at answering the critical question "when are research risks reasonable in relation to anticipated benefits?" We have offered, and continue to develop,² our own answer (Weijer & Miller, 2004). F.G. Miller and colleagues offer many. None are satisfactory.

For starters, Miller and colleagues are not consistent in the way they state the reasonableness requirement.³ At times, they echo their endorsement of component analysis, emphasizing independent evaluation of the therapeutic and non-therapeutic procedures. The former are to be determined reasonable in relation to potential benefits to subjects, the latter in relation to the anticipated value of the study (Miller & Silverman, 2004, p. 562).⁴ On other occasions, the authors endorse a disjunctive statement of the requirement, suggesting that research risks are reasonable in relation to anticipated benefits where the net risks of the study are determined reasonable in relation to potential benefits to subjects *or* the anticipated value of the study (Miller & Shorr, 2002, p. 1340; Litton & Miller, 2005, p. 569).

Most problematic, however, is that F.G. Miller and colleagues never actually specify the reasonableness requirement. They have failed to articulate any standards which identify, secure and balance the interests of subjects and society respectively in receipt of research-related benefits and protection from research-related harms (London and Kadane, 2003, 62; London, 2006a; 219–220). This is a particular concern in respect of the risk/knowledge evaluation, for under a disjunctive approach it will often be the only means by which subjects' interests in protection from research-related harms are served. For their part, the authors have simply denied the possibility of specification:

How can it be determined whether the potential value of knowledge to be gained from a given study can justify the risks posed to research subjects? There are no formulas available. The assessment calls for carefully considered and deliberated judgments by research sponsors, investigators and IRBs. (Miller, 2003b, p. 515)

Miller and colleagues' refusal to specify the reasonableness determination is without justification. Miller wrongly gestures at missing "formulas." The challenge is not to articulate formulas. Risk-benefit evaluation is not an exercise in applied mathematics. Rather, the challenge is to articulate standards that identify, secure and appropriately balance the rights and interests of various stakeholders. The role played by clinical equipoise in component analysis clearly demonstrates the possibility of specifying such standards.

In the absence of standards, the protection of patient-subjects' welfare is left to the unfettered discretion of IRBs and physician-researchers. The process through which reasonableness determinations are to be made must remain entirely mysterious. This is problematic. Presumably, judgments of "reasonableness" relative to the protection of the interests of others may themselves be considered reasonable only where supported by reasons susceptible to public scrutiny (i.e., public reasons). If left unspecified, judgments of reasonableness are not guided by standards capable of supplying

public reasons for judgment. Left unchecked, discretion may be exercised as much through intuition as through reasoned reflection. The result of such a process can only be an inscrutable assertion that risks were reasonable. Miller and colleagues confirm this, illustrating risk/benefit evaluation in the only way they can — i.e., by identifying the risks and benefits of a study, and asserting that they stand in “reasonable” relation (Miller & Shorr, 2002, p. 1340; Miller & Brody, 2003, p. 27; Miller, 2003a, p. 46).

Perhaps sensitive to these problems, Miller and colleagues have devised a new norm, requiring that studies not pose “excessive” or “unreasonable” risks to subjects solely in the interests of science (Miller, 2004, p. 113). At one point, Miller and colleagues attempt to specify this new threshold, but only through resort to a distinct requirement, saying that risks are not “excessive” in part where they are minimized (Miller & Brody, 2002, p. 7). Thus defined, the threshold is vacuous. In the same paper, they supplement the definition with tautology, saying that risks are not excessive when they fall within an “acceptable” or “tolerable” threshold (Miller & Brody, 2002, p. 7). Tautological specifications of norms are obviously not specifications in any sense, thus making meaningless the caveat that the threshold “may vary somewhat depending on the value of the anticipated scientific knowledge” (Miller & Brody, 2002, p. 7).

