The distinction of quality improvement (QI) activities from research:

When is my project considered research and what steps do I take for IRB review and approval?





Outline

- The distinction between research and QI and why does it matter?
- What is research
- What is QI
- Criteria to evaluate whether a QI project is research
- Examples
- Human Subjects Research Requirements
 - How to submit to the IRB





I want to publish (present, etc.).... so I have to submit to the IRB.... Right?

Case example

- Hypothesis that errors might be prevented if ICU clinicians complete a checklist of key steps they must complete to prevent infection during the insertion of lines.
- Each of 5 steps is scientifically validated to help prevent infection; all recommended by the CDC.
- Plan to implement this within the ICUs of a single inner city hospital
- If analysis shows benefits may look more broadly at implementation in >100 ICUs in mid-west US

Research vs. Practice

"Drawing the line between research and accepted practice....[is] the most difficult and complex problem facing the Commission."

Jay Katz, MD, physician and ethicist

From Kay, 1975, as quoted in Levine, 1988: Ethics and Regulation of Clinical Research

Does Uncertainty

Research?

Research vs. Practice

"It is extremely hard to distinguish between clinical research and the practice of good medicine. Because episodes of illness and individual people are so variable, every physician is carrying out a small research project when he treats a patient."

- Thomas Chalmers

From Kay, 1975, as quoted in Levine, 1988: Ethics and Regulation of Clinical Research

The Checklist project (P. Pronovost)

- Implemented checklist of 5 steps to be used in ICUs when inserting central lines
 - Wash hands with soap
 - Full barrier protections: sterile drapes over entire pt; wear sterile mask, hap, gown, gloves
 - Clean pt's skin with chlorhexidine antiseptic
 - Avoid femoral site
 - Remove unnecessary catheters asap
- First implemented at JHH.... Dramatic results
- Implemented at 108 ICUs in MI
 - In 18 mo. prevented more than 1500 infection-related deaths, saved more than \$175 million



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

Peter Pronovost, M.D., Ph.D., Dale Needham, M.D., Ph.D., Sean Berenholtz, M.D., David Sinopoli, M.P.H., M.B.A., Haitao Chu, M.D., Ph.D., Sara Cosgrove, M.D., Bryan Sexton, Ph.D., Robert Hyzy, M.D., Robert Welsh, M.D., Gary Roth, M.D., Joseph Bander, M.D., John Kepros, M.D., and Christine Goeschel, R.N., M.P.A.

ABSTRACT

BACKGROUND

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

METHODS

We conducted a collaborative cohort study predominantly in ICUs in Michigan. An evidence-based intervention was used to reduce the incidence of catheter-related bloodstream infections. Multilevel Poisson regression modeling was used to compare infection rates before, during, and up to 18 months after implementation of the study intervention. Rates of infection per 1000 catheter-days were measured at 3-month intervals, according to the guidelines of the National Nosocomial Infections Surveillance System.

RESULT:

A total of 108 ICUs agreed to participate in the study, and 103 reported data. The analysis included 1981 ICU-months of data and 375,757 catheter-days. The median rate of catheter-leated bloodstream infection per 1000 catheter-days decreased from 2.7 infections at baseline to 0 at 3 months after implementation of the study intervention (P≤0.002), and the mean rate per 1000 catheter-days decreased from 7.7 at baseline to 1.4 at 16 to 18 months of follow-up (P<0.002). The regression model showed a significant decrease in infection rates from baseline, with incidence-rate ratios continuously decreasing from 0.62 (95% confidence interval [CI], 0.47 to 0.81) at 0 to 3 months after implementation of the intervention to 0.34 (95% CI, 0.23 to 0.50) at 16 to 18 months.

CONCLUSION:

An evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of catheter-related bloodstream infection that was maintained throughout the 18-month study period.

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.), and the Bloomberg School of Public Health (H.C.), Johns Hopkins University, Baltimore; and the University of Michigan, Ann Arbor (R.H.); William Beaumont Hospital, Royal Oak (R.W.); Ingham Regional Medical Center, Lansing (G.R.); Harper University Hospital, Detroit (J.B.); Sparrow Health System, Lansing (J.K.); and the Michigan Health and Hospital Association Keystone Center for Patient Safety and Quality, Lansing (C.G.) — all in Michigan.

N Engl J Med 2006;355:2725-32.
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Checklist project

- Written anonymous complaint
- Alleged that research was conducted
 - without prior review and approval by an IRB
 - without informed consent of human subjects who participated
- OHRP opened a compliance oversight evaluation re: allegations of non-compliance with HHS regulations for protection of human subjects.

The New Hork Times Capital One 354 Opinion Opinion All NYT Search N.Y. / REGION WORLD BUSINESS TECHNOLOGY TRAVEL REAL ESTATE AUTOS U.S. SCIENCE SPORTS OPINION ARTS STYLE JOBS COLUMNISTS CONTRIBUTORS LETTERS N.Y./REGION OPINIONS THE PUBLIC EDITOR

OP-ED CONTRIBUTOR

A Lifesaving Checklist

By ATUL GAWANDE Published: December 30, 2007

Boston

Enlarge This Image



IN Bethesda, Md., in a squat building off a suburban parkway, sits a small federal agency called the Office for Human Research Protections. Its aim is to protect people. But lately you have to wonder. Consider this recent case.



A year ago, researchers at Johns Hopkins University published the results of a program that instituted in nearly every intensive care unit in

Michigan a simple five-step checklist designed to prevent certain hospital infections. It reminds doctors to make sure, for example, that before putting large intravenous lines into patients, they actually wash their hands and don a sterile gown and gloves.

The results were stunning. Within three months, the rate of bloodstream infections from these I.V. lines fell by two-thirds. The average I.C.U. cut its infection rate from 4 percent to zero. Over 18 months, the program saved more than 1,500 lives and nearly \$200 million.

Yet this past month, the Office for Human Research Protections shut the program down.

"The government's decision was bizarre and dangerous...."

OHRP and the Checklist

"While some expressed concern that OHRP has prohibited hospitals in Michigan and elsewhere from implementing a program intervention consisting of a checklist and other measures to prevent certain hospital-acquired infections, OHRP has taken no such action. On the contrary, if any hospital or intensive care unit decides to implement the use of checklists or other measures only for the reason that they believe those measures will improve the quality of care provided, they may do so without consideration of the requirements of the Department of Health and Human Services regulations . . ."

"As stated above, the regulations do not apply when institutions are only implementing practices to improve the quality of care. At the same time, if institutions are planning research activities examining the effectiveness of interventions to improve the quality of care, then the regulatory protections are important to protect the rights and welfare of human research subjects..."

(January 15, 2008) - OHRP Statement Regarding The New York Times Op-Ed Entitled "A Lifesaving Checklist"

Why Does it Matter?









Why does it matter?

- For research that involves human subjects, regulations require that an ethics committee (IRB) must review and approve prior to starting.
 - Risks/benefits
 - Informed consent
 - Voluntary participation
- Assures that research is conducted according to ethical principles outlined in the Belmont Report
 - Respect for persons
 - Beneficence
 - Justice

What happens if we don't get it right?

- Possible harm to the patient/subject.
- Breach of ethical obligations to the patient/subject.
- Formal evaluation by OHRP and/or FDA.
 - Determination letters /Warning letters and resulting corrective actions, enforcement actions (including debarment).
 - OHRP holds institution responsible for conduct of its agents;
 FDA holds sponsor, investigator and IRB responsible.
- State licensing board findings/actions.

Erosion of public trust in the research enterprise.

International Committee of Medical Journal Editors (ICMJE) and Protection of Research Participants

"When reporting research involving human data, authors should indicate whether the procedures followed have been assessed by the responsible review committee (institutional and national), or if no formal ethics committee is available, were in accordance with the Helsinki Declaration as revised in 2013........Approval by a responsible review committee does not preclude editors from forming their own judgment whether the conduct of the research was appropriate."

http://www.icmje.org/recommendations/browse/roles-and-responsibilities/protection-of-research-participants.html

Gray Area



Innovations

Novel treatments/procedures

Off-label treatments

Departures from SOC

Non-validated practices

QI/QA projects

Case report vs. "n of 1"

