APPENDIX C

Boundary Between Research and Practice: Reports From the Four Domains

In this appendix, we report the deliberations of four working groups that participated in the April 2011 “think tank” meeting. The challenge to the think tank called for defining conditions within practice which could inform the decision whether or whether not to subject practices to some form of ethics review. A second challenge requested participants to consider ethics review mechanisms short of the institutional review board (IRB) which might suffice for these reviews on the “boundaries” between practice and research.

To prepare for these considerations, members of the think tank were divided into four working groups—one for each of the practice domains—to consider circumstances on the boundary involving clinical practice, public health practice, community engagement, and quality improvement.

Experts with experience in each of the four “boundary domains” were invited to participate in the think tank and were asked to focus on aspects of their specific areas of interest which can lead to ambiguity and confusion (or even contention) around the question of whether independent ethics review should be required and discuss alternative review mechanisms.

CLINICAL INNOVATION

Clinical innovative practice includes medical and surgical activities that are not completely supported by efficacy and safety studies or agreed practice guidelines. Surgical innovative practices include such activities as autologous bone marrow transplants for some non-malignant conditions and use of the latest medical device or surgical equipment. Medical innovation includes off-label use of medications and creative strategies for patients who fail conventional approaches.

Treating physicians frequently have no choice but to “experiment” with a variety of procedures and treatments in an attempt to find the best treatment for their individual patients who do not fit into a convenient or simple category. The “art of medicine” requires it. Some of these activities will have beneficial or harmful results, and yet there is no prescribed or accepted system for collecting the data from these activities. Such activities would not usually meet the regulatory definition of human subjects research.

What constitutes “innovative” may be subject to debate. Innovative practice is sometimes defined as a procedure that lies on a “continuum between research and practice,” in that it derives from completed research (that underwent IRB review), but which is so new that practitioners do not have sufficient experience employing the practice to know when it will be
APPENDIX C

most effective. However, some new applications of a standard practice might also be considered innovative. New uses for approved drugs may also constitute innovative care. Using the image of a continuum between research and practice, such activities might lie in a place that precedes research, and, if done repeatedly or systematically for the purpose of collecting data on the safety and efficacy of the new approach, might fall within the regulatory definition of “human subjects research.” Understanding what type of ethical oversight is warranted for activities along this continuum is the goal of this discussion.

Logistics alone preclude referral of all innovative practice to external review. While exact benchmarks are elusive, reviews estimate that 80% of pediatric and 30% of adult care require decision-making outside of well-agreed evidence and guidelines. Only 20% of medications have been adequately tested in children or the elderly before approval. Evolving use of automated practice-based data and electronic medical records permits routine collection of information about such incompletely proven questions from actual practice and, though systematic, is an integral part of day-to-day practice.

In considering the extent to which an innovative practice might entail more than minimal risk or more risk than other approved or documented interventions, and therefore require a more formal review, the clinician/practitioner must depend on professional training in risk and the evaluation of clinical evidence. Often the presence of a skilled colleague or consultant can help to tip the scales toward or away from more formal review of such practices.

The emergence of formalized networks for practice-based research in clinical care settings poses a specific challenge to formal ethics review. Many practices undertake research which clearly meets the definition of human subjects research; however, these practices may not be based in formal academic settings and may not have connections to local IRB review. Thus, arrangements are necessary to assure that the overall projects from these networks receive the requisite level of human subjects protection review from at least one formally constituted IRB.

Attributes that Require IRB Oversight

- When the proposed activity meets the definition of human subjects research and is not in the category of “exempt” under Federal Regulation

- When the activity entails systematic collection of data (e.g. for the purpose of confirming or contradicting a medical theory or hypothesis).

- When the innovative practice significantly differs from normal practice

- When the innovative practice carries more than the minimal risk for complications, or significantly more risk than alternative, approved interventions

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When the institution engaging in the innovative practice requires explicit consent

**Attributes that Require Other Oversight**

Some type of prospective ethics review is necessary for innovative practice that deviates from the standard of care and entails more than minimal risk (including activities in which the possibility of more than minimal risk is not known until after the practice occurs).

