“Research Ethics Consultation: A Casebook”  

Review by Norman M. Goldfarb

“Research Ethics Consultation: A Casebook” provides a revealing look into real-life bioethical questions and how bioethicists have grappled with them. The book is thus an excellent source for study questions in bioethics educational programs. Practicing bioethicists (and clinical research personnel without ready access to consultants like the NIH Clinical Center’s staff of bioethicists) can compare their own reasoning to that of the consultants in the book.

The following example, one of the shortest in the book, illustrates the format and content of the text. Although this example provided an answer to the clinician’s question, most of the cases are more complex and provide only considerations and options.

CONSULT 2.2: EXCLUSION OF AN INDIVIDUAL BASED ON A NEW COMORBIDITY

Reason for Consult

Dr. Todd Jefferson requested a consultation to determine whether there are ethical reasons not to enroll Mr. Garcia in a Phase I (first in human) protocol in light of his recent psychotic break.

Narrative

The Consultation Service attending and fellow on call, the psychiatrist overseeing Mr. Garcia’s care, and Dr. Jefferson met to discuss Mr. Garcia’s medical history. Dr. Jefferson explained to the research team that Mr. Garcia, a 63-year-old male, has a diagnosis of metastatic cancer. A month ago, he was admitted to the NIH Clinical Center for evaluation and possible enrollment in a Phase I study of an experimental chemotherapeutic regimen. After admission, but prior to enrolling in the study, he experienced periods of increasing confusion, culminating in an acute psychotic break. He was started on haloperidol (an antipsychotic medication) with resolution of his symptoms, and he has remained on low-dose haloperidol since.

Later the same day, the Consultation Service attending and fellow on call met with Mr. Garcia and his daughter. Mr. Garcia appeared nervous but quite lucid and exhibited the capacity to make decisions for himself. He was able to describe what the protocol entailed, including details, such as the name of the medication and the postintervention stay in the intensive care unit. He also described what he saw as alternatives to participating. He seemed to understand that this was an experimental intervention (although he was not clear about the meaning of “Phase I”) and that the decision to participate was his. He said he felt lucky to have the opportunity to participate. He was aware that he may be monitored more closely than other research participants because of his recent psychotic episode. Nevertheless, he

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Essential reading for clinical research professionals
expressed a strong desire to participate in the study, and his daughter supported this desire.

**Analysis and Recommendations**

Mr. Garcia had a reasonable understanding of the study details and clearly stated that it was his choice to participate. There does not appear to be any ethical reason why, with close monitoring of his clinical status, he should not be allowed to enroll in this Phase I protocol.

**Authors’ Commentary**

At the point of enrollment in a study, an investigator may have specific concerns that mental illness could threaten research participant safety by elevating research-related risks or diminish compliance during the course of participation, possibly threatening the scientific integrity of the data. These could be sufficient reasons to exclude a mentally ill individual. For example, a study designed to test the efficacy of a new drug may require participants to go off all other medications; this could be inadvisable for an individual with a history of schizophrenia that is well controlled by medication. Alternatively, the research team may simply be nervous about enrolling a participant with mental illness without being able to fully articulate the basis for their concern. The ability of clinicians and clinical investigators to predict whether participation in a study will be complicated by the comorbidity of a newly diagnosed mental illness is not very good.

While this consultation report does not disclose the precise nature of the investigator’s concerns, an exploratory discussion with Dr. Jefferson might have made a valuable contribution. For example, the ethics consultant can explore with the investigator whether there are any specific procedures in the protocol — such as a stay in intensive care or administration of a medication that frequently causes delirium — that constitute additional risk for a prospective research participant who is potentially prone to psychotic episodes. Similarly, if the Phase I protocol in question is likely to involve long periods of susceptibility to infections, during which it would be very inadvisable for a participant to withdraw from the study, this might be a reason to have reservations about enrollment at the outset.

Other factors relevant to the ethical analysis include the potential of the study to benefit the prospective research participant, the availability of alternatives to research participation, and the prospective participant’s understanding and preferences regarding research participation. As occurred here, it is important to include the prospective mentally ill research participant — or the appropriate surrogate decision maker — as well as the research team in these discussions. In this case, the bioethics consultants might have pointed out that, by enrolling Mr. Garcia, the investigators would assume an obligation to monitor his well-being and may need to terminate his participation early if his mental condition deteriorates.

The book includes 43 consultations in seven chapters:

- Starting Research
- Enrolling Research Participants
- Protecting Research Participants
- Conducting Research with Vulnerable Populations
- Clinical Research and Clinical Care
- Navigating Interpersonal Difficulties
- Ending Research
The book is available in bookstores.

**Reviewer**

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