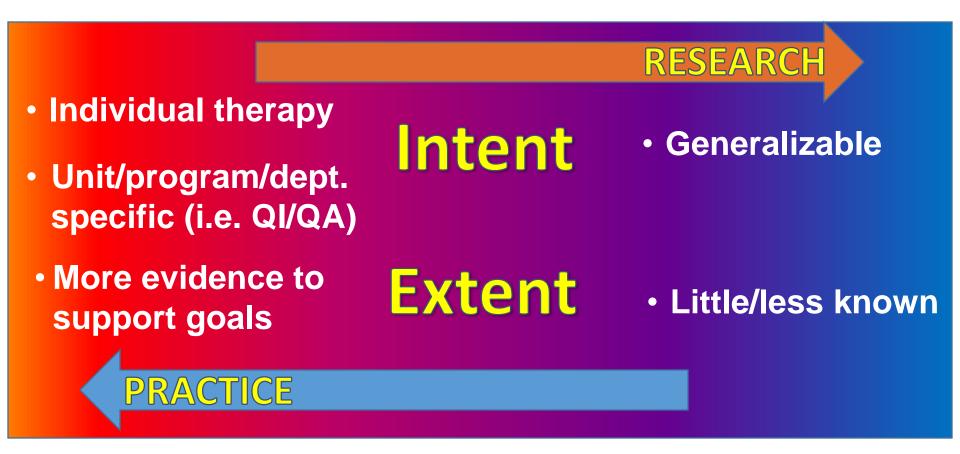
Clinical Research

"When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research."

Belmont Report, 1979

Gray Area

 Significant innovations should be incorporated into a research project to establish safety & efficacy.



What is Research?

 Process of systematic inquiry or study to build knowledge in a discipline (i.e. "generalizable").

- Results

 foundation on which practice decisions and behaviors are laid.
 - "Evidence-based practice"



Overview of Research

- Activities designed to test an hypothesis, permit conclusions to be drawn, and contribute to generalizable knowledge.
- Usually described in a formal protocol with an objective and set of procedures. (systematic)
- Treatment choices made per protocol, not necess. in the best interest of the patient/subject....
 - ex: "random assignment" (systematic)
- Purpose is to gain knowledge, not necessarily to benefit the individual. (generalizable)
- Elements under study may not be of direct benefit to the subject.

QI versus Research: A difference of 'Intent'

- Traditional QI/QA projects are designed, or intended, to principally:
 - improve patient care;
 - compare a program/process/system to an established set of standards such as standard of care, recommended practice guidelines, or other benchmarks;
 - improve the performance of institutional practice or local systems;
 - bring about improvements in health care delivery;







Purpose of HSR

- By comparison, Human Subjects Research is defined by the United States Secretary of Health and Human Services (DHHS) as a "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."
- If any project meets the criteria for research and involves human subjects, prior IRB approval is needed.





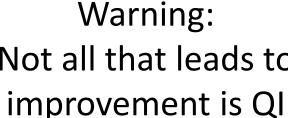
What is QI?

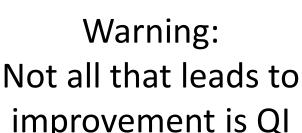
 Systematic, data-guided activities designed to bring about immediate improvements in health care delivery in particular settings

Lynn, et al, Annals of Internal Medicine 2007;
 146:666-673

There is a 'Science' to Improvement

- QI as a <u>methodology</u> is meant to be 'practical' means of realizing improvement
 - Involves hypothesis testing tied to predictions around interventions that will lead to improvement
 - Necessitates measuring what is necessary to realize improvement No 'controls'
 - And improving what needs to be improved based on established best practice
- Key Tenets:
 - Iterative Change (PDSAs)
 - Measuring effect in real time
 - Requires looking at data from beginning to end: not just at the beginning and at the end
 - Systems based
 - **Team Sport**