**Attributes that Require No Other Oversight**

Innovative practices with minimal risk should not require any formal type of ethical oversight. However, the clarification of “minimal” may itself lead the practitioner to seek at least the informal ethical advice of peers.

**Other Items to Consider**

- Under what circumstances can unstructured peer review and expert consultation substitute for more formal review? How explicitly must the inquiry be understood as an ethical consultation?

- When data are collected more systematically than required for clinical care, what are the restrictions on their use (i.e. what is the “boundary” between personal professional accountability and broader information sharing)? Who could advise upon such matters?

**Conclusion**

Clinical innovation can involve sufficient risk and can be sufficiently intrusive to subjects to prompt some kind of ethical review. It is not ethical to vary treatment substantially from the standard of care, when one exists, without external assessment of risk and without informing the subject in advance and permitting the subject to refuse the treatment. Such substantial departures from the standard of care should be carried out only in circumstances in which data are systematically collected to evaluate the safety and efficacy of the innovation.

**PUBLIC HEALTH**

Public health practice has the purpose of improving the health of populations rather than of individuals. However, all populations are made up of individuals, and therefore any public health intervention perforce involves a possible or likely benefit offset by a possible inconvenience or risk of harm. Public health activities involve a wide range of well-tested and widely accepted interventions. While these are imposed on individuals as parts of the communities in which they live, they are overseen by elected general purpose governments at the state and local levels, as well as multiple checks and balances in the public and private oversight of federal, state, and local funding and conduct of programs. Nonetheless, public health is by its nature required to be prepared to respond to the unexpected with extension of underlying public health science to
unprecedented circumstances. Thus, exploratory or innovative practice is part of essential public health service.

Likewise, public health adheres to the application at the practice level of the “ten essential public health services”

The 10 Essential Public Health Services

Assessment
1. Monitor health status to identify community health problems
2. Diagnose and investigate health problems and health hazards in the community

Policy Development
3. Inform, educate, and empower people about health issues
4. Mobilize community partnerships to identify and solve health problems
5. Develop policies and plans that support individual and community health efforts

Assurance
6. Enforce laws and regulations that protect health and ensure safety
7. Link people to needed personal health services and assure the provision of health care when otherwise unavailable
8. Assure a competent public health and personal health care workforce
9. Evaluate effectiveness, accessibility, and quality of personal and population-based health services

Serving All Functions
10. Research for new insights and innovative solutions to health problems

Source: Public Health Functions Steering Committee (1994).

These include collection of extensive data at the individual level for the purposes of disease surveillance and population infection and epidemic control (essential services 1 and 2); data for planning and implementation of population level protections and health promotion activities and medical care access; program evaluation for continuous process improvement (essential

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APPENDIX C

service 9); and research (essential service 10). Stated differently, all public health agencies are expected, as part of their essential mandatory functions, to be collecting and applying information which will contribute to general knowledge for the protection of the public’s health and for improvement of the specific public health practice being applied.

Public health research (and other data collection/interpretation efforts) may be carried out by academic researchers, but may also be part of the responsibilities of practitioners, including epidemiologists, engineers, urban planners, academics, and other government personnel. Practice standards exist for routine public health activities and projects, such as disaster response plans, outbreak investigations, surveillance, and program/project evaluation.

Even the fundamental practice of public health program planning and funding requires often gravely important ethical considerations. What gets funded gets done, and what does not, does not, resulting in depriving whole segments of the population or neglecting whole areas of population need. In the absence of clear practice guidelines, ethical oversight of such interventions (or withholding of interventions) often falls to the governing bodies of public health.

