

LETTERS

Minimal Risk, Administrative Firm Trials, and Informed Consent

In questioning "underlying assumptions" of the recent article by Dr. Goldberg and Ms. McGough (Testing the Implementation of clinical guidelines *IRB* 1991; 13[6]:1-7), I wish to focus closer scrutiny on these assumptions, as relates to their suggestion that administrative experiments with the process of care can be exempt from informed consent. I feel this is a dangerous practice.

Medical care is nondeterministic, and styles of practice arise as a response to random reinforcement when nominally standardized diagnostic and therapeutic modalities are applied to nonuniform patient populations. Hence, the concept of attempted standardization of "styles" under guidelines is as subject to the scientific method as any other area of medicine. However, such manipulations may indeed carry risks other than the random risks of living. In an era when informed consent is routinely required for clinical research requiring as little as a single extra blood drawing, and protocols must be formally amended through IRBs for changes in algorithm as small as a few milliliters of blood taken, a prospective randomized study involving changes in entire systems of care cannot be free from the encumbrances of careful patient-safety scrutiny.

Guidelines for diagnosis and treatment arise as consensus statements clarifying the "fuzzy logic" of thousands of providers seeking optimal pathways. There are certainly risks of delayed, under-, or overdiagnosis and treatment just going from one provider to another. Because beneficence is assumed, those variations in style are tolerated free of any informed consent documentation (ICD) requirement in the setting of a single provider treating a single patient within the vague envelope of the "standard of care."

However, a standardized, mandated algorithmic approach to any disease carries nonrandom risks of delay, under-, or overdiagnosis or treatment, as well as nonrandom risks of side-effects of medications used. Therefore, any prospective

comparative protocol that constrains provider choices exposes the patients involved to the risks, known and unknown, of the assumed superior or cost-effective study protocol. It is not enough to excuse the need for ICD in such cases based on the supposition that such interventions will not *directly* lead to more or different invasive procedures. Since individual providers may be intimidated by "credentialed authorities" in a field as much as patients may, it is not enough to say that an impediment to the use of a given test or drug will not affect care if the provider would not be forced to depart from "personal care."

Intimidation of providers to depart from personal care is real, and is based on the fact that few can feel as in-command of the literature as to persist in the face of a practice restriction or incentive mandated and backed up by a nominal expert. The departure from personal care involved in such administrative experiments would be real and would expose a large proportion of the patients on one arm or other of the study to unknown and unpredictable risks. Because that exposure is backed by a guiding individual or committee, that entity should be humanitarian enough to accept responsibility for those unknown and unpredictable risks by informing the providers and patients of the fact that this is a planned, prospective departure from randomness of "usual" care. Especially when the systems intervention is undertaken for reasons of cost-effectiveness, where the subjects of the study will benefit indirectly at best from the intervention, and those most likely to benefit soonest and most directly are the very individuals proposing the systems intervention, such informed consent alerts the patients and providers to the underlying reasons for the change. It would reinforce ethical behavior on the part of those who administer large self-supporting health care organizations.

The particular example used, that of the low back pain algorithm, if applied to a firm trial, would need careful study to determine, for instance, that the patient group epidemiology being experimented

on matched the 1975 patients in the reference study closely enough for the disease mix causing the pain to be generalizable. Failure of such a firm trial to have to meet the scrutiny of an IRB might mean that a group of systems engineers with little or no knowledge of medicine could assume they could mass-try the algorithm against an inappropriate population. If they indeed found that in their firm trial the results of applying the algorithm resulted in net *harm*, then those patients in the intervention group would have been exposed to risk, and their right to have considered that before joining the firm trial would have been abrogated. It is doubtful such findings would then ever see publication because of legal considerations, whether the standard of practice was to require advance ICD or not.

I argue, in short, that firm trials must be subject to ICD. They are prospective interventions in the health care system, fraught with indirect risks of uncertain type, magnitude, and implication. To conduct such firm trials carries risk of abrogation of patient autonomy and may, by constraining individual providers who can be intimidated, lead to ethical uncertainty. Firm trials free of ICD in a real world where cost-effectiveness leads to personal or organizational wealth may lead to decreased surveillance over the risks and rationales of medical practice, and would therefore constitute a dangerous practice. Organizations running health care systems must accept, as individual clinical researchers do, responsibility in advance for the unplanned consequences of their manipulation of others' lives and health.

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Harold Goldberg and Helen McGough reply:

Our paper was a call for the exercise of discretion on the part of IRBs when faced with protocols involving administrative manipulations of the health delivery system. Current regulations speak only indirectly

this issue, exempting evaluation protocols conducted under federal auspices from IRB review as well as from the need for any informed consent documentation. Indeed, our decision to write the manuscript was in part motivated by a concern that the same exemption might be uncritically applied to all guideline dissemination trials. Doing so could lead to some of the very dangers raised by Dr. O'Neil.

We agree completely that any mandated algorithmic approach to any disease carries nonroutine risks of under- or overdiagnosis and treatment. Hence, our categorization of any protocol involving mandated practice as being a "clinical firm trial." We believe that all clinical firm trials certainly warrant full IRB review and a written informed consent procedure, a point we tried to make clear both in the last line of Table 1, and in the concluding sentence of the section discussing the potential conduct of clinical firm trials.

