TWO ETHICAL EXEMPLARS

Michigan ICU Study

In the United States, 80,000 bloodstream infections related to catheters occur each year in intensive care units (ICUs) leading to increased lengths of stay and costs (Miller & O'Grady, 2012). Researchers continue to investigate interventions to reduce morbidity and costs (Kim, Holtom, & Vigen, 2011). In 2004, clinicians from Johns Hopkins University coordinated a prospective cohort study to examine the impact of introducing evidence-based strategies to reduce infection rates in all ICUs in Michigan (to be referred to in this chapter as the Michigan ICU study). Just over 100 ICUs participated in the 18-month study (Pronovost et al., 2006). A large and sustained reduction in rates of catheter-related infections occurred (up to 66% reduction). The median number of infections per 1,000 catheter-days decreased from 2.7 at baseline to 0 during the final study period ($P < 0.002$).

The study involved a number of educational interventions targeted at ICU personnel to improve patient safety. This included designating one physician and one nurse as team leaders in each ICU. The researchers developed a checklist to promote clinicians' use of five evidence-based procedures recommended by the Centers for Disease Control and Prevention. These were (a) hand washing; (b) using full-barrier precautions during insertion of central venous catheters; (c) cleansing the skin with chlorhexidine prior to catheter insertion; (d) avoiding, where possible, the femoral site for catheter insertion; and (e) removing unnecessary catheters. Neither expensive technology nor additional ICU staff was required, though each hospital provided adequate staff to implement the educational intervention.

The study had limitations and, as with any study, required critical appraisal (Daley, 2007; Jenny-Avital, 2007). Nonetheless, the results were praised in *The New York Times* as "stunning" because of how the study saved more than 1,500 lives during its 18 months (Gawande, 2007). However, a few weeks after the study results were published, the Office for Human Research Protections (OHRP), the federal agency charged with protecting people involved in research in the United States, ordered an investigation into possible ethical violations in the study (Miller & Emanuel, 2008). In November 2007, the OHRP ruled that the project had violated ethics regulations and should be shut down, including planned expansions in other states (Gawande, 2007).

The OHRP held that the Michigan ICU study had violated two ethics regulations. The study was submitted to the Johns Hopkins University IRB, which deemed it exempt from review. The IRB viewed the project as an EBP implementation and QI initiative, not clinical research. The OHRP disagreed and held that it was research. Informed consent was not obtained in the project because it was considered exempt from IRB review (Pronovost et al., 2006). OHRP held that informed consent should not have been waived for this reason because it viewed the project as clinical research.

Wide application of OHRP's approach could mean that "whole swaths of critical work to ensure safe and effective care would either halt or shrink" (Gawande, 2007). In the resolution to the situation, both the parties agreed that the study was clinical research because an educational intervention of unknown efficacy was being tested on clinicians (OHRP, 2008). At the same time, it is most likely that the study would have satisfied the regulations for expedited IRB review since it involved no more than minimal risks (Miller & Emanuel, 2008). The IRB review could also have determined that informed consent was not ethically required since the five infection-control guidelines were evidence-based (i.e., their

expected outcomes previously had been demonstrated through research) and patients were not being put at additional risks (OHRP). The protocol could have been introduced as part of standard clinical practice and covered by patients' general consent to treatment. Thus, their autonomy would still be respected even though explicit informed consent was not obtained. The OHRP also concluded that since the Michigan ICU study demonstrated the effectiveness of its interventions, future implementation and monitoring of the checklists would not be research but improving clinical care.

Spanish ICU Study

The importance of establishing whether a project is research or evidence implementation is revealed by another exemplar, this time in Spain. An educational program on compliance with evidence-based guidelines in patients with severe sepsis was prospectively evaluated for its impact on mortality (Ferrer, Artigas, Levy, et al., 2008). About 20% of Spain's ICUs participated. Based on the results, the authors concluded that if the educational program was implemented in all Spanish hospitals, 490 lives might be saved each year. As with any project or study, this one had limitations and should be critically appraised, especially as its design falls at a lower level of evidence in the study hierarchy for interventions (Kahn & Bates, 2008). This makes causation difficult to establish, but the project remains a good example of an educational program introduced to promote evidence-based guidelines on a national level while also including an objective evaluation of its impact. It would appear to be ethically sound based on its promotion of beneficence and nonmaleficence.

