Ethical Challenges in Knowledge Translation Research

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Learning objectives

1. To be able to define the core principles of research ethics
2. To be able to explain the ways in which KT research both does and does not fit the contemporary research ethics paradigm
3. To be able to list key ethical challenges for KT research

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An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

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ABSTRACT

BACKGROUND

Catheter-related bloodstream infections occurring in the intensive care unit (ICU) are common, costly, and potentially lethal.

From the School of Medicine (P.P., D.N., S.B., S.C., B.S.), the School of Professional Studies in Business and Education (D.S.),

Catheter-related blood stream infections

- Central venous catheters are commonly placed in patients in the ICU
- The catheter may become a site for infection, leading to serious blood stream infection
- 80,000 infections annual in the US
- 28,000 deaths
- $2.3 billion in estimated cost

Evidence

- Targeted clinician use of five evidence-based procedures recommended by the CDC as having the greatest effect on catheter related bloodstream infection:
  - Hand washing;
  - Full-barrier precautions;
  - Clorhexidine;
  - Avoiding the femoral site; and,
  - Removing unnecessary catheters

Intervention

- Education about practices to reduce infection
- Central-line cart created with necessary supplies
- Checklist to ensure adherence and providers were stopped if not adhering
- Removal of catheters discussed at daily rounds
- Feedback on infection rates

The study

- Prospective cohort study
- Invited all Michigan adult ICUs to participate
- 3 month baseline data collection
- 3 month intervention period between March 2004 and September 2005, and by up to 18 months of follow-up
- Data on number of catheter related bloodstream infections and catheter days collected by hospital infection-control practitioner
- Data aggregated into three month blocks by ICU

Hypotheses

- Primary hypothesis: The rate of catheter related blood stream infection would be reduced during the first three months after implementation of the study intervention as compared with baseline.
- Secondary hypothesis: The observed decrease in the rate of infection between 0 and 3 months after implementation of the study intervention would be sustained during the subsequent observation period.

Ethics

“The study was approved by the institutional review board of Johns Hopkins University School of Medicine. Informed consent was waived because the study was considered exempt from review.”

