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The Ethics of Information-Gathering Interventions in Innovative Practice

Jake Earl and David Wendler

jacobcearl [at] gmail.com

<https://www.jakeearl.net/>

ABSTRACT: Innovative practice involves medical interventions that deviate from standard practice in significant ways. For many patients, innovative practice offers the best chance of successful treatment. Because little is known about most innovative treatments, clinicians who engage in innovative practice might consider including extra procedures, such as scans or blood draws, to gather information about the innovation. Such information-gathering interventions can yield valuable information for modifying the innovation to benefit future patients and for designing scientific studies of the innovation. However, existing guidelines do not say when or whether it is appropriate to add potentially risky information-gathering interventions for these purposes. As a result, clinicians may assume that information-gathering interventions are ethically inappropriate and should not be used in innovative practice. This assumption can lead to seriously negative consequences, such as increasing the likelihood that harmful or ineffective innovations will be adopted and creating new barriers to the development of genuinely beneficial treatments. We argue that health care institutions need to promote the responsible use of information-gathering interventions as an adjunct to innovative practice, and that these interventions are not clinical research and should not be subject to research oversight.

Clinicians typically offer their patients standard interventions. However, there are no standard interventions for some conditions, and standard interventions are ineffective for some patients. Clinicians thus sometimes engage in *innovative practice*, offering their patients interventions that “depart in a significant way from standard or accepted practice.”[[1]](#endnote-2) Many therapeutic, diagnostic, and preventive interventions were developed at least in part through innovative practice, ranging from modest alterations in practice (e.g., antiseptic wound cleaning) to major technological leaps (e.g., robotics-assisted telesurgery).[[2]](#endnote-3),[[3]](#endnote-4) Innovative practice remains common in many fields, including surgery and reproductive medicine.[[4]](#endnote-5),[[5]](#endnote-6)

Despite its continued prevalence, innovative practice is poorly understood and ethically controversial. Critics worry that innovative practice has the potential to exploit patients and expose them to unwarranted risks. This is particularly troubling given that innovative practice is frequently not subjected to rigorous oversight.[[6]](#endnote-7) Proposed ethics guidelines would mitigate the risks of innovative practice by requiring prospective review by other professionals, enhanced informed consent procedures, and careful patient safety monitoring.[[7]](#endnote-8),[[8]](#endnote-9),[[9]](#endnote-10),[[10]](#endnote-11) Another way to mitigate the risks of innovative practice would be to include interventions that are not medically indicated—such as an extra blood draw, scan, or behavioral evaluation—but can yield valuable information about the innovation. Gathering this information has the potential to significantly improve clinical research and clinical care. However, there are few documented cases of such *information-gathering interventions* being performed as an adjunct to innovative practice, and their use appears to be rare. This is likely for several reasons.

First, there has been almost no discussion in the literature about information-gatheringinterventions. Hence, clinicians who offer innovative treatments to their patients may not be aware of the possibility of adding information-gatheringinterventions. Second, the few existing ethics guidelines on innovative practice do not address when information-gatheringinterventions might be appropriate. As a result, clinicians who would otherwise consider their inclusion might assume that they are ethically problematic. Third, given the lack of explicit guidance, clinicians who do perform information-gatheringinterventions as an adjunct to innovative practice might be reluctant to disclose their actions.

The current failure to add appropriate information-gatheringinterventions to innovative practice represents a missed opportunity to gather information that could be valuable for improving clinical care and clinical research. To address this problem, we argue that guidelines for innovative practice should be revised to encourage the responsible use of information-gathering interventions.

***Information-Gathering Interventions: Neither Care nor Research***

In 2010, a team of clinicians in Germany reported treating a patient using a novel deep brain stimulation (DBS) intervention.[[11]](#endnote-12) The patient had suffered from major depressive episodes for decades, and in recent years her symptoms could not be controlled by standard therapies. Based on their understanding of the neurology of depression, as well as ongoing investigations of DBS, the team concluded that the best option for the patient was stimulation of a new target area of the brain. Roughly four months after the first-in-human use of this innovative treatment for refractory depression, the patient achieved a full remission.

Prior to the innovative DBS treatment, the team performed a positron emission tomography (PET) scan to exclude other treatable causes of the patient’s depression. Several months after placing the DBS device, the team performed a second PET scan. The second scan was not medically indicated and was not used to guide the patient’s care. The Hamilton Depression Rating Scale was sufficient for monitoring the patient’s illness. Nonetheless, the second PET scan provided valuable information: it helped the team to verify successful modulation of the target area of the brain and to exclude alternative mechanisms of action for the patient’s observed improvement.

It is commonly assumed that clinical interventions are ethical in two contexts only. They are ethical when they are medically indicated and they can be ethical as part of valuable research studies. On this basis, one might argue that the second, information-gathering PET scan was unethical. It was clearly not medically indicated, as it exposed the patient to risks and burdens in order to gather information about the novel DBS treatment, not to promote her health. But the second PET scan was not part of clinical research either. The Council for International Organizations of Medical Sciences (CIOMS) defines health-related research as “activities designed to develop or contribute to generalizable health knowledge.”[[12]](#endnote-13) Although the second scan was intended to gather health-related information, it was not designed to yield *generalizable* health knowledge. The clinicians selected the patient for the DBS treatment because they believed it might benefit her, not because she was representative of the population of patients with refractory depression.[[13]](#endnote-14)

In our view, the fact that the second PET scan was neither medically indicated care nor clinical research does not necessarily mean that it was unethical. