Rational Protection of Subjects in Research and Quality Improvement Activities

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This Open Forum illuminates shortcomings with the basis for determining degree of oversight of health services research and quality improvement activities. Using a federally regulated definition of research rather than a direct appraisal of risk to patients can misallocate effort from activities with higher risk for patients to those with lower risk. The case of the Johns Hopkins multicenter study of central line safety checklists in intensive care units is cited. Definitions of research promulgated by the Office of Human Research Protection are reviewed, and an alternative model based on patient risk is proposed. Suggestions for how quality improvement work fits into the larger paradigm of research are made. (*Psychiatric Services* 61: 180–183, 2010)

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In the past 20 years we have seen the emergence of new data-driven efforts to improve the quality of care in clinical settings. These efforts sometimes fall under the rubric of quality improvement and sometimes under the rubric of research, specifically health services research—a new research area in which investigators attempt to acquire generalizable knowledge regarding how best to shape systems in order to deliver high-quality cost-effective health care.

Institutional review boards (IRBs) serve an essential role in the protection of human participants in research and help ensure that research is conducted safely and ethically. However, the development and increasing sophistication of health services research as a quality improvement science beyond traditional biomedical research has created challenges in the designation of such projects as "research" as well as in the implementation of IRB oversight. In addition, advances in quality improvement science underscore a potential lack of oversight of quality improvement activities that do not meet the technical definition of research. This situation may paradoxically increase risk to individuals receiving health care rather than reduce risk and increase benefits. Although there is no simple solution to this unfortunate situation, our goal in this Open Forum is to elucidate the issues and further a process that creates solutions.

Johns Hopkins multicenter study

A recent well-publicized episode drew our attention and that of many others to the thorny application of research procedures to quality improvement science. In 2007 the Office for Human Research Protections (OHRP) halted a Johns Hopkins University quality improvement research study that was initiated in 2003 to evaluate the use of a checklist to reduce central line infections in intensive care units. The checklist included five simple actions, all of which are known to decrease the possibility of infection: hand washing, barrier precautions during venous catheter insertion, cleaning the patient's skin, avoiding the femoral site for catheter insertion, and if possible, removing unnecessary catheters. All of these actions should be a routine part of catheter insertion and pose no additional risk to a patient. These procedures were implemented in 67 hospitals in Michigan and dramatically reduced infection rates; the results were published in the *New England Journal of Medicine* (1,2). An anonymous complaint about the Johns Hopkins study generated an investigation by the OHRP.

The OHRP determined that the investigators at Hopkins had failed to ensure that the requirements for obtaining informed consent and documenting that the criteria for "legally effective informed consent of the subjects . . . were satisfied" (3). OHRP disagreed with the ruling of the Johns Hopkins IRB that the study was exempt from oversight based on its "collection of or study of existing data" because, in fact, hospital procedures were being manipulated as part of the study. OHRP's actions also implied that the IRBs of individual hospitals had to consider this study and require that informed consent be obtained. Although each hospital's IRB could expedite the review of the protocol and permit a waiver of informed consent, these decisions needed to be made at the local IRB level. As a result of the OHRP ruling, the delivery of data to the Hopkins group was ended. Public discussion and editorials clarified the implications of the OHRP ruling: essentially, OHRP was saying, "institutions can freely implement practices they think will improve care as long as they don't investigate whether improvement actually occurs" (4). OHRP eventually reversed its decision and permitted the research to move forward (5,6), but ambiguity persists in the current regulatory framework guiding the relationship between quality improvement, research, protection of human subjects, and the role of the IRB.

Why did the government halt a research initiative that involved no additional risk to patients and was likely only to benefit the patients and the public at large? Although this decision was clearly determined by multiple factors and involved a variety of complex processes, we want to highlight an issue we have not heretofore seen discussed regarding conduct of quality improvement activities and quality improvement research. We worry that decision makers have become focused on whether data-driven activities are "research" or not (or instead are quality improvement activities) and have failed to focus on the issue of primary importance—the degree of risk that patients may experience, regardless of whether an activity is research or quality improvement.

Editor's Note: This Open Forum is the second contribution to an occasional series in which the Group for the Advancement of Psychiatry (GAP) (www.ourgap.org) will present ideas to further the understanding of mental illness and improve access to care and quality of treatment for persons with mental disorders. Since its beginnings in the post–World War II era of providing modern psychiatric care, GAP has continued to be a think tank operating through its committee structure of national experts to present reports and position statements that are disseminated nationally and internationally.

Rationale for regulations

Regulations on research involving human subjects were established in response to egregious violations of peoples' rights, such as the Tuskegee Syphilis Study and Nazi medical experimentation. Specifically, federal standards now mandate that all research involving human subjects and receiving federal funds be independently reviewed. (These same standards are generally applied to all research regardless of funding.) As defined in federal policy 45CFR46.102(f) research means "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge"(7). Notably, many consider that the intention to publish is a proxy for the intention of producing generalizable knowledge. A human subject is a "living individual about whom an investigator (whether professional or student) conducting research obtains (a) data through intervention or interaction with the individual, or (b) identifiable private information" (7). A key component of the definition of research is intent, which may be very difficult to capture and may also change over time.

Once a project is defined as research, the first task is to consider whether it is exempt from human research protections. The specific criteria for exemption (8) are listed in the box on this page. Here, a key point is that even if anonymous data are collected, the data must already exist in order for the project to be considered exempt. Importantly, if a new intervention, even a program with no risk, is being tested prospectively, the data probably cannot be considered already existing and the exempt status would not apply. This creates an almost bizarre situation that may discourage prospective collection of data because researchers would be faced with the potentially onerous prospect of working through IRBs, and these regulations favor retrospective and frequently less efficient and valid program evaluation.

