APPENDIX B

Boundary Between Research and Practice Report: Case Studies

These cases were collected from a variety of sources. They were submitted for discussion at the April 2011 meeting, they were discussed at the town hall meeting that took place during the 2011 Advancing Ethical Research Conference, and they were sent to the PRIM&R office in response to a blog post. Depending on the extent of the information provided, some of the cases describe how they were actually resolved. This information is provided under the “results” heading for applicable cases.

A. CLINICAL INNOVATION

Case Study #1: Innovative Imaging and Surgery for Maternal and Fetal Medicine Program

This case exemplifies the development of a successful alternative review system.

Great advances in imaging have increased surgeons’ ability to detect and diagnose fetal anomalies as early as the first trimester. Some anomalies are fatal; some anomalies are fatal unless corrected in utero; and other anomalies can wait until after parturition for repair.

Surgeons in the Maternal and Fetal Medicine Program at an academic research center had begun conducting fetal interventions to correct heart, respiratory, and urologic problems that had not been previously been detected and treated prenatally. The institutional review board (IRB) was uncertain whether to regard these interventions as new surgical approaches to correct novel defects or as human subjects research to assess whether such surgical approaches were beneficial. Sometimes, new surgical approaches to remedy such defects were proposed with some clinical urgency. The most difficult problems were: (a) determining whether the diagnosis of a defect warranting surgical action was based on a recognized clinical procedure or on an unverified research procedure; and (b) determining whether a proposed remedial surgical procedure was “innovative” but within the scope of a clinician’s practice, was research, or was a combination of the two.

Resolution: To facilitate the ethical oversight of these activities, the human research protection program identified a team of specialists with no direct relationship to the fetal medicine program that included a neonatologist, a pediatric surgeon, an OB-GYN, an anesthesiologist, an ethicist, and an experienced maternity nurse. This Fetal Intervention Advisory Committee was trained in human protections principles and IRB regulations, and met regularly to become familiar with one another and with the fetal medicine program, in preparation for consultations as a committee. The Maternal and Fetal Medicine Program submitted protocols describing procedures they were ready to undertake, and the advisory committee helped the human protections program to parse the protocols, sorting them into groups—innovative clinical care and not research; pure research protocols; and clinical protocols with elements of research.
These distinctions were difficult to make, but through frequent meetings and dialogue the Advisory Committee and the Program were able to work together to create an effective system for distinguishing between “innovative surgical care” and “surgery research.”

Case Study #2: Electronic Surveys
A social scientist submits to an IRB an article abstract and requests IRB approval. In reviewing the abstract, the IRB learns for the first time that he has placed an "electronic terminal" in each clinic of the institution that presented a letter from a physician and a quality of life survey that posed questions such as: “do you find your disease status depressing,” “do you have suicidal thoughts,” and “would you like help dealing with your depression?”

Resolution: The institution determined that this activity was "research" as defined in the federal regulations and required IRB review.

Case Study #3: New Procedure at Trauma Center
A level-one, non-military trauma center adopts a military practice of using plasma for resuscitation of severely injured soldiers, and subsequently publishes the results. In applying the criteria for ethics review, should the center have considered this practice "standard of care" or "research" requiring IRB review?

Resolution: "Standard of care" was established by the military practice, and the use of plasma was not considered a significant departure from standard practice.

B. QUALITY IMPROVEMENT/ASSURANCE

Case Study #1: Iron Levels for Dialysis Patients
A group of nephrologists sought to discuss quality improvement of their practice. They wanted to determine what level of iron was optimal for their dialysis patients. They decide that some of the doctors will give 50 milligrams while others will give 100; then they will reconvene to compare results.

Resolution: The nephrologists did not consider this activity to be "research" requiring IRB review because it was their “intention” to conduct quality improvement. Although opinion was a split on whether this activity should have received IRB review, broad consensus existed that the activity warranted some kind of ethical review due to the potential risks to patients. The team agreed to apply the following standard: every proposal to conduct an activity that is not "usual and customary" should be presented to an ethics services provider such as an auditor, an ethicist, or an ethics review committee.

