RESPONSIBLE CONDUCT OF QI AND QI RESEARCH

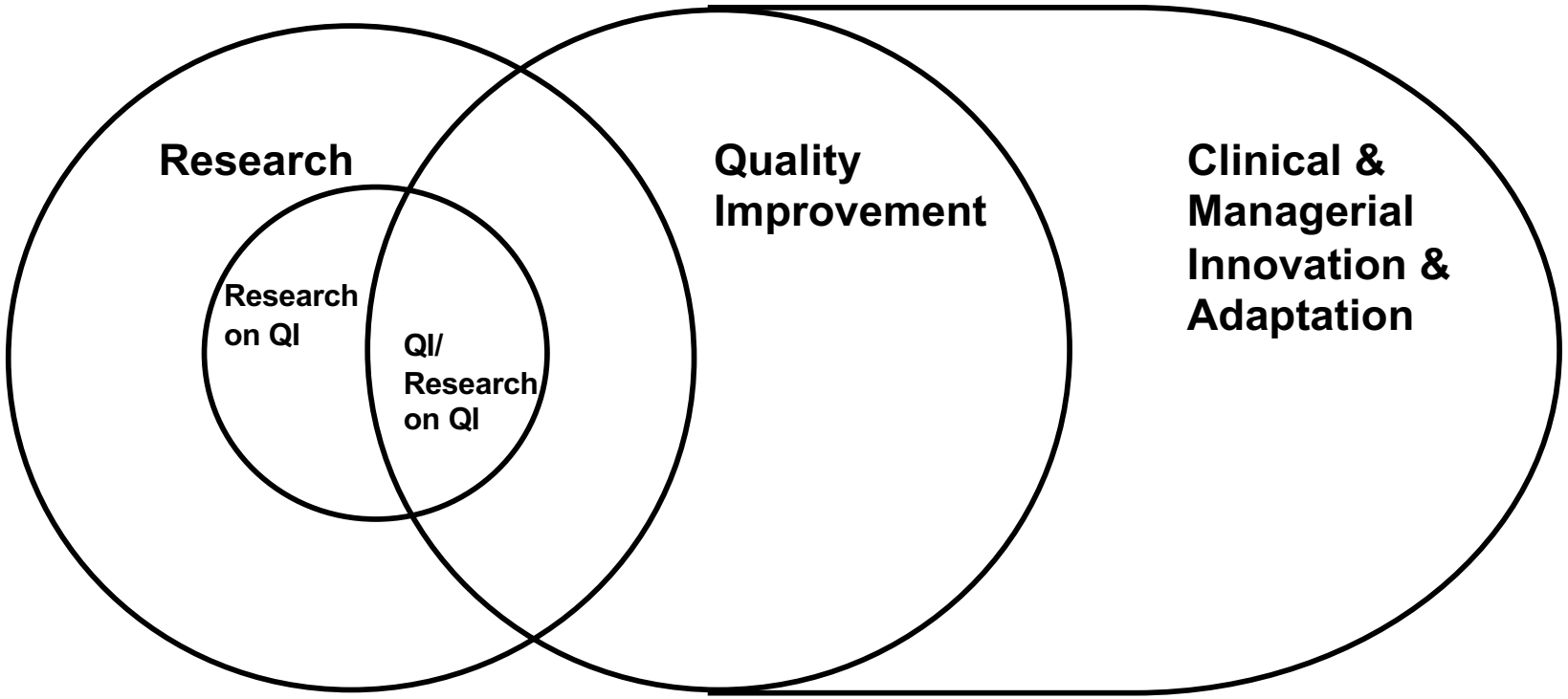
TO IRB OR NOT TO IRB, THAT IS THE QUESTION

JON FINKELSTEIN, MD, MPH- BOSTON CHILDREN'S HOSPITAL
DAN HYMAN, MD- COLORADO CHILDREN'S HOSPITAL

First, we digress…QI, QI Science, Implementation Science, and how I sleep at night

- QI- a structured activity using specific principles and methods, to improve care, service, or outcomes, generally by bringing them in line with accepted (or best) clinical practice
- QI Science- the science underlying the activity of QI
- QI Research- generation of new knowledge (about a clinical practice or process) using QI methods, or that contributes generally to QI science

Overlap between Improvement and Research (from Peter's Talk)