Where we appear to differ from Dr. O'Neil's position is in our handling of administrative interventions that would encourage, advocate, or provide incentives for a given approach, but would not mandate that it be followed. Dr. O'Neil offers two arguments suggesting that even these kinds of interventions carry risks greater than the routine risks of everyday living. In effect, he is disputing our contention that certain administrative manipulations can be appropriately considered to pose no more than minimal risks, the first prerequisite considered by IRBs in waving the requirement for ICD.

His first argument is a normative one. Given that we live in an era in which informed consent is routinely required for a single extra venipuncture involving a "few milliliters of blood," certainly any prospective randomized trial involving a change in an entire system of care must involve sufficient risks that they should not be "free from the encumbrances of careful patient-safety scrutiny." This argument confuses the important distinction between the risks of specific interventions and the risks of randomization. We agree that the physical risks of an additional venipuncture are very small, so small that venipuncture is included in the regulatory listing of procedures whose performance as part of a research protocol presents only minimal risks. However, in the absence of the other waiver prerequisites

mentioned in regulations (45 CFR 46.116(d)), IRBs routinely require ICD *not* because of the minimal physical risks incurred in one more needle stick, but because the uninformed imposition of a procedure even as low risk as a venipuncture violates the principle of respect for persons. Having blood drawn or receiving therapy as a result of chance assignment to this or that arm of a clinical trial (as opposed to the individualized, consensual calculus inherent in the concept of personal care) is not a risk routinely encountered in daily life.

Administrative manipulations indirectly affect patient outcomes for better or worse. That is, they may also present intervention-specific risks. Yet as long as administrative changes do not involve any decrement in access or benefits that trial participants would have otherwise received, their specific risks are generally considered to be minimal precisely because they are indirect and noninvasive. Unlike the situation that pertains to clinical interventions, no presumption of "personal administrative care" exists. As part of the everyday process of obtaining health care, patients are routinely exposed to differing and changing administrative fiat without their input or consent. To the extent that both the intervention-specific and randomization risks involved in administrative trials are no greater than those routinely encountered, the prior notification process that we described is an adequate expression of respect for persons. We have never suggested that administrative firm trials be free of careful IRB scrutiny; only that customary system changes that preserve access, benefits, and the provision of personal care can be considered to present no more than minimal risks. Whenever more than minimal risks are presented, as would our example involving restrictive insurance coverage, full committee review and ICD are warranted.

Dr. O'Neil's second argument is a crucial one because it raises the issue of exactly what constitutes constraint of practice. He is concerned that even if compliance with guidelines was not mandated as part of an administrative firm trial, the fact that the guidelines were promulgated by "credentialed authorities" or "nominal experts" would be sufficiently intimidating to the average provider to affect and thereby to preclude the uninhibited

exercise of personal care. First, this theoretical concern is not supported by empirical evidence. Widely accepted guidelines for preventive practices, for example, have existed for some time in the form of reported recommendations from both Canadian and United States task forces. Yet studies have demonstrated that overall compliance rates are not markedly changed by the issuance of such reports, remaining generally at less than 50 percent. Second, this argument appears to equate any potential effect of any magnitude with a "real" departure from personal care. This is an inflexible position that we feel fails to take into account the multitude of influences that now routinely affect physicians' judgments as to what is in the best interest of individual patients. The envelope of standard care is indeed so vague because in addition to considering medical efficacy physicians must routinely factor everything from dollar costs to patient expectations to the exhortations of pharmaceutical salespeople into their final recommendations. We feel that to be proclaimed capable of precluding personal care, proposed interventions must do more than simply affect medical judgment; they should be likely to distort medical judgment in a meaningful way. In essence, we are suggesting that a "minimal risk standard" be applied. Influences no more inhibiting than those to which physicians are routinely exposed represent only minimal additional threats to personal care. This is why we, and others, have drawn distinctions between protocols involving group versus individual financial incentives for providers. The former can certainly affect physician judgment; the latter are likely to distort it. In any event, at the risk of becoming redundant we would prefer the more discretionary approach of allowing disinterested IRB members to determine at what point on the continuum of increasingly constraining interventions personal care is sufficiently jeopardized to warrant declaring the risks involved to be non-minimal and hence deserving of the application of ICD.

In summary, we are chagrined by Dr. O'Neil's concluding blanket remark that firm trials (independent of the level of risk involved) must be

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subject to ICD. This position is unnecessarily absolutist. Determining the type and magnitude of risks and benefits involved in educational or administrative interventions is no more difficult or uncertain a task than that faced by IRBs during their deliberations concerning either traditional clinical research or clinical firm trials. Because we have recommended that all administrative and clinical firm trials undergo IRB review, the implication that the conduct of firm trials in an avaricious world populated by renegade systems engineers will necessarily lead to decreased surveillance of the rights and welfare of participants is gratuitous. In those instances where an IRB has determined risks

to be minimal and the waiver of ICD appropriate, the prior notification process preserves rather than abrogates patient autonomy.

Both clinical and health services researchers currently face a real world where an estimated 80 percent of what physicians do lacks adequate experimental justification. The dangers to patients posed by this intolerable situation dwarf any of the supposed dangers of firm trials raised in Dr. O'Neil's letter. We desperately need imaginative solutions to this vexing problem, one that will surely remain intractable if the only allowable response is the steadfast application of present-day methodologic and ethical approaches.

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