The project was subsequently criticized for ethical reasons similar to those of the Michigan ICU study. Based on viewing the Spanish project as clinical research, the project coordinators were criticized for not obtaining informed consent from the patients involved and thus not respecting their autonomy (Lemaire, 2008). The authors defended their decision on the basis that the project was EBQI and thus part of good clinical care (Ferrer, Artigas, & Levy, 2008). They gave several reasons for not viewing their project as clinical research. Foremost among these was that the educational program taught previously established evidence-based guidelines and did not expose patients to test interventions. In particular, they noted that the project was reviewed by the research ethics committee at every participating hospital and in that way ensured that appropriate ethical standards were maintained.

If the people who make the decisions are the people who will also bear the consequences of those decisions, perhaps better decisions will result.
—John Abrams

PRACTICAL CONSEQUENCES

Much of the controversy has revolved around establishing whether evidence implementation activities fall within the definition of clinical research. The focus of this chapter is on the ethical aspects of this distinction, which have important practical and regulatory implications. The OHRP can impose severe penalties on organizations found to be in violation of U.S. regulations. The OHRP has regularly defined research very broadly and thereby often included QI activities within its oversight (Lynn et al., 2007). Similar regulatory uncertainty and confusion can exist in the United Kingdom (Hill & Small, 2006) and elsewhere in Europe (Lemaire, Ravoire, & Golinelli, 2008).

Another practical consequence of "getting it wrong" can arise if clinicians decide to pursue publication of their findings. Many journals will not publish articles they deem to be clinical research if they have not already had IRB review (Lynn et al., 2007). Sometimes clinicians conducting evidence implementation activities decide to pursue publication only after the project is completed and the findings are viewed as having broader interest (Hill & Small, 2006). Some journals evaluate the ethics of a study or

This serves to highlight that the important factor for ethical review is not how a project or study is classified, but whether the activity is ethically appropriate. EBP does not fall into this overlapping region as the basis for all EBP projects is an already ethically reviewed body of evidence that has been deemed safe for patients; however, the ethical responsibility to protect patient information still remains.

ETHICAL PRINCIPLES AS APPLIED TO RESEARCH, EBP, AND EBQI

Much has been written on research ethics (Emanuel et al., 2008). A set of seven ethical requirements have been proposed as the ethical foundations upon which clinical research should be based (Emanuel, Wendler, & Grady, 2000):

1. Social or scientific value
2. Scientific validity
3. Fair subject selection
4. Favorable risk–benefit ratio
5. Independent review
6. Respect for potential and enrolled subjects
7. Informed consent

They are summarized in the following sections as originally proposed for clinical research, and their relevance for EBQI activities is also described, where appropriate (Baily et al., 2006). All the seven principles are ethically important and are not listed in any order of priority.

Social or Scientific Value

For research to be ethical, it should be worth doing. Appropriate use of resources is an ethical issue because of the principle of justice. Further research on questions that have been adequately answered by prior studies is ethically questionable. Exposing human subjects to any level of risk is unethical if the research does not have value to society or health care. This also places an ethical obligation on researchers to share their results and findings with others so that they can benefit from the new knowledge.

Similarly, EBP and EBQI activities are only ethical if they are worth doing. The value of the activity may initially be very local. Practitioners should identify significant clinical outcomes that could benefit from improvements. The value of different proposed activities may need to be compared to determine which have the potential to improve care the most, which is the essence of EBP. After conducting a local project or study, its wider value may be noted. For example, the results of the Michigan ICU study were extremely valuable worldwide, and it would have been unethical not to disseminate them broadly.