Public health research raises similar ethical concerns to those of other practice-based research activities. Respect for autonomy, for example, may or may not be relevant in the context of certain public health initiatives. On the one hand, we elect government to oversee its own activities; on the other hand, not all government is adequately sensitive or responsive to the populations upon which its public health interventions may have adverse impact. Members of the population under study (or subject to an innovative or untested intervention) may not be able to either consent or withdraw from the activity, even research. ³ And, yet, individuals may be at risk from such research. Stigmatization of the study population is a potential risk of public health research. Invasion of privacy, breach of confidentiality, infringement of certain liberties are all risks relevant to public health research. For these reasons, many public health interventions border on research. Like the dilemma with innovative clinical practice, innovative public health practice occurs along a continuum that differs only slightly from “standard practice” (e.g., to accommodate a special circumstance) to that which is required to address conditions for which there is no standard response. Likewise, the risk of such innovative interventions will vary along a continuum, from those with minimal apparent inconvenience (e.g., recommending paved sidewalks as a “likely” strategy to reduce obesity) to those with considerable potential risk (e.g., requiring immunization against smallpox in a vaccine-naïve population because of the theoretical, unproven, threat of a bioterror attack). When a program or intervention outside of standard, evidence-based practice is undertaken, and when the risk of potential harm is substantial, formal ethical review is needed.

Even in cases where practitioners/researchers never come into contact with research subjects, these may demand ethical review to ensure that the risks and uncertainties of such projects are

justified by the potential benefits. Such analysis may best be achieved through the review and monitoring by some objective independent body, other than an IRB. Conversely, however, most innovative public health interventions do not involve significant or unanticipated risks to individuals or uncertainties about their efficacy. They occur every day in the course of public health practice and cannot reasonably be expected to undergo regular or formal review. Rather, they are overseen as part of responsible governance.

Thus, however, it is imperative that those conducting public health practice and its oversight be trained in the ethical principles of human subjects protection and, themselves, be regularly held accountable.

Attributes that Require IRB Oversight

- When the proposed activity meets the definition of human subjects research
- When public health intervention involves substantial risks to humans beyond those of daily living in the communities in which the effort is undertaken

Attributes that Require Other Oversight

- When the activity does not meet the regulatory definition of “research” but is outside the parameters of accepted clinical practice
- When the activity falls under the jurisdiction of agencies that require governance and/or review by entities other than the IRB
- When the activity involves risk to investigators or their staff
- When there is modest/less than substantial risk of physical harm or infringement to dignity
- When there is a risk that encrypted information will be reassembled and de-anonymized by those outside the immediate agency with professional and/or research responsibility

Attributes that Require No Other Oversight

All activities constituting “accepted” public health practice within the framework of widely understood evidence based endeavors (e.g. those supported by adequate evidence),[^4] and those along the minimal exposure end of continuum of risk and uncertainty. In general, these include those activities mandated by statute and/or in implementation of public health rules and regulations.

Other Items to Consider

- Who consents when a community is the subject of the innovative practice or research?

APPENDIX C

- Who determines the value of the program goals?\(^5\)
- When is the public health program manager/implementer the patient advocate and when is he or she acting as the researcher or on behalf of the larger community?
- Who is the arbiter of harm and uncertainty and how is it assured that adverse consequences are incorporated into public health program evaluation?
- Who should determine the circumstances under which an ordinarily exempt activity should be referred for prior ethical review and who can decide in the absence on an impractical “every project” review basis?
- Who assesses, and how, the consequences of infringement on rights, including dignity and privacy?
- Who should determine where to commit resources for ethical safeguards?

Conclusion

As for all research, an oversight body should consider whether the risks of harm are reasonable in the light of the potential benefits of the activity. However, public health activities and interventions, including innovative practices or even specified research, may fall under the jurisdiction of agencies that provide oversight independent of formally constituted ethics boards or IRBs. For most innovative public health practices with minimal deviation from standard activity and low risk of harm, no formal external review is feasible or necessary.

QUALITY IMPROVEMENT

Quality improvement (QI) activities involve ongoing monitoring of clinical and/or organizational activities, introduction of innovative methods which might be expected to improve things, and evaluation of the impact(s) of those interventions, with an eye toward adoption or possible further improvement. Thus, all quality improvement activities represent some form of deviation from standard practice, whether clinical or managerial. When conducted correctly, quality improvement activities are systematic and evidence-based efforts that have the intention of improving the quality and efficiency of a local healthcare practice.