Adapted from *The Ethics of Using QI Methods to Improve Health Care Quality and Safety. A Hastings Center Special Report.*

First, we digress…QI, QI Science, Implementation Science, and how I sleep at night

- Implementation- the activity of introducing something into actual practice in real world settings
- Implementation Science- the science underlying implementation, drawing from psychology, organizational behavior, antropolgy, heavily focused on how context influences implementation
- Implementation Science Research- generation of new knowledge about factors that influence successful implementation or that contributes generally to implementation science

Goals of session

- Describe two or more ways in which typical QI projects differ from human subjects research;
- Assess whether your own project should require IRB review from an ethical perspective, and whether it does require IRB review in your own institution;
- In two minutes or less, make a logical argument for why local IRB's should create an alternate and simplified pathway for review and approval of QI projects

In 1979... Twenty years before To Err is Human

Billboard Top 40

1. My Sharona, The Knack
2. Bad Girls, Donna Summer
3. Le Freak, Chic
4. Da Ya Think I'm Sexy, Rod Stewart
5. Reunited, Peaches and Herb
6. I Will Survive, Gloria Gaynor
7. Hot Stuff, Donna Summer
8. Y.M.C.A., Village People


Weather

The Washington Post

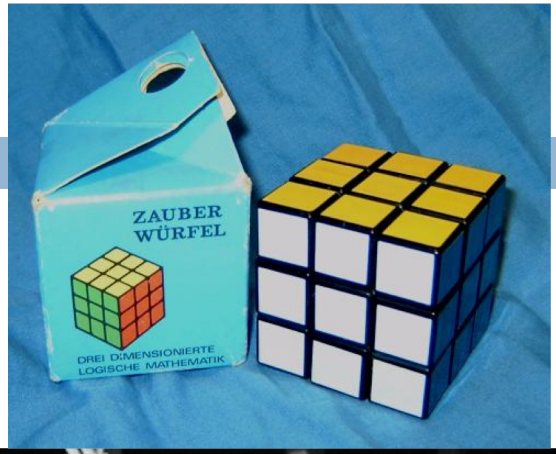
FINAL

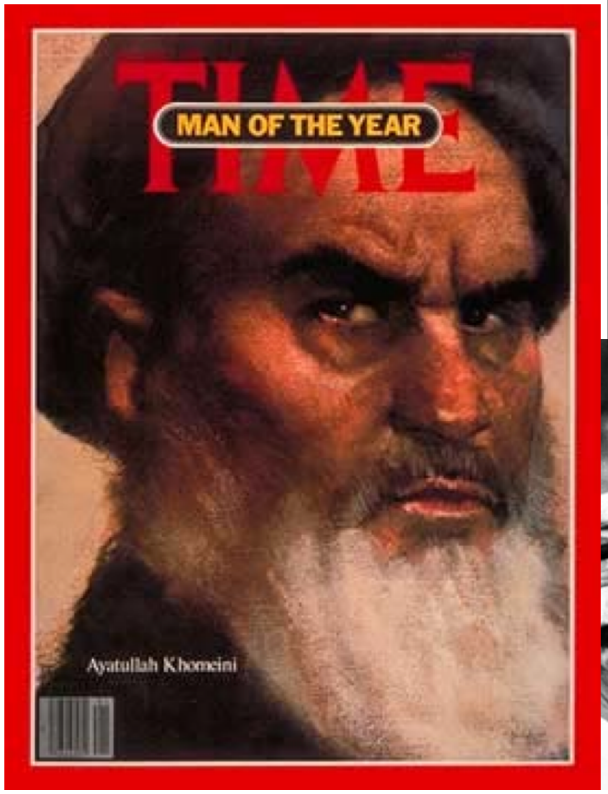
TUESDAY, NOVEMBER 6, 1979

Americans Still Captive in Tehran Embassy

U.S. Firmly Refuses To Extradite the Shah

British Mission Held 5 Hours by Students





…and, the Belmont Report is released

- 1974 National Research Act creates the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research
- 1979 Belmont Report Released
  - "statement of basic ethical principles and guidelines to assist in resolving research problems"
  - Respect for Persons
  - Beneficence
  - Justice

Belmont Report Applications

- Informed Consent
  - Information, comprehension, voluntariness
- Assessment of Risks and Benefits
  - Nature and scope, systematic assessment
- Selection of Subjects
- Office of Human Research Protection, *45 CFR Part 46, part A, (the Common Rule)*
- Special protections for children

Federal definitions

- *Research*-a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge
- *Human Subject* - a living individual about whom an investigator conducting research obtains:
  - data through intervention or interaction with the individual, or
  - identifiable private information

The centrality of "intent"

- Research: Intent of the project is to develop or contribute to generalizable knowledge (e.g., testing hypotheses). Dissemination is also intended end-product.
- But, what is "generalizable knowledge??"