Scientific Validity

To be ethical, a research project must be methodologically rigorous to ensure a well-done study that can produce generalizable, valid findings. In addition, nonadherence to the EBP process or various processes of QI can result in poorly designed or implemented projects that waste resources and the time of those involved. The goal of EBQI is usually local improvement, not generalizable knowledge, so different methods may be used, but they should still be rigorously applied. Context and local factors are embedded in EBP and EBQI, while they are usually minimized in research by its methodological rigor. Nevertheless, exposing people to any risk in a flawed study or project is unethical.

Fair Subject Selection

The selection of subjects for research studies should be fair so that risks and benefits are shared equally. Inclusion and exclusion criteria for recruiting study participants should be based on good scientific reasons, not convenience or vulnerability. People should not be selected *because* they are marginalized, powerless, or poor. Such groups may become human subjects or participants, but only if the research is

relevant to people in those groups. Those groups that bear the risks and burdens of research should have the potential to benefit from the results.

The same criteria should apply in EBP and EBQI activities. Those involved in an EBP or EBQI project should be determined more by where the project is conducted and a population of patients than recruitment techniques aimed at representative sampling. If resources prevent improving care in all areas, decisions about where to focus should be made fairly and not based on people's status or other irrelevant factors. EBP and EBQI should be present across health care, including clinics or services that serve the underprivileged. Funding for services for the underprivileged should include resources for EBP and EBQI, just as they should for fee-paying or profitable services.

Favorable Risk–Benefit Ratio

Both research and EBQI should be committed to minimizing the risks and maximizing the gains of all studies and projects. Risks in research can range from very high to none, while risks in EBQI are usually low. Risks may be physical but can also include risks to privacy and respect. Wherever possible, the risk–benefit ratio should be improved as much as possible. This way both beneficence and nonmaleficence are promoted. With EBP, risks are known because of the body of evidence that guides practice and defines expected outcomes. No new risks should be associated with EBP when the fidelity (how the evidence is implemented) is high.

Independent Review

Independent review of research is ethically required because of the potential conflicts of interest. Research subjects are inherently used as means to a goal of securing new knowledge. They may be placed at risk of harm for the good of others. In clinical contexts, the potential exists to exploit patients as research subjects because what is best for the research project may not be what is best for patients.

Different views exist on the nature of the review that EBP and EBQI activities ethically require. The author's view is that different types of ethical review are best for different types of EBP and EBQI activities. The reasons for this will be developed in the following sections and will be brought together in the chapter's conclusion.

Respect for Potential and Enrolled Subjects

Research has scientific goals, with respect for the participants involved in the research remaining paramount. As the Declaration of Helsinki states, "In medical research involving human subjects [participants], the well-being of the individual research subject must take precedence over all other interests" (World Medical Association, 2008). This respect applies to those who are asked to participate in the research and decide not to do so. It includes protecting privacy and confidentiality, maintaining participants' welfare during the project, keeping them informed of significant changes during the research, and allowing them to withdraw from research.

In EBP and EBQI activities, respect for patients must also take precedence. Improving their outcomes is the goal of EBQI and inherent to the nature of the activities. As with research, it includes protecting privacy and confidentiality, maintaining welfare, and keeping patients informed. However, the issue of withdrawing from EBQI (i.e., initiatives designed to produce known improvement in outcomes) is tied up with informed consent and its appropriateness to EBQI is discussed later in this chapter. The focus of EBP is best care for patients to achieve best outcomes. It does not seem logical or ethical to exclude patients from these projects or to allow them to remove themselves. However, refusal of treatment is always a right of patients and should be respected in these EBP projects as well.

Informed Consent

Informed consent is one of the bedrocks of clinical ethics and research ethics. Participating in research is viewed as voluntary, and this places an ethical obligation on researchers to provide information so that people can make informed decisions to enroll or not. This requirement is based on the importance of

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