After a research project is determined not to be exempt, a next step is

Exempt from oversight

1. Research conducted in established or commonly accepted educational settings involving normal educational practices
2. Research involving use of educational tests as long as the test results cannot be linked to the individual
3. Research involving the collection of existing data or specimens if the sources are publicly available or if subjects cannot be identified or linked to the data or specimen
4. Research or demonstration projects that are conducted by or approved by department or agency heads and are designed to evaluate public service or service programs
5. Taste and food quality evaluation as long as the foods are wholesome or contain very low levels of additives

Eligible for expedited review

1. Clinical studies of drugs and medical devices if an investigational new drug application is not required or an investigational device exemption application is not required or if the device is cleared for marketing and the device is used in accordance with its approved labeling
2. Collection of blood samples via stick or venipuncture as long as certain weight, health, and blood volume restrictions apply
3. Prospective collection of biological specimens for research purposes by noninvasive means. Specimen types include items such as hair, buccal scrapings, and saliva
4. Collection of data through noninvasive procedures routinely employed in clinical practice, excluding procedures involving general anesthesia or X rays or microwaves
5. Research involving materials (data, records, and specimens) that have been or are being collected solely for nonresearch purposes, such as treatment or diagnosis
6. Collection of data from voice, digital, or image recordings made for research purposes
7. Research on individual or group characteristics and behavior employing survey, interview, focus group, program evaluation, or other quality assurance methodologies
8. Continuing review of previously approved IRB research where enrollment and intervention is complete, for long-term follow-up of subjects or where either no subjects have been enrolled or the remaining research activities are limited to data analysis
9. Continuing review of previously approved IRB research that has been determined to involve no greater than minimal risk and no additional risks have been identified

to determine whether the research qualifies for expedited review (9) (box on this page). Expedited means that an IRB reviews the study but does not require the review of a fully convened board. The criteria for approval are not altered in expedited review—that is, the risk-benefit ratio is considered. The possibility of a waiver of informed consent is also considered at this stage. Of note, because there are no national standards, not all IRBs expedite minimal-risk studies, and every local IRB has autonomy to make its own decision. Different IRBs might come to differing conclusions about the appropriateness of a waiver of informed consent and any other aspect of the study. Increasingly quality improvement studies have waivers of consent sometimes reviewed by IRBs. Thus quality improvement research involving a number of facilities might not receive uniform IRB decisions. In the setting of minimal or no risk, this situation incurs a tremendous cost in time and effort, may erode the validity of the studies, and ultimately may reduce the likelihood that these studies will be done (10–12).

An alternative model

The checklist case described above has stimulated a great deal of discussion and has highlighted numerous challenges and ambiguities associated with implementing our current system to protect human subjects in research. Utilizing the "research" versus "not research" dichotomy as the decision point on whether IRB review is necessary can result (as in the example above) in activities meeting the criteria for research that have minimal patient risk receiving intensive review within the research oversight mechanism. In contrast, other projects with substantive patient risk that become defined as quality improvement rather than research may receive insufficient oversight. An alternative is to consider the degree of risk as the determining factor for assigning degree of oversight for projects that are designed to improve the quality of care. Projects that are assessed as having minimal risk could be spared the burden of intensive, laborious, comprehensive review, and those that are assessed as having more than minimal risk could be subject to independent oversight, regardless of whether the project meets criteria for research.

These issues also apply for instance to the mental health arena. Consider the following examples. One very common quality improvement activity is the reduction of seclusion and restraint on psychiatric units. Quality improvement efforts directed toward reducing the use of seclusion and restraint are not research because they are not intended to increase knowledge beyond the individual setting but instead are intended to meet an institutional goal. Thus these activities are not currently subject to IRB review. However, the irony is that such activities could result in significant risk to patients and staff and might benefit from careful and ongoing review. On the other hand, a study implementing the evidence-based practice of the "5 A's" (ask, advise, assess, assist, and arrange for follow up) of smoking cessation in outpatient mental health clinics would pose virtually no risk and could have large benefits if used widely. The 5 A's reduce smoking when delivered in primary care. Such a study could be stymied if subject to IRB review.

If the degree of risk rather than the definition of research is the critical factor in defining need for oversight, we would need to focus our energy on defining risk. This may be particularly important among patients with psychiatric illnesses, who are especially vulnerable (13). Although this is no easy task, it seems more directly relevant to the individual's potential experience of benefit or harm from a project than is the theoretical, ever-shifting definition of what constitutes "research" versus quality improvement projects. Yanos and colleagues (13) have provided a useful framework for defining three categories of risk: minimal, minor increment, and greater than minor increment over minimal risk. Further, a focus on risk would allow a much clearer differentiation of research to develop new treatments and interventions from organizational efforts to implement proven effective treatments. Adequate protections could then be ensured for participants in all projects, whether the issues or risks involved are physiologi-

cal, psychological, social, vocational, informational, or financial. At the same time, unwieldy and unnecessary obstacles could be minimized for the gathering of important guiding information aimed at increasing the welfare and functionality of our patients and the providers and institutions that serve them.

We understand that triaging quality improvement trials according to risk rather than research requires some yet-to-be-defined organizational entity to make a decision about risk level. This could be a combined research–quality improvement committee. We believe that current definitions are sufficient to determine the level of risk and that many quality improvement projects would meet the criteria of expedited review. We also understand that our suggestion will not necessarily reduce the amount of work and attention dedicated to protecting individuals from the risks that might be involved in developing new health care improvement approaches. But we submit that a protocol of oversight driven by risk rather than a somewhat arbitrary definition of research will increase the efficiency and appropriateness of the energy devoted to these protections.

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