The 'James Moses' Definition of QI

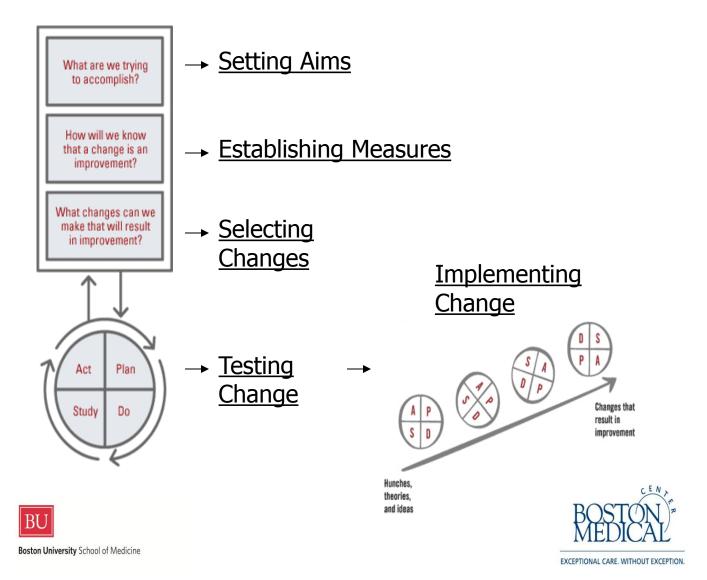
Quality Improvement is:

Creating Sustainable Improvement in Patient Care by LEARNING what is effective via a structured process aka, methodology

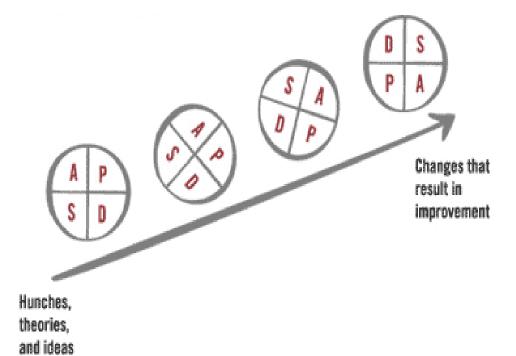




Model for Improvement



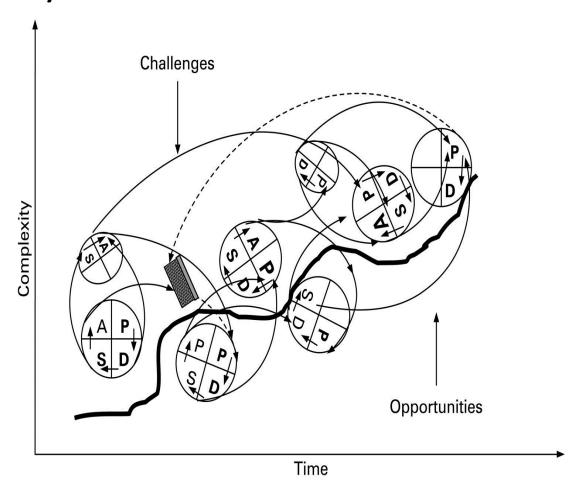
Ideally







Reality







Discerning Research from QI

Not so straightforward

- Features such as methodology, publication of findings, or the systematic collection of data, do not necessarily discern QI/QA initiatives from regulated human research
 - Such attributes can be shared by both research and non-research projects
 - According to federal guidance, "the intent to publish is an insufficient criterion for determining whether a QI activity involves research."
- Activities that start out as QI/QA projects may eventually lead to regulated human research when a decision is made to use previously collected QI/QA data for research purposes.
 - Use of previously-collected QI/QA data for research purposes requires IRB submission and review.





Premise of no IRB review needed for QI

- Do no harm as ethical/moral imperative in practice of medicine
- Context of 'Do No Harm' in current context is tied to continuous improvement to adopt best practice into the point of care
- QI therefore is a moral obligation in practice of medicine both at individual level and at system level
 - Research is optional and not a moral obligation
- QI becomes part of every day work of individuals and health care institution, part of the 'practice of medicine'
 - Not separate and distinct warranting 'research review'







Implications

- In applying QI (without IRB approval), the approach taken must live up to the 'First, Do No Harm' principle
 - No risk (including HIPAA considerations)
 - Improvement tied to broader and more consistent application of standard of care, best practice
 - If randomization of intervention (benefit) then needs to be with care process in which best practice is not defined
 - Assessment of possible harm assimilated into QI approach
 - Balancing Measures
 - Measurement as necessary to derive improvement
 - Not prove effectiveness first and foremost





- After completing QI project, resident wants to see if any outcomes (post-discharge utilization) improved since the intervention was 'implemented'.
- Resident looks at all discharges from inpatient service the year prior and assesses for repeat presentation to ED within 30 days and admissions. Compares patients who received intervention with those that didn't via chisquare/ttest:
 - Intent: Improvement? Or generalizable knowledge?
 - Intervention: No active intervention, intervention previously implemented.
 - Iteration: No iteration
 - Measurement: Intervention group compared to control to assess outcome improvement



Should the resident now submit an IRB to complete the above?





