When is it Research and When is it Not? The Special Cases of Quality Assurance Studies and Medical Device Improvement

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Why are we here?

When Johns Hopkins launched its quality assurance study of central line infection control practices, they exposed a fault line in the medical research community that continues to generate strong opinions about when IRB approval is appropriate
In addition to the ongoing debate about whether their intervention required IRB approval due to human exposure to harm, the OHRP reaction to the Hopkins study triggered a debate about the need for IRB review as a condition of scholarly publication.

This presentation will explore the lingering impact of the OHRP-Johns Hopkins confrontation. We will discuss how to evaluate application of the common rule to non-patient focused research and medical device improvement efforts.
So, what’s the problem?

It’s the word RESEARCH.

It’s a Homonym Problem.
Research

What does the word mean from a IRB perspective?

Which begs the question, why do we have IRBs?
Which begs the question, what is an IRB?

45 CFR 46

Subpart A—Basic HHS Policy for Protection of Human Research Subjects
Source: 82 FR 7259, 7273, Jan. 19, 2017, unless otherwise noted.

§46.101 To what does this policy apply?
(a) Except as detailed in §46.104, this policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency that takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States. Institutions that are engaged in research described in this paragraph and institutional review boards (IRBs) reviewing research that is subject to this policy must comply with this policy.
• (l) Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

And Yet,

IRB approval is required for other reasons and in other settings.
The requirement for publication

What does that have to do with IRB protection of Human Subjects?

How do we solve this problem?

ELEMENTS IN AN ETHICAL DECISION-MAKING PROCESS

What is the problem?  What are key considerations?  How should the decision be made?  Consider possible solutions

Note: This presentation is for educational purposes only.
1. What is the problem?
   - What are the key ethical issues/questions?
   - Gather the facts (who, what, when, where, why?)
   - Identify the affected parties (e.g., stakeholders)

2. What are the key considerations?
   - Assess relevant laws– Identify the relevant ethical principles
   - Identify the risks and benefits (short/long-term, magnitude/probability)
   - Identify the rights/role of autonomy
   - Consider issues of justice
   - Consider other obligations/responsibilities
   - Consider your moral intuitions (“gut feelings”)
   - Consider your biases
   - Weigh competing principles
   - May need to revisit Step 1, to gather additional facts

3. How should the decision be made?
   - Consider processes–Transparency– Consulting with others
   - Experts– Stakeholders – e.g., community representatives

4. What are the possible solutions?
   - Think creatively about potential actions/solutions
   - Consider possible objections/alternatives
   - Decide on the proper ethical action

THE CENTRAL LINE INFECTION CONTROL STUDY

- Every year, physicians insert catheters into the blood vessels of millions of patients, of whom 80,000 unfortunately develop infections, and 28,000 die.
- In 2003, Peter Provonost, a prominent researcher at Johns Hopkins, and his colleagues, with support from a grant from the Agency for Health Care Research and Quality, studied whether a five item check list that included use of certain type of approved central lines and cleansers, and hand washing would reduce these infections at 67 hospitals in Michigan.
- Regulations exempt from IRB review studies that are not "research", defined as, "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”
- Federal agencies have clarified:
  - Investigators who intend to publish their results are, by definition, conducting “research that requires IRB review,” because the researchers are thereby seeking “to contribute to generalizable knowledge.”
  - Studies may be exempt if they are of normal educational practices or QI studies of “public benefit and service programs” (i.e., are not seeking to contribute to “generalizable knowledge”).
THE CENTRAL LINE INFECTION CONTROL STUDY

• The researchers submitted the protocol to the Hopkins IRB as research and requested an exemption from IRB review, saying the study was only quality improvement research. The IRB granted the exemption.
• The Hopkins IRB thus did not review the study, and said the protocol was exempt from IRB review at Hopkins or at any the 67 hospitals, and that informed consent was therefore not needed.
• After three months, the study found that the median rate of infections dropped dramatically from 2.7 to 0 infections for every 1,000 patient days with a catheter (i.e., the total number of days on which patients, cumulatively, have these tubes in them). Over the next 16 to 18 months, the mean rate continued to fall (from 7.7 to 1.4).
• Yet the Office for Human Research Protections (ORHP) then rebuked the investigators and the IRB.