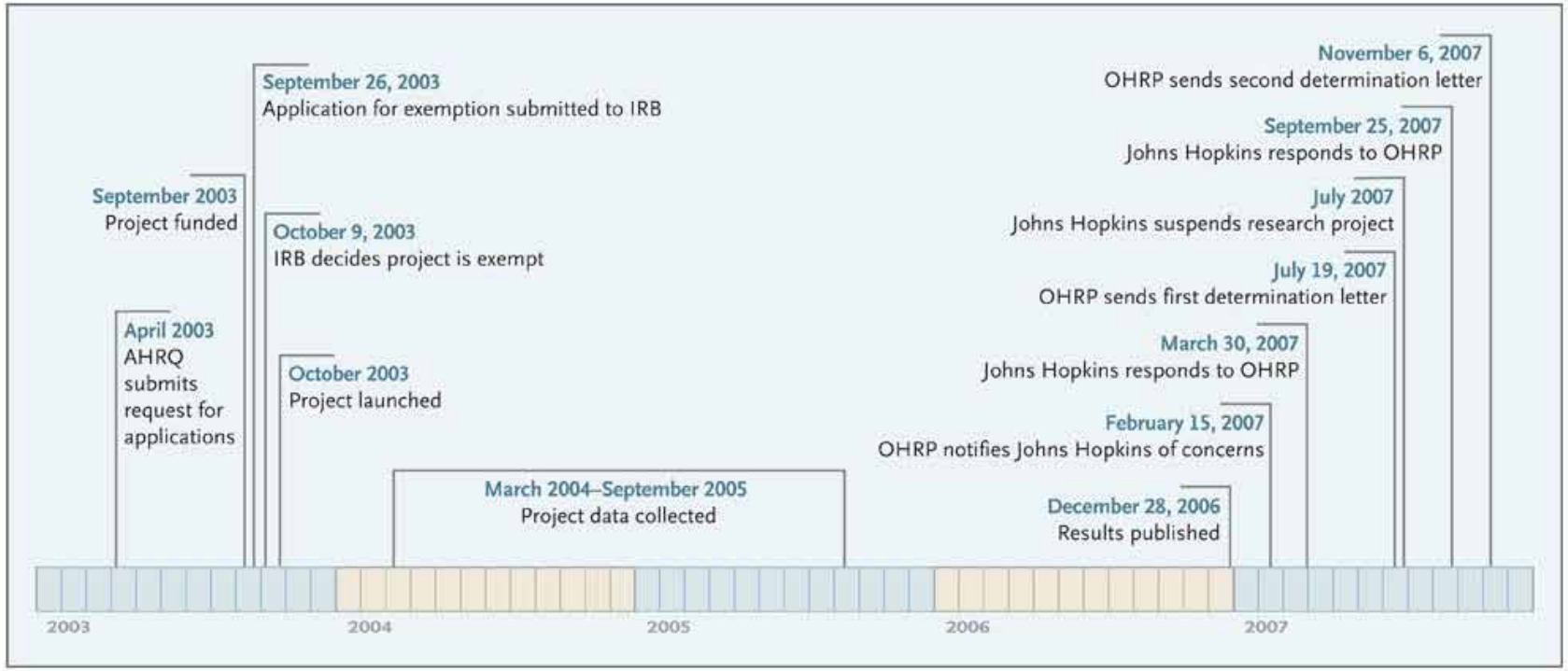
Results

Table 3. Rates of Catheter-Related Bloodstream Infection from Baseline (before Implementation of the Study Intervention) to 18 Months of Follow-up.*

Study Period	No. of ICUs	No. of Bloodstream Infections per 1000 Catheter-Days				
		Overall	Teaching Hospital	Nonteaching Hospital	<200 Beds	≥200 Beds
		median (interquartile range)				
Baseline	55	2.7 (0.6–4.8)	2.7 (1.3–4.7)	2.6 (0–4.9)	2.1 (0–3.0)	2.7 (1.3–4.8)
During implementation	96	1.6 (0–4.4)†	1.7 (0–4.5)	0 (0–3.5)	0 (0–5.8)	1.7 (0–4.3)†
After implementation						
0– 3 mo	96	0 (0–3.0)‡	1.3 (0–3.1)†	0 (0–1.6)†	0 (0–2.7)	1.1 (0–3.1)‡
4–6 mo	96	0 (0–2.7)‡	1.1 (0–3.6)†	0 (0–0)‡	0 (0–0)†	0 (0–3.2)‡
7–9 mo	95	0 (0–2.1)‡	0.8 (0–2.4)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.2)‡
10–12 mo	90	0 (0–1.9)‡	0 (0–2.3)‡	0 (0–1.5)‡	0 (0–0)†	0.2 (0–2.3)‡
13–15 mo	85	0 (0–1.6)‡	0 (0–2.2)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.0)‡
16–18 mo	70	0 (0–2.4)‡	0 (0–2.7)‡	0 (0–1.2)†	0 (0–0)†	0 (0–2.6)‡

* Because the ICUs implemented the study intervention at different times, the total number of ICUs contributing data for each period varies. Of the 103 participating ICUs, 48 did not contribute baseline data. P values were calculated by the two-sample Wilcoxon rank-sum test.
† $P \leq 0.05$ for the comparison with the baseline (preimplementation) period.
‡ $P \leq 0.002$ for the comparison with the baseline (preimplementation) period.

What happened



OHRP

- Study was not a quality-improvement initiative, but was research and therefore was not exempt from IRB review
- Johns Hopkins "failed to ensure that the requirements for obtaining and documenting the legally effective and informed consent of the subjects or the subjects' legally authorized representatives under regulations…"
- Failed to get required review at all participating institutions
- OHRP halted the study.

What is research?

- Research "*involves a systematic investigation to establish facts, principles or generalizable knowledge*." *(TCPS p.1.1)*
- It is not research if:
  - It isn't a systematic investigation; or,
  - It doesn't seek to establish facts, principles, or generalizable knowledge.
- Quality assurance initiatives – systematic investigations to inform change in only local practice or policy -- are not research and are not subject to REB review. (*TCPS 1.1(d)*)

What research requires REB review?