Key Considerations/questions: Intent



Proof of Effectiveness versus Sustained Improvement





What requires IRB Review?

1) Is it research?2) Are there human subjects?

Definitions

- Research (OHRP regs: 45 CFR 46.102 (d))
 - "... a systematic investigation, including research development, testing and evaluation, <u>designed</u> to develop or contribute to <u>generalizable</u> knowledge."
- Clinical Investigation (FDA regs: 21 CFR 312.3 (b))
 - "... any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice."

Definitions

What is "generalizable knowledge"?

 An activity may be thought to develop or contribute to generalizable knowledge if the information collected is intended to be applied beyond a particular patient/setting/program. **US Dept. Justice:** http://www.ojp.usdoj.gov/funding/

decision tree.htm

- Intent of the research is to add info to the field of study. Results applied beyond the subject population to other settings.
- Intent to test or develop scientific hypotheses, draw conclusions to be shared beyond the populations or situations being studied.

More on generalizable knowledge

- The knowledge contributes to a theoretical framework of an established body of knowledge.
- The primary beneficiaries: other researchers, scholars and practitioners in the field of study.
- Publication, presentation or other distribution of the results is *intended to inform the field of study*.
- The results are expected to be generalized to a larger population beyond the site of data collection.
- The results are intended to be replicated in other settings.

I want to publish (present, etc.).... Does this mean I have to submit to the IRB?

OHRP response:

"Planning to publish an account of a quality improvement project does not necessarily mean that the project fits the definition of research; people seek to publish descriptions of nonresearch activities for a variety of reasons, if they believe others may be interested in learning about those activities. Conversely, a quality improvement project may involve research even if there is no intent to publish the results."

Definitions

- Human Subject (OHRP regs: 45 CFR 46.102 (f))
 - "... a living individual <u>about whom</u> an investigator..... conducting research obtains:
 - Data through interventions or interactions with the individual, or
 - Identifiable private information."
- Subject (FDA regs: 21 CFR 312.3 (b))
 - "...a human who participates in an investigation, either as a recipient of the investigational new drug or as a control.
 A subject may be a healthy human or a patient with a disease."

Definitions

- Interaction/Intervention (45 CFR 46.102 (f))
 - physical procedures by which data are gathered...
 - manipulations of the subject or the subject's environment
 - performed for research purposes.
 - interaction includes communication or interpersonal contact between investigator and subject.

Definitions

- Private information (45 CFR 46.102 (f))
 - Includes information about behavior that occurs in a context in which an individual can reasonable expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
 - ... must be individually identifiable (i.e. the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects."

(See also OHRP guidance on coded data/specimens: http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm)

Determining when OHRP regs re: IRB review and informed consent apply...

- 1) Does activity involve Research? (46.102(c)) If yes then....
- 2) Does research involve Human Subjects? (46.102(f))

If yes, then....

3) Does the human subjects research meet criteria for Exempt from 45 CFR 46? (46.101(b))

Exempt determination... 45 CFR 46.101 (b)*

- 1. Normal educational, practices in established educational settings
- 2. Educational tests, surveys, interviews, or observation of public behavior -unless identified & sensitive**
- 3. Research on elected or appointed public officials or candidates for public office
- 4. Research using, <u>existing data</u> if publicly available or recorded without identifiers (existing = at time of submission to IRB)
- 5. Evaluation of public benefit service programs
- 6. Taste and food quality evaluation and consumer acceptance studies

** does not apply to research with children except for research involving observation of public behavior when investigator(s) do not participate in the activities being observed.

^{*}None of the categories apply to Prisoner research (Subpart C).