Most often, Miller and colleagues simply leave the threshold unspecified (Miller, 2004, p. 114; Litton & Miller, 2005, p. 572). Left unspecified, it is problematic for precisely the reasons reviewed above. The ostensible protection the threshold provides is illusory given that it simply calls for yet another inscrutable exercise of unfettered discretion. As above, Miller and colleagues illustrate the operation of the threshold in the only way they can — i.e., by identifying the potential risks of a study, and asserting that they are “reasonable” or “not excessive” (Miller, 2003, p. 46; Miller, 2004, p. 113).

Given that, inconsistencies aside, Miller and colleagues’ efforts have resulted in mere prescriptions to exercise unchecked discretion, one wonders why they have not given up pretence to specification of norms. Why not simply say “use judgment”? They have done that as well. According to Miller and Brody, “risk-benefit assessment of research protocols ultimately comes down to a matter of judgment” (Miller & Brody, 2003, p. 27). While there is little reason for confidence that unchecked discretion will provide effective protection for patient-subjects, the clarity of the admission is welcome.

IV. FOUNDATION OF NORMS

Miller and colleagues’ work has identified five distinct foundational ideas or theories for their approach. Never are these reconciled through argument. In the absence of such argument, positing distinct foundations for a set of norms renders work of normative theory incoherent. That being said, there

are other problems. First, in some cases, the claimed foundations are problematic when posited as such. Second, in most cases, the claimed foundations are left underdeveloped. Third, in every case, left entirely unexplored is *the* critical question — that of the relationship between foundation and particular norms. Fourth, in every case, one can readily anticipate serious difficulties establishing these relationships. We presently consider these problems in respect of each of the five distinct foundational ideas identified by Miller and colleagues.

The first such idea is that goals of activities determine the norms governing participants in them. As Miller and Brody put it, “The basic goal and nature of the activity determines the ethical standards that ought to apply” (Miller & Brody, 2003, p. 22; see also Brody & Miller, 2003, p. 334). Buchanan and Miller echo the claim, saying “it is imperative to recognize that the different contexts generate different moral obligations” (Buchanan & Miller, 2005, p. 170). Miller and colleagues have, accordingly, claimed that the distinct goal of clinical research — the production of valid and medically useful knowledge — founds a distinct set of norms governing it.

There are several problems with this approach. First, the assertion that the goals of activities are normative is problematic. Why should we think that the goals of activities are normative at all, let alone in the sense of “determining the ethical standards that ought to apply”? Examples reveal absurdity. Suppose the goal brushing one’s teeth is to make them clean and healthy. Does anything of normative significance follow? Shall we say that those engaged in the activity of brushing teeth are obliged relative to the goal of the activity (i.e., to make teeth clean and healthy)? Say that transportation is the goal of driving a car. Shall we say that traffic regulations must be justified on the basis of the goal of driving rather than, say, out of concern for universal interests, such as freedom and security from harm? The assertion that goals of activities “determine” norms is counter-intuitive. It thus requires argument.

Second, Miller and colleagues’ specification of the goal of clinical research is question-begging (London, 2006b). The authors never consider that clinical research might have multiple goals. One might be to advance scientific knowledge for its own sake. Another might be to advance generally useful scientific knowledge. Another might be to advance public health. Another might be to advance the health of a distinct population. Yet another might be to advance the health of distinct individuals, including patient-subjects. Another common goal is to advance the commercial interests of private enterprise. Others might be to further the mission of universities or other public and private institutions.

Third, Miller and colleagues’ fail to explain the relationship between the goal of clinical research and particular norms governing it. Instead, they have been preoccupied with disputing the applicability of the duty of care. In any event, in some cases, the assertion of a relationship

would strain reason and imagination. How, for example, are requirements for informed consent and fair subject selection to be derived from the goal of producing generalizable knowledge? Why should we not think they are instead derived from principles of equal freedom and distributive justice?

Fourth, and finally, the argument is contradictory. If norms are “determined” by the goals of activities, logic dictates that entirely distinct goals will give rise to entirely distinct norms. Miller and colleagues have posited entirely distinct goals for medicine and clinical research. They also suggest that these goals give rise to entirely distinct norms. However, the suggestion is false, as they recognize the informed consent requirement as applying equally in medicine and clinical research.