Informed Consent in Low-risk Research (may include much of QI research)

- Even if a project is research, IRB's can use to waive informed consent requirements
  - Minimal risk
  - Rights and welfare not adversely effected
  - Not practicable to obtain consent
  - Subjects will be provided with pertinent information after, if applicable

Routine healthcare operations do not require oversight as human subjects research.

Quality Improvement is operations…

What is Quality Improvement?

- "… systematic, data-guided activities designed to bring about immediate improvements in health care delivery in particular settings."*
- Not primarily intended to have application beyond the specific unit within the organization that carries out the operation
- Broader benchmarking and multi-institutional QI efforts are increasingly common

*Hastings Center Report

What's special about QI related research

- Potential harms generally different in both magnitude and type.
- Interventions often at the system level
- Interventions could typically be implemented within current care, often without measurement to assess whether they worked.
- We are studying "meta" issues (implementation fidelity, variation by context, etc.) compared to direct biological/clinical effect

QI and Research: where do we draw the line

- When does “learning from data” become “seeking generalizable knowledge”?
- When does “measurement” become “systematic collection”?
- How do we think about “routine operations” in a Learning Health System with “best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience”? (IOM Roundtable on Value and Science-driven Health Care)

Example: Improving Asthma discharges

- Children's Colorado identified that 35% of the time patients with asthma were discharged with a written asthma treatment plan that included all 7 elements as required by The Joint Commission
  - A multidisciplinary team convened to define set roles, responsibilities for improving this process
  - Data was collected monthly and reported to team and oversight committee
  - PDSA cycles run to test different strategies for improvement
  - The team was interested in presenting their work at various regional and national meetings

What QI activities are research?

- If a project involves introducing an untested clinical intervention for purposes which include not only improving the quality of care but also collecting new information about patient outcomes for the purpose of establishing scientific evidence to determine how well the intervention achieves its intended results

  OHRP Quality Improvement FAQs

- What's a "clinical intervention"???

QI collaboratives and other multisite initiatives: considerations

- Does engaging multiple delivery systems change the balance of intent regarding local learning/improvement and generalizable knowledge?
- Does transfer of identifiable or non-identifiable information change the requirement for IRB-review?

The Pronovost Affair

- "Classic" large-scale safety program/checklist implementation to decrease CLABSI in 103 ICU's- a collaboration between investigator at Johns Hopkins (Pronovost) and Michigan Health and Hospital Assoc.[1,2]
- Funding from AHRQ
- No randomization, all received intervention, pre-post design
- Data on catheter-days and CLABSI's aggregated to the ICU-level collected by MHA- sent to JHU.
- Median CLABSI rate dropped from 2.7/1000 days to 0 at 3 mos.

[1]Pronovost P et al. NEJM 2006; 355:2725
[2]Kass N et al. Joint Commission Journal 2008 34:349-353

The Pronovost Affair

- Categorized as "exempt" by JHU IRB- no transfer of identifiable data and minimal risk.
- Anonymous complaint:
  - Should not have been exempt
  - Each hospital should have had IRB approval
  - Patient informed consent
- OHRP found
  - The JHU IRB erred in declaring it exempt
  - Subjects were both providers and patients
  - Consent should have been addressed

[1]Pronovost P et al. NEJM 2006; 355:2725

The Pronovost Affair

- Was it research from the perspective of the investigators at Hopkins?
- How about at the participating sites?
- How would one consent for:
  - System-wide change
  - Promoting evidence-based practice
  - Collecting data that hospitals are required to collect
- Or, an intrusion on patients to generate broadly applicable knowledge[2]

[2]Kass N et al. Joint Commission Journal 2008 34:349-353

Evolution at OHRP?