Possible types of IRB submissions

- NHSR: The QI project is NOT research
 - Submit to the IRB only if you need a formal determination from the IRB that it is not research.
 - Your subsequent publication should make it clear that it is QI and not research.
- NHSR: The QI project IS research, but no human subjects are involved.
- Exempt: The QI project IS research, but meets one of the exempt criteria under the regulations.
- Non-exempt (Expedited or full board): The QI project is research and does not meet exempt or NHSR criteria.

IRB Submission for QI projects:

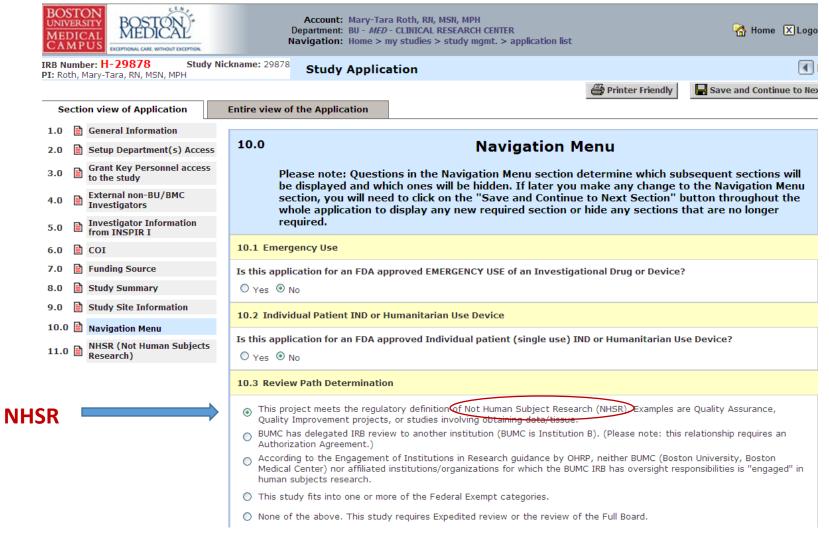
NHSR (because there are no human subjects) or

NHSR (because it's NOT research)

 QI-only, because it's not designed to contribute to generalizable knowledge

- IRB submission and review/approval not required
- But, in this case you want to have a formal determination from the IRB that this is QI-only (not research) or there no human subjects**)
 - (This would be a determination, not an approval)

INSPIR and NHSR Submission



Then, make your case for WHY it is NHSR in Section 11.

- What are two examples of justification that you might use?

IRB Submission for QI projects:

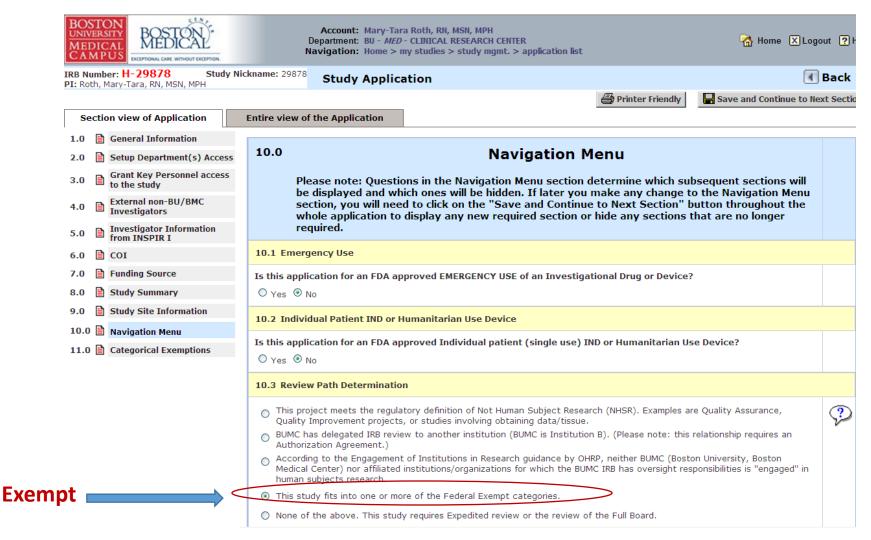
Exempt

- You did a QI-only project; afterwards you decide want to generalize the results as research (exempt category 4)
 - IMPT: This is NOT retrospective approval for something initially intended to be research! That is NOT an option!