Questions:
1. Should the IRB have reviewed the study?
2. Should the researchers have obtained informed consent and if so, from whom?
3. What if the researchers were including in the protocol the use of a new type of central line, the safety and efficacy of which have not yet been established, and which therefore does not yet have FDA approval?
   • Would that change your considerations?, and if so, how?
4. Should the current regulations be changed?
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2. What are the key considerations?
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Peter Pronovost

From Wikipedia, the free encyclopedia

Peter J. Pronovost is Chief Clinical Transformation Officer at University Hospitals (UH) health system in Northeast Ohio. At UH, Pronovost is responsible for improving value across the health system, helping people stay well, get well and manage their most acute medical conditions. He is the clinical lead for population health and the lead for high-reliability medicine, with direct responsibility for the UH employee accountable care organization. He is also responsible for telehealth and virtual health programs serving patient and provider communities.

He previously served as an intensive care specialist physician at Johns Hopkins Hospital in Baltimore, Maryland. He is a Professor at the Johns Hopkins School of Medicine in the Departments of Anesthesiology and Critical Care Medicine, and Surgery, Professor of Healthcare Management at the Carey Business School, Professor of Health Policy and Management at the Johns Hopkins Bloomberg School of Public Health, and is Medical Director for the Center for Innovation in Quality Patient Care.

He introduced an intensive care checklist protocol that during an 18-month period saved 1500 lives and $100 million in the state of Michigan. According to Atul Gawande in The New Yorker, Pronovost's "work has already saved more lives than that of any laboratory scientist in the past decade." In 2008 Time named Pronovost one of the 100 most influential people in the world. That same year, Pronovost was awarded a MacArthur Fellowship.

Pronovost's book Safe Patients, Smart Hospitals: How One Doctor's Checklist Can Help Us Change Health Care from the Inside Out was released in February 2010.

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THE NEW ENGLAND JOURNAL OF MEDICINE

Quality-Improvement Research and Informed Consent

Franklin G. Miller, Ph.D., and Emanuel J. Emanuel, M.D., Ph.D.

A tens of thousands of patients die each year because of hospital failure to adhere consistently to standard procedures of safe and effective medical care. Accordingly, quality-improvement researchers are increasingly focusing on programs designed to implement standard practices for the safety and care of hospitalized patients.

Perspective

February 23, 2006

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Tens of thousands of patients die each year because of hospitals’ failure to adhere consistently to standard procedures of safe and effective medical care. Accordingly, improving the quality of routine hospital care is a public health imperative. An effective way to promote quality improvement is to conduct evaluative research on programs designed to implement standard practices for the safety and care of hospitalized patients.

Such research, however, poses an apparent ethical conundrum: it is often impossible to obtain informed consent from patients enrolled in quality-improvement research programs because interventions must be routinely adopted for entire hospitals or hospital units. When, for instance, research on a quality-improvement initiative that affects routine care is conducted in an intensive care unit (ICU), surgical suite, or emergency room, individual patients have no opportunity to decide whether or not to participate. Can it be ethical to conduct such research without informed consent? A recent investigation by the Office for Human Research Protections (OHRP) — the federal agency charged with overseeing human-subjects research — places this issue in bold relief.
Researchers at Johns Hopkins University coordinated a quality-improvement research project aimed at reducing catheter-related infections in 103 ICUs at 67 Michigan hospitals. The study evaluated a protocol designed to routinely implement five evidence-based procedures: having clinicians wash their hands, using full-barrier precautions during insertion of central venous catheters, using chlorhexidine for skin cleansing before catheter insertion, minimizing the use of the femoral site for catheter insertion, and removing unnecessary catheters. In addition to the training of clinicians in such standard infection-control procedures, the project involved the use of a checklist to ensure adherence to the protocol. The result was a dramatic decrease in catheter-related infections: at baseline, the participating hospitals had a median of 2.7 infections per 1000 catheter-days; after 3 months, the median had dropped to 0, and it remained there for 18 months. Publication of the results, however, triggered an investigation by the OHRP (see timeline).1

Timeline of Johns Hopkins Quality-Improvement Project.

The October 9 decision by the institutional review board (IRB) was made by the IRB chair and one committee member, in accordance with Johns Hopkins policy. AHRQ denotes Agency for Healthcare Research and Quality, and OHRP Office for Human Research Protections.
MILLER, EMANUEL:

In view of the provision for waiving consent, the OHRP’s about the need for patients or surrogates to grant “legally effective informed consent” in its two determination letters seems unjustifiable.

Can we live in a world where the word RESEARCH means two different things?
OF course we can.

In the Hopkins study who needed the protection of the IRB?

Who was the subject?

Who was the participant?

What did OHRP accomplish by its investigation?

ANYTHING?
IN CONCLUSION,

Let’s stop tripping over the English language.

http://sps.columbia.edu/bioethics

Questions, Concerns?
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