Case Study #2: Hand Hygiene
Eight hospitals agreed to work with an accrediting body to identify solutions to the seemingly intractable problem of low rates of hand hygiene. Evidence clearly establishes that washing
hands or using alcohol gel between patients is essential to preventing transmission of infection. Before initiating this quality improvement project, the participating hospitals estimated that their hand hygiene rates were about 85%. Each hospital agreed to use standardized, rigorous techniques to measure its actual rate of hand hygiene, to identify the causes of its low hand hygiene rate, and to develop cause-specific solutions for these organization-specific causes. The hospitals discovered that they had an average hand hygiene rate of 48% at the start of the quality improvement project. After the cause-specific solutions were implemented in each hospital, the participating hospitals achieved and sustained an average hand hygiene rate of 82%.

The hospitals agreed to provide to the accrediting body the organization-specific causes each identified and the successful cause-specific solutions that they implemented. The accrediting body used this information to develop a tool available at no cost to accredited hospitals. The tool enabled each hospital to determine its own rate of hand hygiene, to identify the specific causes for its low rate, and to then choose from a database of cause-specific solutions those solutions applicable to its specific causes.

Resolution: This project was considered quality improvement only, with no research component. Since it did not involve the collection of patient-specific or personal health information data, it did not pose any risk to patients. Ethics review was not considered warranted.

Case Study #3: New Disease Management Plan
The care that University Hospital provides for chronic Disease X compares very favorably with the care provided by other health care organizations, both in the immediate area and nationwide. Nevertheless, the administration would like to improve.

A group of employees developed a new management plan for Disease X patients. They began by reviewing recent literature on the disease to look for clinical and administrative practices that have been shown to improve the process and/or the outcome of care for patients. They selected the most promising, combined them into an integrated system of care, and then consulted extensively with the hospital’s physicians, nurses, and support staff who work with Disease X patients to fine-tune the plan and ensure that it would be appropriate for its environment. The result was a program that the administration believed would provide superior care for the disease at affordable cost. The goal was to make this program the standard of care for all patients with Disease X; however, the administrators decided that it would be prudent to begin implementing it as a pilot program, for three reasons:

1. Staff could monitor processes and outcomes carefully to confirm that it is a clear improvement over the current standard of care.
2. By beginning the program on a trial basis, the administration could use actual experience to fine-tune training materials.
3. A pilot program would allow the administration to further assess the cost-benefit impact of the program.
Since the trial treatment could not be provided to everyone during the pilot stage, the administration decided that the fairest way to determine access was by lottery. Patients would be chosen at random for enrollment in the pilot program. In addition to giving everyone an equal chance to participate, this would allow staff to assess how the program worked for a diverse group of patients with Disease X. Patients selected for the pilot program could refuse to participate and remain in standard care.

Resolution: Since the trial was not considered “human subjects research” it was not reviewed by an IRB. However, given that there was some chance of benefit for patients, an ethical concern about access to the trial was considered and managed through the lottery process.

Case Study #4: Public Benefit Program
A protocol was developed to ensure that male circumcision (MC) services for HIV prevention funded by the Centers for Disease Control and Prevention (CDC) were being provided according to the best clinical practices and that the services meet CDC standards. The results were to be provided to local-governments in charge of service delivery in various African countries. This study included:

- Monitoring, assessment, and evaluation of health systems, including cost effectiveness and cost-outcomes
- HIV antenatal care sentinel surveillance
- Drug resistance surveillance, including HIV drug resistance threshold surveys
- Population-based surveys with biological testing
- Measurement or estimation of fertility, mortality, and migration

Data was collected through: interviews with relevant health facility staff involved in MC service delivery; review of clinic supplies and other materials; data abstraction from MC patient records and review of MC clinic registers; and observation of counseling sessions and MC clinical/surgical procedures.

Resolution: The project was determined to be “human subjects research” exempt from IRB review under category 5 as a program evaluation of a “public benefit/service” program.