- *TCPS Article 1.1(a-c)*
- *(a) All research that involves living human subjects requires review and approval by an REB in accordance with this Policy Statement, before the research is started, except as stipulated below.*
- *(b) Research involving human remains, cadavers, tissues, biological fluids, embryos or fetuses shall also be reviewed by the REB.*
- *(c) Research about a living individual involved in the public arena…only requires ethics review if the subject is approached directly for interviews or for access to private papers…*

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- The distinction between research and quality-assurance initiatives is unclear at times, and much follows from the classification
- Currently, there is little oversight of QI initiatives, and this may push regulators to extend the scope of the definition of research
- In this case, it seems clear the study
  - Was research; and,
  - Required ethics review.

Moral principle	Moral rules
Respect for persons	Obtain the informed consent of prospective research subjects
	Protect the confidentiality of private information
Beneficence	Therapeutic procedures must satisfy clinical equipoise
	Risks of non-therapeutic procedures must be (1) minimized and (2) reasonable in relation to knowledge to be gained
Justice	Subject selection procedures must be fair
	Compensate subjects harmed as a result of research participation
Respect for communities	Respect communal values, protect and empower social institutions
	Where applicable, abide by the decisions of legitimate communal authority

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Informed consent

- General presumption that informed consent must be obtained from research subjects (*TCPS 2.1*)
- Additional protections for those who cannot provide informed consent (*TCPS 2.5*)
  - Inclusion must be necessary to answering the study hypothesis
  - Consent from a surrogate decision maker
  - Threshold for non-therapeutic risks to which they may be exposed (minimal risk)

Waiver of consent (*TCPS 2.1(c)*)

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration;
- Whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation; and
- The waivered or altered consent does not involve a therapeutic intervention.

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- OHRP concluded that because the study was research, in effect, informed consent was required
- Requirements for REB review and informed consent are separable (e.g., secondary use of data)
- Who is the research subject here?
  - Health care team?
  - Patient?
- At whom was the intervention directed?
- Waiver of consent for the patients?

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Therapeutic procedures

- A state of clinical equipoise must exist at the start of a study (*TCPS p. 7.1*)
- The various therapeutic procedures within the study must be consistent with competent medical care
- At the start of the trial there must exist a state of honest, professional disagreement in the community of expert practitioners as to the preferred treatment

Non-therapeutic procedures

- Two requirements:
  - Risks to subjects are minimized consistent with sound scientific design
  - Risks reasonable in relation to knowledge to be gained
- If the study involves a vulnerable population:
  - Risks of nontherapeutic procedures must be no more than
    - Minimal risk (Canada)
    - Minor increase above minimal risk (US)

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- How do we determine that the various study procedures in a KT study have benefits that outweigh risks?
- Intervention is directed at health care workers and only indirectly effect patients
- Does clinical equipoise apply?
- Generally thought to stem from the fiduciary duty of care that the physician-research owes to the patient-subject
- Are there concerns about “placebo controls” or “substandard care”?

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Selection of subjects

- *TCPS Section 5*
- Undue burdens:
  - Those who will not share in study benefits
  - Groups exposed to repeated study may be unduly burdened by research participation
- Access to benefits:
  - Exclusion of groups may lead to systematic gaps in medical knowledge
  - Children, women (*TCPS 5.3*), elderly, members of minority groups may not be excluded without careful justification

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- May certain groups be unduly burdened by KT studies?
- Concern applies most directly to overburdened health care workers.
- Also applies to settings involving vulnerable subjects, e.g., prisons, patients who lack capacity for decision making.

- May certain groups be unfairly denied access to the benefits of research?

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Communities

- Recognizing the heterogeneity of communities, researchers may in particular instances have obligations to:
  - Engage the community in the development of the study
  - Disclose information to the community and, where appropriate, seek community consent
  - Involve the community in the conduct of the study
  - Negotiate access to and storage of data and samples
  - Involve the community in the dissemination and publication of study findings

KT

- KT research may, as in community participatory action research, target an entire community
- The challenge of many KT studies is they involve groups who are not communities and whose moral status is unclear
  - Is consent from groups (e.g., group medical practice) included in studies required?
  - Must all in the group agree?
  - May a representative consent on their behalf? Who represents a group (e.g., the practice manager)?

Conclusion

- We have a poor understanding of the ethics of KT research and this may lead to good research not being done
- Difficult questions include:
  - When is a KT study research as opposed to QI?
  - Who is the research subject?
  - When must consent be obtained and from whom?
  - Does clinical equipoise apply?
  - Are there over-studied or understudied groups?
  - How do we deal with groups included in research?