Quality review and improvement are inherent in the managerial process, and lack specific involvement of human subjects. Traditional IRB review would not be relevant. However, there are some ethical questions that are raised by these activities even when they do not require informed consent or a higher scrutiny review.

In some cases it is difficult to discern whether an activity that is described as QI is more like clinical innovation (discussed above) or a managerial change intended to improve outcomes or reduce costs. Like other innovative practice, QI activities are frequently modified as the activity progresses. Changes are made, then assessed and then tweaked and reassessed in a continuous cycle (e.g., continuous quality improvement or CQI). Changes are ongoing, often ad hoc based on interim experience, making it difficult to use the traditional IRB model as a review.

mechanism. Patients do not expect to be informed of some of these changes institutions make (e.g., changes in soap brands or shift changes). However, when it comes to changes involving clinical innovations with more than minimal differences in risk of harms beyond those of customary care, such as spinal taps after new operating procedures, some argue that the institution should seek patients’ consent, and the intervention should be required to receive human subjects protection review. Even then, such interventions, conducted within the institution and based on other standards for CQI, may be understood as not “designed to contribute to generalizable knowledge” and still exempt from IRB review.6

**Attributes that Require IRB Oversight**
- When the proposed activity meets the definition of human subjects research

**Attributes that Require Other Oversight**
- When the activity is intrusive for the patient
- When the predicted level of risk is more than minimal
- When clinical practices are directly affected
- When the activity is part of a general operational change
- When the activity is to be implemented throughout the organization
- When the proposed system for collecting data carries risk to privacy or confidentiality
- When there is potential conflicts of interest such as may exist when funding for the activity is from an external source
- When patients must consent to the release of information

**Attributes that Require No Oversight**
Perhaps, the most effective approach to ensure ethical conduct of quality improvement is at the overall program/organizational level. Within the context of an ethical organizational program, individual quality improvement activities should be excused from detailed ethical review.

**Other Items to Consider**
- How do you create ethical benchmarks in the area of quality improvement, in which changes are constantly being implemented and revised?

**COMMUNITY ENGAGEMENT FOR COMMUNITY-BASED PARTICIPATORY RESEARCH**

Community engagement entails efforts beyond those historically required or pursued to achieve health practice objectives, including improvements in health care delivery, cultural adaptation of public health programs, and, of course research.

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APPENDIX C

Those engaged in research and knowledge development activities have often aggressively pursued community engagement as a means to ensure the quality and relevance, as well as acceptance, of their work. Community-based participatory research (CBPR) is a "collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities."\(^7\)

Such research has become more prevalent in recent years as a way to assess the impact of social and environmental factors on health and behavior. The chief distinction between CBPR and more traditional models of research is that in the case of CBPR the research “subjects” play an active role in carrying out the research itself, whereas in more traditional research models the subjects play a more passive role. In addition, CBPR may create risk for an entire community, and not just the actual participants. The scope of CBPR is also more difficult to define than traditional research depending on the numbers of people and organizations that may be involved in developing the research question and negotiating the respective responsibilities of the participants.

Certain mechanisms have been developed to handle some of these issues. Since collaboration between researchers and communities is critical to the success of CBPR, Community Advisory Boards made up of prominent members of the community to be studied are often formed to promote community engagement in the research. In addition, research collaborations may be strengthened by well-developed memoranda of understanding that describe the project, its goals and the responsibilities of the parties. These tools are useful for minimizing the risks of CBPR.

Despite its different nature from more conventional research approaches, there is no explicit exemption from current regulations for CBPR, although in some cases exemptions may apply as they would to any other type of research. As a result there is uncertainty about how to minimize risks and conduct such research ethically.

When research is conducted within and about a particular community it is sometimes difficult to identify the subjects and the researchers. For example, if the research involves the study of participants in a chat room, how would the researcher go about obtaining informed consent? Sometimes the “researchers” are members of the community who initiate a project for the benefit of the community. They are members of the community studying the community.