Case Study #5: PhD Nursing Programs
Some PhD nursing programs require applicants to conduct a quality improvement project to show that they are improving their profession. PhD nursing program projects are usually evidenced-based practice initiatives, so not strictly "research." They involve the collection of evidence that a change in practice made a difference. The practice itself is not considered "experimental."

Resolution: The group determined that a relevant factor for managing the oversight of these projects is whether the nurse is evaluating the impact of an intervention that is already in place, or is implementing an intervention to achieve an improved practice, followed by an evaluation.
C. COMMUNITY BASED PARTICIPATORY RESEARCH

Case Study #1: Heritability of Schizophrenia
Dr. Spencer is studying the genetic component to schizophrenia and whether its expression is related to substance use. As she begins designing her study, she consults some recently published articles on participant attitudes toward, and knowledge of, genetic screening and discovers some concerns she had not considered, including the fact that most participants exaggerate the genetic component and heritability of major mental disorders. She establishes a community advisory board consisting of a few patients, a few family members, and the director of a local peer support group that serves mental health consumers. They will provide input on the study design, including the protections offered to participants. Moreover, in an attempt to build trust with the community, she employs an individual with schizophrenia to serve as a recruiter, who will also administer some surveys to peers.

Resolution: Dr. Spencer included a brief educational intervention during the enrollment process of her study. Many participants expressed surprise at the facts shared and some expressed gratitude for the information. Her advisory committee recommended that she hire a mental health consumer to assist with recruitment at the local peer-support center. After interviewing several candidates, she hired Mr. Jones, who received human subjects protection training that was tailored to community members and focused on confidentiality protection. Mr. Jones helped Dr. Spencer meet her enrollment goals a month earlier than planned after he convinced her to increase the payment for participant time by $10 per visit. He told her participants at his center view payments as a sign of respect and being valued, not as manipulation. Dr. Spencer was also surprised to learn through Mr. Jones that most participants wanted their data to be confidential but identifiable so they could be contacted in the future if the research yielded any information that could be useful to improving their own health. She could not accommodate this request in the current study, but decided to pursue this possibility in future research.

Dr. Spencer’s advisory committee encouraged her to spend some “observation time” with Mr. Jones at the peer-support center and to conduct a focus group with regulars to ensure that she was taking cues from the larger group and not just one member (Mr. Jones). They also encouraged her to work harder to retain participants in her study; she found that many participants missed meetings, particularly if they were actively using drugs. The advisory committee shared with her strategies for finding participants. Dr. Spencer was able to implement new contact procedures with participants, and her retention rate increased 25%. Additionally, Dr. Spencer began holding her quarterly community advisory board (CAB) meetings in different locations affiliated with members to indicate that she was concerned about their convenience and that she viewed them as team members. These various acts made it easier for participants to accept that she had their best interests in mind, even though the study would have no immediate therapeutic value for them.
D. PUBLIC HEALTH

Case Study #1: Evaluation of Public Health Initiative
A researcher is invited to lead an evaluation of the national Public Health Improvement Initiative, guiding development of the evaluation, working with evaluation consultants, crafting data collection strategies, collecting and analyzing data, and preparing reports. The Office of Sponsored Research at the researcher’s institution will not issue a contract number to allow payment for this work to proceed without paperwork from the IRB even though “just-in-time” approval had been entered into the federal database.

Resolution: The researcher submitted a determination form to the IRB requesting that the evaluation project not be considered research, which was approved. Nearly all evaluation work conducted by the institution now receives a determination that it is not research even though the findings are published and presented and add to generalizeable knowledge in that the work is conducted to improve the public health system.

Case Study #2: Prison Study
An epidemiological study of HIV transmission was proposed for a Los Angeles prison. The proposed population was the gay and transgender prisoners who were housed in a designated area of the prison that was generally a preferred area as one that was safer. Prisoners entering that area of the prison were required to be HIV tested. If they did not agree to this they would be placed in solitary confinement or in a less safe area of prison.