- July 2008- Pronovost asks for guidance on a new study- to expand CLABSI intervention to multiple hospital systems and study whether Michigan effects were replicated.
- OHRP determined that
  - At each hospital site, the intervention was not research
  - The analysis of aggregate data was research, but not human subjects research (since no identifiable private information, and no interaction with participants).

OHRP says:

- …where the implementation of a program is being studied, and important issue is whether the the regulations apply to the program itself, or only the information collection activities used to study the program….The question to ask is 'Is the program implemented for a research purpose, or altered or controlled in some way to answer a research question? If project leaders, [and hospital leaders] answer this question 'no' then the program is separable from the research for that hospital."

OHRP Letter to Johns Hopkins, July 30, 2008

Does prospective data collection always constitute research?

- From medical records
- From patient reports
- Does the magnitude of the burden matter?
- How about risks to privacy– or is that now "covered" under HIPAA?

IRB needed? Considerations for single site improvement projects

- Are interventions to promote standard or established care?
- Does the project further the goals of the clinical leadership and team?
- Are there additional risks to patients because the project is underway?
- Are data collection burdens consistent with what is expected in routine care and organizational improvement?
- Are there reasonable additional privacy concerns?

Do the following always constitute research?

- Comparison groups?
- Factorial designs?
- Randomization at any level?
  - Hospitals
  - Wards
  - Individuals

CAN FEDERAL REGULATIONS EVOLVE?…

…well, sort of.

Notice of Proposed Rule Making (NPRM) to Modernize the Common Rule (9/8/15)

- By HHS and 15 federal agencies
- Followed an Advanced Notice of Proposed Rule
  - Exclusions for activities that are not research, are low risk, or covered by other protections
  - New process for exemption without IRB review
  - Requirement for a single IRB for multi-center studies
  - Extend scope to cover all clinical trials (regardless of funding source) at any institution that receives federal funding

The New Common Rule

- Process of revision of the Common Rule undertaken over a 3 year period (ANPRM, NPRM, comment, comment, comment).
- Proposed rule **would have** explicitly excluded "*Quality assurance or improvement activities involving the implementation of an accepted practice to improve the delivery or quality of care or services if the purposes are limited to altering the utilization of the accepted practice and collecting data or biospecimens to evaluate the effects on the utilization of the practice.*"

The New Common Rule

- The QA/QI exclusion got lots of pushback from many.
- It was **NOT** adopted as part of the final rule which is silent on QI…"The proposed exclusion for certain quality assurance/quality improvement (QA/QI) activities has been dropped because it could create more confusion than it resolved, and it might have inadvertently created inappropriate obstacles to those QA/QI activities that should not fall under the rule." {Common rule, federal register (link below)}
- Leaving us to existing definitions and determinations of research vs. operations.
- **Revised Common Rule Regulatory Text**
- **OHRP Quality Improvement FAQs**
- **OHRP Decision Charts**

But…a fair bit of clarity from OHRP-FAQ's

- https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html
- QI does not need IRB review. Research does. QI includes:
  - Implementing a practice to improve the quality of care
  - Collecting patient or provider data regarding implementation for "clinical, practical, or administrative uses."
- Research definition remains based on "systematic investigation…to contribute to generalizable knowledge"
- Human subjects definition per HHS
- Minimal risk research can receive expedited review (not exemption).

[1]See https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html

Intent to publish as a sole criterion: a clear "no." (Not new)

- OHRP: "No, the intent to publish is an insufficient criterion for determining whether a quality improvement activity involves research. …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."[1]
- **However, such dissemination must be described as a QI activity, and not make claims of new knowledge generation using typical standards of clinical or health services research.**

[1] https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html

We haven't revoked the need to act ethically just because we do QI

PCORnet Task Force on Ethical Issues in Pragmatic Trials

- What QI activities should have explicit ethical oversight in order to help ensure adherence to fundamental ethical principles of health care?
- Are there special considerations in the oversight of pragmatic QI research activities that optimally protect patients and other participants yet allow for rapid system learning?

Finkelstein et al.

