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COMMENTARY

Informed Consent

For many years, as members of our hospital network's Institutional Review Board (IRB), we have been involved in supervising clinical research trials. As such, we have had the opportunity to identify a number of issues related to informed consent for clinical research that we consider to be problematic. The focus of this article will be on clinical research trials as we will address issues related to routine clinical practice in another article.

The basis for all medical practice is the trust relationship that physicians and patients develop in each other. Most often this is an unspoken arrangement, but because there are no guarantees as to outcome, it is the element of risk that requires consent. The principles underpinning informed consent were first established in the US 100 years ago by Justice Benjamin Cardozo when he wrote "Every human being of adult years, and sound mind, has the right to determine what shall be done with his own body."[1] This concept has been refined and confirmed over the years by the Nuremberg Code (1947), the Declaration of Helsinki (1964), the Belmont Report (1974), and the 1991 establishment of (what is now called) the Office for Human Research Protection.[2] What this has come to mean is that a person volunteering to enter a clinical research trial has a "sound" mind and is fully informed as to the risk/value of a study that conforms to the laws of the land. It is a fact that in virtually all medical interventions, "there is no bright line between significant and insignificant risk."[3] Under certain circumstances, community notification involving therapeutic privilege may supervene. This entails widespread notification of the community, media, and local governmental agencies. Also needed are approval of the local hospitals' IRBs and appropriate federal governmental agencies for studies in which the patient cannot provide consent, no authorized person is available, and life or limb is threatened.[4]

Illiteracy was identified as a significant national problem when the results of the National Literacy Survey (1993) revealed that 48% of adults across all sectors of American society were literacy challenged.[5] Health care document illiteracy is even more ubiquitous,[6-12] with some authors citing a 60% incidence;[11] Spanish speakers had more difficulty,[11] as did those over age 65.[13] Janofsky et al[14] designed consents for the 6th, 8th, and 12th grade reading levels so as to determine comprehension. Ogloff and Otto[8] have recommended that consents be written at no higher than a 7th or 8th grade reading level, and they and Hopper et al[9] recommended "trial runs" of consent documents by a lay audience (preferably similar to the target of the study profile). Patients are often ashamed of telling their spouse, their children, and even their physicians of their illiteracy.[15] Joffe et al have noted that patients' unawareness increased the "potential for incremental risk of discomfort in the unproven nature of study treatment and uncertain benefits to self."[16] Patients may not even be aware that they are participating in a clinical trial.[17] Coyne et al presented 2 consents to his patients involved in a cancer chemotherapy study—one a standard consent and one an "easy to read."[18] In each group, half of the patients did not understand that cure was unlikely as a result of their participation. Patients also frequently forget what they are told by their physicians,[19,20] with one such misperception leading to serious legal consequences for a group of UK surgeons.[21]

The language used by physicians (a kind of "medicalese," a mixture of medical and anatomical terms as well as standard English) can be confusing to patients[22] and lead to misperception. In addition, most consent documents are reviewed by the sponsor's legal department, where often arcane legal language is added. The language of the consent is then designed "less to inform the patient, then to list all possible adverse events, irrespective of probability."[23] By attempting to match the physician's vocabulary to that of the patients, Williams and Ogden found a significant improvement in patient satisfaction and adherence to medical recommendations.[24]

The mental competence of patients to understand the consent document is an issue that usually arises in the course of trials addressing dementia, most often Alzheimer's disease.[25] Utilizing a number of different neuropsychological tools, Moye et al recommended that at the bedside the clinician should focus on whether the patient can describe a logical reason for his consent decision and evaluate whether the patient has an idea of the consequences of his decision.[26] In our experience, the clinician usually makes a judgment about mental competency on the basis of a "gestalt clinical judgment." Two bedside assessments, however, that appear to be useful in assessing a patient's competency to make an informed consent are the Mini

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Mental Status Examination[25] and the Hopkins Competency Assessment Test.[14]

The process by which a consent is obtained also may influence comprehension.[12] In one study, half of the patients remembered the oral content of a consent document while 3% remembered the written consent.[12] What appeared to influence comprehension was the "perceived duration" of the explanation but not the educational level or participation in previous studies.[12] The process itself may be viewed differently by researchers. In one multinational study, 47% of researchers thought that few patients understood that they were taking part in a controlled clinical experiment, and for many physicians the "informed consent process seemed little more than a ritual."[27] Furthermore, 75% of responding physicians thought that their patients rarely understood all of the information provided.[27] Failure to treat the consent process as more than a ritual recently led to a successful class action suit against an academic hospital in which the central issue was the consent.[28] A recent court action in Texas made national headlines, indicating the interest by the media and public in consent issues.[29] Utilizing videotape consents, one study resulted in improved patient satisfaction with the consent process[30] and opened the door to further studies of the use of technology in improving the process.