Results: The Centers for Disease Control and Prevention ruled that the activity did not constitute "research." In spite of this determination, the IRB stopped the project on the grounds that the project design was coercive.

BRIEF FACT SCENARIOS FOR DISCUSSION
The following scenarios provide examples of cases that may or may not meet the definition of research ethics, but which raise ethical issues. They were presented at the April 2011 meeting without resolutions for discussion:

1. A doctor develops a test order tracking system that makes it easy for him to identify what tests have been ordered for a patient, access the test results, and make timely and appropriate adjustments in the patient’s care. He monitors its performance, and refines it over time in response to his observations until he is satisfied with it.

2. After multiple doctors develop personal test order tracking systems, they ask the nurses who care for their patients to use them. The nurses point out that using a dozen different doctors’ systems would create complexity for them and lead to mistakes. They recommend initiating a systematic project to develop a common tracking system incorporating the best features of the individual systems. The project is then carried out
under supervision at the management level, which covers all parts of the organization affected by the change, with one supervisory task being review of the project’s design for conformity with ethical requirements.

3. Several nurses find that they are each using a different method to perform a routine nursing procedure. The methods are all within standard nursing practice and are used interchangeably in various clinical settings; however, the nurses wonder whether the methods differ in the time they take and the effect they have on the patients. The nurses try each method in sequence over a few months, keep track of how long the procedure takes with each method, and ask patients whether there is any difference in comfort. At the end of this activity, they conclude that one method works better than the others in their local setting and all decide to use it.

4. New evidence-based guidelines for managing a particular health condition are published in a respected medical journal. A large medical group decides to adopt the new guidelines for the relevant patient group. A committee is formed to study existing practices and develop a plan to identify the changes needed in the local setting, educate clinicians and support staff about the changes, and collect data during the transition so that the group can monitor to ensure that the new guidelines are being followed correctly and the new practices produce no unexpected adverse consequences.

5. A large hospital is concerned about the incidence of post-operative infections in its patients. Someone suggests that the timing of the administration of prophylactic antibiotics may be a factor in infection incidence. Currently, the hospital has no standard protocol for antibiotic administration and the timing varies considerably within the patient population. An epidemiologist on the hospital staff performs statistical analyses on data from medical records on post-operative infections and discovers that giving antibiotics within a specific window of time seems to be associated with a lower rate of infection. Physicians are informed of this and most adopt the suggested timing. The results are monitored over time and the incidence of post-operative infection is significantly reduced, producing both an improvement in patient outcomes and a reduction in hospital costs.

6. A doctor at a community health center has many patients who have chronic health conditions that might be improved by exercise. The local YMCA sells institutional memberships that can be used as an employee benefit. She arranges for the health center to purchase some memberships and allow its patients to use them. The YMCA fitness instructors want medical information on the patients who are exercising, so a simple referral form is developed. The form must be signed by both patient and provider and contains basic information about the patient’s health and recommendations from the health care provider about type and intensity of exercise. The program is very popular, and at the end of the first year, there have been over six thousand exercise visits. The doctor decides to see whether the exercise is having any health effects, and by cross-
matching the exercise list with patient registration data, is able to identify patients with diabetes who have started to exercise. She finds that many of these patients have experienced clinically significant improvements. [Note: This is a real example. For the whole story, see Lucy M. Candib, "How Turning a QI Project into 'Research' Almost Sank a Great Program," Hastings Center Report 37, no. 1 (2007): 26-30. Available for download at www.thehastingscenter.org.]

7. The routine process for intra-operative care for hip surgery in a hospital involves substantial loss of blood during surgery and post-operative transfusions to replace the blood, usually several days out. New equipment becomes available that enables lost blood to be captured and re-transfused immediately, and some studies show that the equipment is effective. The equipment vendor approaches the hospital and proposes that it try out the equipment.