In most cases, community based research is dynamic and not suited to adherence to a strict process of protocol development and implementation. Nevertheless, there are risks involved in CBPR that may warrant IRB review such as community stigmatization (e.g., a study of parental attitudes toward optometry for children in a Latino, immigrant population). In this example the stigma might be that the community develops an adverse reputation for providing inadequate parenting or health care for its children. Other risks such as maintenance of sensitive data may

\(^7\) Kellogg Health Scholars. 2012. Accessible at: http://www.kellogghealthscholars.org/about/community.cfm.
be one that could be monitored by a group other than a formal IRB, such as a Community Advisory Board.

Finally, there are many, perhaps most, community engagement activities that may require no ethics oversight at all. The community is engaged when practitioners formally educate the community about their health care and rallying their support for improvements (including continuous improvements).

Much community based health improvement work involves descriptive, non-interventional studies and secondary analyses of public data. (For example: an examination of the number of children born to immigrants within five years of moving to the community, or a focus group on shopping habits.) When data are collected to inform a specific effort or answer a specific question, often an oversight body is designated or created to monitor the project’s data ownership, including such issues as what happens to the collected data and information after the research project finishes; whether damaging information will be exposed; and how the information is being collected and vetted. Ideally, this oversight body also monitors those activities in which data collection is a peripheral part of the project and is not the focus of the intended intervention. Such an oversight body should also review any formative and preparatory activities in which the field workers themselves are facing harm.

Often, those conducting CBPR draw up a memorandum of understanding with community groups with which they are working to detail what falls under the purview of the community advisory board or other body that is overseeing the project. Additionally, small panel groups could meet regularly with community members to review ethical issues. There could also be a body that oversees student research and student mentorship.

In some situations, planning and development activities comprising personal interviews and focus groups may require some sort of oversight. Again, it is given that activities that meet the regulatory definition of “human subjects research” would be reviewed and monitored in accordance with the applicable regulations regardless of whether the activity takes place in collaboration with and in the context of a defined “community” and with its active participation. Such activities may have some or all of the following characteristics:

- Intended to test a hypothesis
- Participants or the community are exposed to a risk of harm that is tangentially connected to the larger research project
- Involve risks to physical and emotional well being and activities that risk stigmatization of the entire community

Attributes that Require IRB Research Oversight

- When the proposed activity meets the definition of human subjects research
- When the community engagement itself involves substantial risks of harm beyond those of daily living in the communities in which the effort is undertaken
APPENDIX C

Attributes that Require Other Oversight

- When the activity falls under the jurisdiction of agencies or entities outside the purview of the academic institution which have their own requirements for ethical review
- When the activity involves risk to investigators from outside and within the community or their staff
- When there is risk of physical harm or infringement to dignity to any individual or community group

Attributes that Require No Other Oversight

Ethical oversight is not necessary in reviewing many aspects of formative and preparatory work in which field workers and community participants or potential subjects do not face any significant risk of harm. Similarly no oversight is required for minimal-risk data collection activities, particularly assembly of secondary data for project planning and prioritization.

Other Items to Consider

- Does the intent of the activity determine what oversight body reviews the project? When academics are working in an engaged community, must the ethics mechanisms in academia and community both be consulted/approval from both sought?
- In activities that involve community-level harms, what oversight body is capable of assessing and mitigating those harms?
- What is the definition of ‘risk of harm’ to a community? Is it a term relative to the benefits of the activity?

Conclusion

Community engagement for the purposes of health improvement poses potential ethical challenges. CBPR is particularly challenging in that projects are made up of multifaceted components, some involving research-like interventions in addition to the research focus of the project. Whether a component requires IRB review may depend on whether it is looked at as its own entity or as part of a larger project. Community engagement per se must be understood as an innovative practice, with the potential for harm as well as benefit.

The best way to ensure human subjects protection is by having an ethical researcher and research team. Since CBPR is initiated by different types of parties for different reasons, and by definition outside the four walls of the academic institution, not all of the engaged groups are familiar with IRBs and many do not have mechanisms that trigger or sustain ethics review. Good mentoring practices are needed within any institution engaged in CBPR to educate students, practitioners, researchers, and those engaged in human subjects protections.