The media has, over the last several years, documented a number of ethical lapses in the conduct of and payment for research trials by the pharmaceutical and device manufacturing industry.[31-33] Recently, Stossel has defended the role of industry in the support of academic research, suggesting that strengthening the internal controls can deal with the conflict of interest charges.[34]

Considering the issues of illiteracy, misperception of language, mental competence and ethics, advances in medicine are achieved only through carefully done research trials with patients who understand the risk/value encapsulated in a properly constructed informed consent. Often patients are unable to distinguish therapy taking place in a clinical trial from what is considered to be "standard,"[18] and many patients enter clinical trials expecting to personally benefit.[27] Patients are scarcely "volunteering" for entrance to such trials when they "desperately believe" that such treatment is their last "best hope."[35] This has generated a lively debate as to whether all patients who meet inclusion/exclusion criteria for a research trial should be offered such therapy[36] or should the option to enter a research trial be only one of a number of possible treatments.[37,38] Should researchers "shepherd" patients to a decision even when their own assessment of the risk/value is uncertain?[39] In a meta-analysis of numerous forms of the informed consent process, Flory and Emanuel found issues with virtually all of the methods (from person to person interviews to prolonged interviews to the use of videotapes, etc.).[40] They concluded that although there is no perfect method yet published, person-to-person consents seemed to be the best at informing patients of the risk/value.[40]

With this in mind and based on our personal experience dealing with these issues, we propose the following as the basis of a pilot project in an effort to improve the process:

- Initiate the consent process utilizing a computerized reading level assessment program (a number are available) written in the language appropriate to the patient (eg, Spanish or English).[10,14] The computerized program would then proceed to the consent document, appropriate to the reading level of the patient. The consent document itself, which would be presented in DVD,CD-ROM or videotape format, should be constructed by the appropriate scientific personnel, should conform to the sponsors' ethical requests, and should follow Office for Human Research Protections and Food and Drug Administration guidelines. It would then be reviewed by a panel of lay individuals who represent the target audience for the study. The additional advantage of this program would be to standardize the information presented to patients at multiple sites.
- Touch-screen technology could help with feedback and serve to ensure that patients can interact as necessary. Person-to-person feedback should be provided by appropriate clinic personnel (eg, a research nurse). Hard copies of the consents and Health Insurance Portability and Accountability Act forms would then be provided. This also could be an opportunity to assess the patient's mental competence, for example, utilizing the Hopkins Competency Assessment Test or the Mini Mental Status form (adds marginally to the time required).
- Consent should be a 2-step process. In one study only 28% of patients signed a consent at the first meeting.[16] The first step could be informational and the second step, enrollment. Experience could determine the spacing (preferably a few days to a week). Bringing a trusted advisor to accompany the enrollee would be encouraged.

Biomedical research is, more often than not, an extremely expensive proposition, critical to medical progress.[41] The majority of Americans surveyed in 2004 (68%) perceived medical research to be of great value, and 55% (down from 63% in 2001) said they would participate in a clinical research trial.[42] Media reports of the influence of bio-pharmaceutical companies and ethical issues involving a few physicians influence public perception of the nature of clinical research[31-33] and add to misperception of clinical trials. Every effort needs to be made to enhance the trust relationship that physicians still are able to encourage in their patients. Improving the flow of information by improving communication contributes to patient satisfaction.[24] Registering clinical trials in a publicly accessible registry will enhance the openness necessary to encourage the public's confidence in the process.[43]

With the passage of the Health Insurance Portability and Accountability Act of 1996, Kulynych and Korn[44] reviewed the impact on research trials. They pointed to the problems associated with developing 3 consents for each trial (although 2 of them could be formed into 1), issues related to

de-identification and even just the problem of identifying what is a privacy right. In addition, the responsibility (and liability) of the IRB in some situations is murky. Because it is the IRB that supervises this process, Sugarman et al[45] have commented on the financial and administrative burden academic IRBs bear. Without appropriate assistance, IRBs will scarcely be able to fulfill their current supervisory function, much less assume the burdens generated by such new technologies as stem cell research and the fruits of the genomic revolution.

CONCLUSION

This article reviewed those issues we consider to be of importance to the informed consent process. Any progress in the management of illness requires the nurturing of the special trust relationship between researchers and patients, which can then assist patients in their decision to enroll in well-designed clinical research trials that meet ethical and legal standards. The informed consent process is the tool that enables people to understand the risk/value of such a decision. It is clear that for many patients, issues of health care document literacy, the language used in the process, and the patients' ability to comprehend what is being presented, can lead to a misperception of the true nature of research trials. Although enrollees may personally benefit from participating in a research trial, it is primarily future patients who are the targets of the studies. This fact is occasionally lost on the researchers themselves. How often patients make a decision to enter a research trial because they really understand versus their "obedience to the physicians authority" is uncertain.[46] We present specific recommendations to improve this process with the hope that this will educate patients, give them more faith that they are being fully consulted and informed, and that they will understand the risk/value of the trial and thus enhance the prospects of increasing the acquisition of (informed, voluntary) patients for well-designed studies. If so, then we hope to be able to fulfill the admonition, attributed to Hippocrates, "to help, or at least to do no harm."[47] At the same time, IRBs, responsible for supervising the process, must be given adequate support to carry out their mission to protect the safety of patients.

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