8. Primary care providers in a large managed care organization participate in an educational conference regarding prescribing practices and the use of clinical reminders. They are then randomized into three groups that will work with three different clinical reminder systems (patient directed mailed reminders, computer/chart reminders, and automatic consults). Questionnaires are used to gather information about the providers' experiences with the educational intervention and the clinical reminder systems being evaluated.

9. Survivors of patients who have recently died in a hospital's palliative care unit are interviewed by telephone by palliative care nurses to determine their satisfaction with care.

10. A hospital conducts a one-day screening of all outpatients to determine the prevalence of hepatitis C.

11. A managed care organization (MCO) has multiple delivery sites. Management notices that a clinical care quality measure varies significantly across sites. It sends letters to the sites that are clustered at the bottom on the measure and asks them to take action to improve their performance. After an interval, it looks at overall performance on the measure and also at the performance of the sites that received the letter to see whether they have improved relative to the average.

   a. Same facts, but this time the letter instructs the low performing sites to take action to improve and—to make sure they actually do something—submit a report documenting what they did.

   b. Story (a) continued—In its review of the quality measure performance, management notices that some sites have improved dramatically and others have hardly improved at all. A staff member uses the site reports to put together
APPENDIX B

a. a document that describes the various strategies tried and the results, congratulates the sites that have improved the most, and exhorts the sites that haven’t improved to keep trying. The document is sent to the sites that received the original letter. After an interval, management again looks at overall performance and the performance of the targeted group. Now, all the sites are clustered around a very respectable average and there are no distinct low performers.

c. Same facts, but this time, before sending the letter, a small quality improvement team consults the literature and has informal conversations with people at the sites to identify possible strategies for improving performance. Of the three identified, the team picks the one that they think is most suited to their organization. The letter tells the targeted sites to adapt this strategy to the individual site, implement it, and document what they did in a report.

d. Story (c) continued—The review of quality measure performance is a disappointment; the performance of the targeted sites is practically unchanged. Management sends a new letter instructing the sites to try the second most promising strategy. This time, the performance on the quality measure actually declines. The process is repeated with the third strategy. Fortunately, this strategy seems to work—all sites are clustered around a respectable average and there are no distinct low performers.

e. Story (d)—but this time, the quality improvement group considers the three strategies equally promising, and decides to try all three at once. The letter describes the strategies, asks the sites to pick one, adapt it, implement it, and document the results. They do (and fortunately, they don’t all pick the same one). Review of the new quality measure stats suggests that one strategy has been much more successful than the other two. This information is reported to the target sites, and all are instructed to use that strategy.

f. Story (e)—but this time, rather than let the sites pick a strategy, the sites are divided into three roughly equal groups and each group is assigned one of the strategies. The sites are told that if one strategy looks to be superior when performance on the quality measure is reviewed, they will be informed and can then switch to that one.

g. The MCO belongs to several organizational networks that are concerned about the quality of health care. Managers and health care professionals informally consult with their peers in other organizations and have periodic meetings in which they make presentations on experiences in their own organizations that might be of interest to others. Of course, all the interactions are carefully constructed to appropriately protect the privacy and confidentiality of individual
patient information. Assume that in each of the above stories, someone in the MCO eventually decides that a description of what was done and what the results were would interest others in this networking group and makes a presentation.

12. An institution grappling with the distinction between research that involves private health information (PHI) and quality improvement projects and outcomes books data establishes a strict rule that requires IRB oversight when a request is made for data that contains PHI.

13. An institution receives Magnet status in nursing. As part of the Magnet designation, the institution must conduct ongoing research in nursing practice. When projects were designated as “quality improvement” rather than “research” the nurse researchers were disappointed because they would not count towards their research quota.

14. Advanced practice nurse works on projects to improve practice. The process involves asking questions about the practice. When they publish the results they are told not to use the word "research" in the article and to only refer to the activity as quality improvement.

15. Military intelligence officers are placed in communities within combat regions to obtain information about how people "on the ground" are thinking about the occupiers, and how they might get better cooperation. This activity places officers and community residents at risk of physical harm.