or

 You have implemented an evidence-based quality improvement measure, and as part of follow-up you want to survey patients and staff and you consider this evaluation to be research (exempt category 2)

INSPIR and Exempt Submission



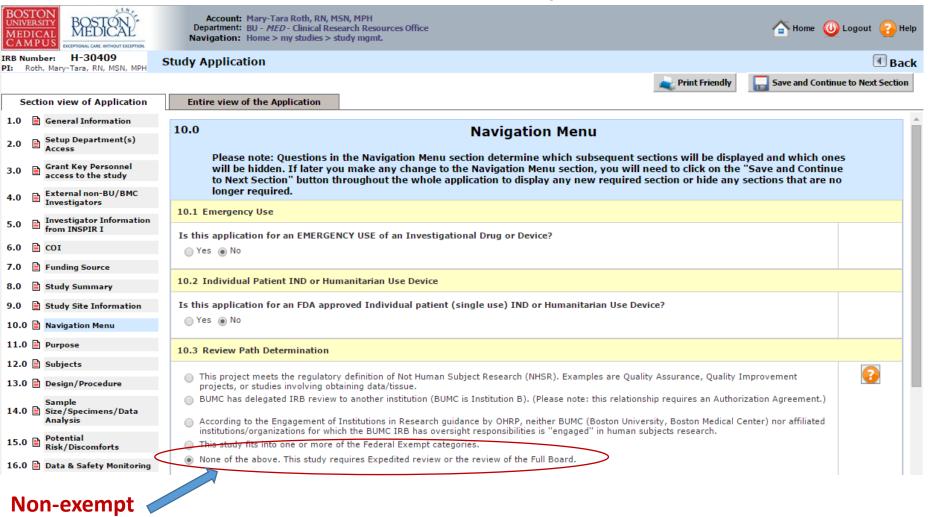
In Section 11, choose Exempt category 4 if data is all existing at the time of submission, and it is anonymous (no link back to the record) or Exempt category 2 if you have a survey.

IRB Submission for QI projects:

Non-exempt (expedited or full-board review/approval)

 You want to implement a new practice to improve care that does not have sufficient evidence base to support its safety and/or efficacy.

INSPIR and Non-exempt Submission



Complete the full application, that "builds" based on your responses in Section 10. Consider requesting "waiver of consent" if applicable.

Flexibility in Regs re: Consent

Waiving Informed Consent for Research (45 CFR 46.116 (d))



- 1. Minimal Risk
- 2. Does not adversely affect subject rights and welfare
- 3. Not practicable to conduct research without the waiver
- 4. When appropriate, subjects provided with pertinent info after participation.

SQUIRE Guidelines

http://squire-statement.org/

BU Boston University School of Medicine

SQUIRE Guidelines (Standards for QUality Improvement Reporting Excellence) Version 2.62 SHORT – 10/2/08

- These guidelines provide a framework for reporting formal, planned studies designed to assess the
 nature and effectiveness of interventions to improve the quality and safety of care.
- It may not be possible to include information about every numbered guideline item in reports of
 original studies, but authors should at least consider every item in writing their reports.
- Although each major section (i.e., Introduction, Methods, Results, and Discussion) of published studies generally contains some information about all of the numbered items within that section, information about items from one guideline section (for example, the Introduction) is often also needed in other sections (for example, the Discussion).