Some of the issues

- Routine vs. non-routine
- Who decides?
- Who oversees?

nder review)

One more example: cluster randomized trial

- Randomized 43 hospitals (in a single for-profit chain) to 3 arms commonly used to address MRSA colonization in ICUs
- All were in routine practice at some hospitals
  - Decolonize everyone on entry
  - Surveillance cultures- isolate those positive
  - Surveillance cultures- decolonize those positive
- Implemented by local ICU, quality, and infection control staff
- Outcome data from automated systems

- QI or Research?
- Informed consent needed by patients? Providers?

Huang SS et al. NEJM 2013

- Deemed research, most hospitals delegated to a single IRB.
- Individual consent deemed unnecessary. IRB required posted signs informing patients of the study.
- Results: 44% fewer blood stream infections

Examples

- A clinic increasingly utilized by decisionally impaired patients implements a widely accepted capacity assessment as part of routine standard of care in order to identify patients requiring special services and staff expertise. The clinic expects to audit patient charts in order to see if the assessments are performed with appropriate patients, and will implement additional in-service training of clinic staff regarding the use of the capacity assessment in geriatric patients if it finds that the assessments are not being administered routinely.

Examples

- A radiology clinic uses a database to help monitor and forecast radiation dosimetry. This practice has been demonstrated to reduce over-exposure incidents in patients having multiple procedures. Patient data are collected from medical records and entered into the database. The database is later analyzed to determine if over-exposures have decreased as expected.
- A group of affiliated hospitals implements a procedure known to reduce pharmacy prescription error rates, and collects prescription information from medical charts to assess adherence to the procedure and determine whether medication error rates have decreased as expected.

Example Continued

- Research
  - Problem : There is variation in hospital regarding the implementation of visitor policies and it is unknown whether these variations impact patient satisfaction.
  - Hypothesis: Liberal visitation decreases family anxiety and increases satisfaction
  - Research-There are two surgical floors. One floor is randomized to follow the strict visitation policy the other floor is to be more liberal (study defines what that will be)
  - Obtain consent for 50 patients on each floor
    - Anxiety score and patient satisfaction to be determined on each subject at discharge on validated visitor instrument
    - Perform t tests for significant differences in mean score

Children's Hospital Colorado

- Organizational Research Risk and Quality Improvement Review panel (ORRQIRP)
  - IRB sanctioned with ad hoc members from IRB
  - Multidisciplinary- legal, risk, med staff, quality, nursing, research
- Considers IRB approved studies that might pose institutional risk (e.g. brain biopsy in fatal tumor; study of use of TCH by patients with epilepsy)
- Reviews quality improvement projects upon request of investigator (nursing requires submission)

COMPARISON OF THE CHARACTERISTICS OF RESEARCH, QUALITY IMPROVEMENT, AND PROGRAM EVALUATION ACTIV

	RESEARCH	QUALITY IMPROVEMENT	PROGRAM EVALUATION
INTENT	☐ Intent of project is to develop or contribute to generalizable knowledge (e.g., testing hypotheses)	☐ Intent of project is to improve a practice or process within a particular institution or ensure it confirms with expected norms	☐ Intent of project is to improve a specific program
DESIGN	☐ Designed to develop or contribute to generalizable knowledge; may involve randomization of individuals to different treatments, regimens, or processes	☐ Not designed to develop or contribute to generalizable knowledge; generally does not involve randomization to different practices or processes	☐ Not designed to develop or contribute to generalizable knowledge; does not involve randomization of individuals, but may involve comparison of variations in programs
MANDATE or ENDORSEMENT	☐ Activities not mandated by institution or program	☐ Activity endorsed or mandated by the institution or clinic as part of its operations	☐ Activity endorsed or mandated by the program, usually its funder, as part of its operations
EFFECT ON PROGRAM OR PRACTICE EVALUATED	☐ Findings of the study are not expected to directly affect institutional or programmatic practice	☐ Findings of the study are expected to directly affect institutional practice and identify corrective action(s) needed	☐ Findings of the evaluation are expected to directly affect the conduct of the program and identify improvements
POPULATION	☐ Usually involves a subset of individuals - universal participation of an entire clinic, program, or department is not expected; generally, statistical justification for sample size used to ensure endpoints can be met	☐ Information on all or most receiving a particular treatment or undergoing a particular practice or process expected to be included; exclusion of information from some individuals significantly affects conclusions. Initial work can be limited to a smaller subgroup to identify and plan for implementation or feasibility etc. with the expectation that the practice or process will be extended to the broader population.	☐ Information on all or most participants within or affected by receiving a particular treatment or undergoing a particular practice or process expected to be used; exclusion of information from some individuals significantly affects conclusions
BENEFITS	☐ Participants may or may not benefit directly – benefit, if any, to individuals incidental or delayed	☐ Participants expected to benefit directly from the activities	☐ No benefit to participants expected; evaluation concentrates on program improvements or whether the program should continue
DISSEMINATION OF RESULTS	☐ Intent to publish or present generally presumed at the outset of project as part of professional expectations, obligations; dissemination of information usually occurs in research/scientific publications or other research/scientific fora; results expected to develop or contribute to generalizable knowledge by filling a gap in	☐ Dissemination of information may occur in quality improvement publications/fora; when published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable knowledge. Any publication should footnote that the project was carried out as QA and did not meet the definition of	☐ Intent to publish or present generally presumed at the outset of the project; dissemination of information to program stakeholders and participants; may be publicly posted (e.g., website) to ensure transparency of results; when published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable

Boston

- Quality committee of the Department of Pediatrics reviews projects submitted by project leaders to provide guidance on whether IRB review is appropriate.
- Brief (2-3 page proposal)
- Final decision remains with project leader/investigator
- If deemed QI, clinical program leaders must take responsibility for ethical oversight, as they do for clinical processes

Boston

Criteria for consideration (none are determinative)

Consideration	Yes	No	Explanation (if needed)
Is the project primarily designed to improve care locally (i.e. bring care in line with accepted standards)?			
Is the project designed primarily to create new, generalizable knowledge?			
Are personnel who provide the care involved in the project, and do they view it as desirable for improving care?			
Does the project use any experimental medications or devices, or processes of care that others in your field would consider experimental?			
Does the project test a specific scientific hypothesis about biology or human behavior?			
Does the project test a change (or multiple cycles of change) in how care is delivered?			

Boston

- Criteria for consideration (none are determinative)

Is there randomization at the patient level?			
Is there randomization at another level (e.g. physician, unit, day of week)?			
Does the project receive any research funding (internal or external)?			
Is the data collection commensurate with that commonly used in quality improvement activities?			
Will data be transferred outside of Boston Children's Hospital (if so, please note whether all data transferred will be de-identified)?			
Are there any risks to subjects beyond a minimal risk of loss of privacy?			

Even if it's QI…BCH QI Letter

- If you move forward with this work as QI, it does not fall under the authority of the IRB…. the clinical division or program continues to have responsibility for the QI work undertaken as part of this project- just as in all aspects of clinical service delivery and uses of health information. The Division Chief (Dr. XXXXXXXXX) is copied on this communication and must be made aware of all aspects of this project that involve patients or their data and ensure that adequate protections are in place. For example, patients should understand that direct participation in quality improvement related data collection beyond direct clinical care (e.g. patient surveys) is voluntary. Of course, patients may be indirectly engaged in quality improvement activities as clinical processes of care are changed to better align with accepted standards. Consent for participation in this way is not required, since such improvements are part of changes in routine care processes.

BCH QI Letter

- Publication: This is acceptable as long as the primary goal of the activity was not primarily generalizable research, but rather local care improvement, and that no research funding was used to support the activity. Of course, the published work must be reported as QI (and not research), no identifiable individual patient level data can be included, and all HIPAA regulations apply, including having appropriate Data Use Agreements (DUA) or Business Associate Agreements (BAA) in place. Some journals still maintain requirements for IRB approval for any work considered for publication. Project leaders should investigate the requirements for journals to which they might submit.
- If any aspects of this project change in ways that might impact this determination (e.g. significant additional data collection burden for patients) you should submit them in writing …for an opinion prior to implementation. Questions about whether particular activities constitute human subjects research can also be directed to the Human Subjects Committee.

Summary

- QI as part of health care operations does not require *IRB oversight*, but still may require *oversight*.
- The current definitions and requirements were not designed with current types of QI-research in mind- and can cause difficulties in the evolution of an efficient, learning health care system…
- …but the fog is starting to clear.
- We are <u>all</u> responsible for acting within current regulations *and* facilitating the evolution within our institutions and nationally of improved processes.