Miller and colleagues have also hinted at utilitarianism. They have, for instance, said that, “Clinical research is dedicated primarily to promoting the medical good of future patients by means of scientific knowledge derived from experimentation with current research participants — a frankly utilitarian purpose” (Miller & Brody, 2003, p. 21). By logic, when read in conjunction with the above-mentioned claim (advanced in the same paper), they are bound to a form of utilitarianism. Such leanings are also evident in Litton and Miller saying that: “If a proposed set of ethical guidelines is more conducive to producing valid and medically useful knowledge ... then there is a *prima facie* reason to endorse the proposed set” (2005, p. 568). Finally, we have the utilitarian logic of weighing harms and benefits in F.G. Miller and colleagues’ discussion of the reasonableness standards for the favorable risk-benefit requirement. In espousing utilitarianism, the authors seem to be saying two things. First, that the purpose of research is utilitarian in that the activity is a means by which to maximize general welfare (i.e., through production of useful knowledge). Second, that the norms governing clinical research are (or ought to be) utilitarian in that their justification turns on whether they advance the welfare-maximizing goal of clinical research.

If Miller and colleagues’ approach is utilitarian, none of the hallmarks of sophisticated utilitarianism are present. There is, for instance, no reference to an underlying theory of welfare, elaboration of kinds of benefits and harms to be recognized, and no argument as to how rights (including that to competent care) are founded on, or opposed to, utilitarian footings.

Even were Miller and colleagues to establish sophisticated utilitarian footings, they would face considerable challenges. They would need first to revisit their question-begging specification of the goal of clinical research. The sophisticated utilitarian might find several goals worthy of recognition. Those of advancing the health of patient-subjects, the commercial interests of private enterprise, and the mission of universities or other public and private institutions might all be thought worthy for their tendency to maximize general welfare. If multiple goals were recognized, challenges of

prioritization and conflicts await. The further task of establishing a utilitarian footing for particular norms presents obvious challenges.

But there is an additional problem. Rule utilitarianism has a peculiar structure of justification. Because norms are understood as justified to the extent they further or diminish specified welfare endpoint(s), justification of particular norms requires detailed empirical argument. If, following F.G. Miller and colleagues, we suppose that the endpoint here is the production of useful knowledge, they are obliged to demonstrate that each norm furthers that endpoint. Further, to reject a particular norm — say, the duty of care — they are obliged to demonstrate that it diminishes the endpoint. One way the duty of care might impact the production of useful knowledge is in respect of recruitment of patient-subjects. If the duty of care is to be recognized in medicine, but not clinical research, presumably this must be disclosed to prospective patient-subjects. But if patients were told in clear terms that they must waive their entitlement to competent care to participate in clinical research, it seems likely many would be disinclined to participate, thus jeopardizing recruitment. F.G. Miller and colleagues apparently agree:

Clinical research generally depends on a more or less explicit *quid pro quo* between investigators and patient volunteers, namely that patients agree to participate in studies in exchange for the chance of therapeutic benefit. A complete purging of the therapeutic milieu of clinical research would likely undercut the motivations of patients to volunteer, and it is improbable that the altruism of contributing to scientific knowledge would sustain the enterprise. (Miller, Rosenstein, & DeRenzo, 1998, p. 1451)

If empirical evidence supports our shared intuition, the authors face an uphill battle demonstrating that their “proposed set of ethical guidelines is more conducive to producing valid and medically useful knowledge” (Litton & Miller, 2005, p. 568).

In yet other work, Miller and colleagues suggest the norms they commend are founded on concepts of personal and professional integrity (Brody & Miller, 2003, p. 333, Figure 1). This builds on earlier work in which the authors spoke of “the nature and role of professional integrity of physician investigators, a conscientious framework for guiding investigators in the socially important but morally complex activity of clinical research” (Miller, Rosenstein, & DeRenzo, 1998, p. 1449).