Text section; Item number and name	Section or Item description Did you provide clear and accurate information for finding, indexing, and scanning your paper?			
Title and abstract				
1. Title	 Indicates the article concerns improvement of health care quality, and the specific aim of the intervention 			
2. Abstract	 Summarizes all key information using chosen journal's abstract format 			
Introduction	Why did you start?			
3. Background Knowledge	Summarizes knowledge about the care problem, and characteristics of organizations in which it occurs			
4. Local problem	 Describes the nature and severity of the local problem that was addressed 			
5. Intended improvement	 Describes the specific aim of the proposed intervention; also who and what triggered the decision to make changes, and why now 			
6. Study question	 States the primary and secondary study questions 			
Methods	What did you do?			
7. Ethical issues	 Describes the ethical aspects of implementing and studying the improvement, and how ethical concerns were addressed 			
8. Setting	 Specifies how relevant context factors were identified and characterized 			
9. Planning the intervention	Describes the intervention itself; why it was chosen; and what was to be done initially, and by whom			
10. Planning the study of the intervention	 Describes plans for assessing how effectively the intervention was implemented; mechanisms by which intervention components were expected to cause changes; study design chosen; and efforts to maximiz internal and external validity 			
11. Methods of evaluation	Describes instruments used to assess effectiveness of implementation; contributions of intervention components and context factors to intervention effectiveness, primary and secondary outcomes, validation of instruments, methods for assuring data quality and adequacy			
12. Analysis	 Describes qualitative and quantitative analytic methods; variability expected in implementing the intervention; expected change in outcomes; power of study to detect such effects; methods used to demonstrate effects of time as a variable 			
	CENA			
	POSTON > -			

Journal	SQUIRE Development Article	Editorial on SQUIRE	Recommends for Authors
American Journal of Nursing	Not Available	It's 'Improved,' but Is It Better?	<u>Yes</u>
Clinical Journal of Oncology Nursing	Not Available	Not Available	<u>Yes</u>
Japanese Society for Quality and Safety in Healthcare	Not Available	Not Available	Yes
Joint Commission Journal on Quality and Patient Safety	Publication guidelines for quality improvement in health care: evolution of the SQUIRE project	Not Available	Please contact your local biomedical library or consult the Joint Commission website to order a copy any of these articles
Journal of General Internal Medicine	<u>Yes</u>	Not Available	<u>Yes</u>
Journal of Hospital Medicine	Not Available	Not Available	Yes
Journal of Nursing Care Quality	Not Available	Not Available	<u>Yes</u>
Pediatrics-American Academy of Pediatrics	Not Available	Not Available	<u>Yes</u>
<u>Spine</u>	Not Available	Not Available	<u>Yes</u>
The Permanente Journal	Not Available	Not Available	<u>Yes</u>





HIPAA regs versus Human Subjects Protection regs

- Human Subject: a living individual about whom an investigator conducting research obtains
 - data through interaction or intervention with the individual, or
 - identifiable private information
- HIPAA: Health Insurance Portability and Accountability Act
 - Establishes security and privacy standards for the use and disclosure of 'protected health information' (PHI)
 - Not well designed to deal with research issues
 - Uses different definitions regarding personal information (PHI versus identifiable private information)

EXCEPTIONAL CARE, WITHOUT EXCEPTION



- Resident takes on a 'QI' project tied to improving meds in hand prior to discharge for patients admitted to inpatient service.
 - Intent: Improvement for Patients
 - Intervention: Meds in hand for patients that opt in delivered by pharmacy.
 - Iteration: No iteration planned with intervention.
 - Measurement: Pre/Post assessment to assess effectiveness at end of year



Resident then wants to publish project in a journal. Is IRB needed?





- Faculty member has a patient safety grant to improve follow-up for pulmonary nodules.
- 3 different frames for follow-up being tested via randomization:
 - letters
 - low intensity navigation
 - high intensity navigation
- Outcome being follow-up completion rate.



Faculty wants to know if she should submit an IRB. What do you think?





- Faculty member attains implementation grant tied to developing new model of care (intensive outpatient management) for patients with special health care needs
- Request for data is made to help identify population and to start developing model.
- As part of grant there is an outcomes assessment with sharing of intervention as possible 'best practice'

Clinical analytics wants to know if the request for data is for QI or for research? And ask the faculty member if they should submit an IRB? What do you think?







Regardless of Research or QI...

HIPAA, QI, and You

- No PHI should exist outside BMC's Firewall
 - No thumbdrives
 - No personal computers, nonencrpyted
 - No google drive
 - No BU email, gmail, yahoo, Hotmail
- Use BMC email only
- Get access for students (BMC email, network drive, shared drive)
- New resource: box.com





Takeaways

- Tools:
 - QI/IRB checklist
 - SQUIRE Guidelines
- Mary-Tara Roth (Research) and James Moses (QI) as point people to touch base with regarding 'grey areas'