Miller and colleagues’ ongoing appeal to professional integrity is problematic for several reasons. First, they never explain why the norms governing professionals should be thought founded on essential characteristics of a “professional,” nor do they identify those characteristics. Interestingly, others suggest that the essential characteristics shared by professionals are precisely those of fiduciaries (Arras, 2001, p. 661). If professional integrity is to

be understood in fiduciary terms, obvious problems arise for Miller and colleagues (Miller & Weijer, 2006b). Second, Miller and colleagues never establish a relationship between the norms they commend and any essential characteristics of professionals. Third, Miller and colleagues imply that professional integrity falls within a theory of personal integrity, but they say nothing of the latter. Finally, Miller and colleagues fail to consider that notions of integrity are incapable of founding norms. Integrity is arguably best understood as a virtue — a quality of character possessed by one who consistently acts in accord with a coherent set of principles, regardless what they are (Cox, La Caze, & Levine, 2003).

Miller and colleagues also repeatedly suggest that their approach is founded on a theory of exploitation. This is particularly evident in respect of their presentation of the seven-point framework (Miller & Brody, 2003, p. 26; Brody & Miller, 2003, p. 334). However, the authors never provide a theory of exploitation, even in outline. The confidence with which they dub the seven-point framework one of “nonexploitation” suggests it is to be taken as a self-conscious articulation of norms based on a theory of exploitation.

This suggestion cannot be sustained. First, it misinterprets the framework. The framework ought to be recognized for what it is — a useful summary of well-established ethical requirements drawn from a wide range of academic and policy contributions. If the framework carries any moral authority, it is self-consciously derived from these contributions (Emanuel, Wendler, & Grady, 2000, p. 2702). The framework does not derive authority from arguments rooted in normative moral theory because it is not supported by such arguments.

Second, the concept of exploitation plays a minimal role in the framework as originally articulated. The authors identified exploitation as a non-exclusive “justifying ethical value” for only three of the seven requirements (Emanuel, Wendler, & Grady, 2000, p. 2703, Table 2).

Third, the historical foundations of the framework resist the reinterpretation Miller and colleagues seek to impose. F.G. Miller and colleagues have recognized that the authors of the framework endorsed clinical equipose. They, have, however, failed to recognize that this endorsement is anchored by the historical foundations upon which the framework rests. Several of the academic contributions relied upon support the duty of care and clinical equipose or a cognate. The same is true of three of four policy documents cited as “fundamental by the authors of the framework.” For instance, the *Belmont Report* states that investigators must both “maximize possible benefits and minimize possible harms.” Paragraph Five of the *Declaration of Helsinki* states that, “In medical research, considerations related to the well-being of the human subject should take precedence over the interests of science and society.” Guideline 8 of the CIOMS *Guidelines* state that, “Interventions or procedures that hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual subject must be justified

by the expectation that they will be at least as advantageous to the individual subject, in the light of foreseeable risks and benefits, as any available alternative,” with the Commentary stating that, “Beneficial interventions are justified as they are in medical practice.”

Given that Miller and colleagues’ presentation of the framework is inconsistent with its original exposition and historical moorings, they must explain why it should be divorced from the latter, and how each particular norm is founded on a normative theory of exploitation.

More recently, Miller and colleagues have suggested that their approach enjoys contractualist footings. For example, Buchanan and Miller assert that “[t]he non-exploitation framework represents a fair contract with the participants” (2005, p. 163). Most recently, invoking Scanlon, Litton and Miller present it as articulating “principles [that] serve as terms of mutual respect among persons,” where persons are understood to be autonomous (“self-directed”) agents (Litton & Miller, 2005, p. 567).

There are several problems with this shift in strategy. First, it is difficult to reconcile the repeated invocation of “fair contract” with Scanlon’s contractualism. This is because, as Scanlon indicated, “‘contract’ and its cognates ... suggest a process of self-interested bargaining that is foreign to my account” (Scanlon, 1998, p. 5).

Buchanan and Miller discuss “fair contract” in conventional terms, even employing terms of art like unconscionability (2005, p. 175). However, as Scanlon rightly noted, contractual fairness is distinct from fairness in contractualism. As exemplified by unconscionability, contractual unfairness requires a defect in the process of contracting (i.e., in the process of establishing a common will). Substantive unfairness is pertinent only inasmuch as it is determined a product of such a defect. Contractual fairness therefore provides no support whatever for protectionist norms that constrain bargaining processes or contractual terms (e.g., requirements for fair subject selection, independent review and favorable risk-benefit ratio). Richer contractualist arguments on fairness may provide requisite support, but despite promises to the contrary, Litton and Miller never offer such arguments. They simply wield Scanlon’s work as an instrument by which to criticize clinical equipoise and the duty of care. Further, the contractualist strategy is self-defeating. First, given that contractualist arguments predominantly presume rationally self-interested⁵ individuals, they incline for rather than against the duty of care. Contemplating future illness and the possibility of participation in research, such individuals would surely want their interest in competent care protected as of right. Of course, recognition of this right (and the correlative duty) does not entail its inalienability. In their haste to reject it, Litton and Miller conflate the question whether the duty of care should be recognized with the analytically distinct question whether it may be waived (Litton & Miller, 2005, p. 570–571). Second, as a result, Litton and Miller wrongly accuse advocates of clinical equipoise of espousing paternalism. In any event, the accusation

trades on historical revulsion for the “p-word” in bioethics, and as Feinberg recognized, it “is derogatory and thus tends to be tendentious and question-begging in its bare application” (Feinberg, 1986, p. 4).

Furthermore, a number of the norms Miller and colleagues commend are open to the same accusation. Operating independently of the requirement for consent, the duty of protection and requirement for favorable risk-benefit ratio may attract the same accusation, as they grant others the discretion to judge whether research-related risks to the latter are reasonable.

V. CONCLUSION

To the extent it has stimulated renewed interest in research ethics, the work of F.G. Miller and colleagues has been salutatory. Their work is certainly partly responsible for our ongoing efforts to develop and improve our position. That being said, for meaningful debate to be possible, F.G. Miller and colleagues need to articulate a coherent alternative. This they have not done. Their work to date has traded on false contrasts and analogies, thereby frustrating the clarity essential to healthy debate. Further, preoccupied by their negative ambitions, F.G. Miller and colleagues have neglected the positive dimension of their work. As a result, inconsistency and contradiction are rife, manifest in their work on the identification, specification, and foundation of norms governing the conduct of clinical research. In recognition of the importance of healthy debate, we look forward to F.G. Miller and colleagues’ articulation of a coherent alternative.

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NOTES

1. F.G. Miller and colleagues never expressly consider whether the requirement applies equally to individual physician-researchers and IRBs, and if so, whether it should be specified distinctly for each. The authors seem merely to presume that the requirement applies equally to IRBs and individual physician-researchers, and that it is to be identically specified for each. Because F.G. Miller and colleagues vacillate in referring to IRBs and individual physician-researchers when discussing the requirement, our analysis will at times reflect that vacillation.

2. For example, we are working on specification of the requirement that the risks of non-therapeutic procedures be deemed reasonable in relation to the value of the knowledge to be gained from the study, and we are contemplating whether to add a threshold limiting the risks of non-therapeutic procedures for research involving competent adults.

3. Note that the reasonableness requirement is actually one of three risk-related requirements. The other two include the minimal risk threshold, and the requirement that risks be minimized consistent with sound scientific design. The distinct nature of these requirements is obscured by the general label “favorable risk-benefit ratio” in the seven-point framework.

4. Note, however, that in contrast to component analysis, key terms such as “experimental interventions” and “research procedures” are left undefined (see Miller & Silverman, 2004, p. 564).

5. Which is not to say exclusively or inordinately self-interested.

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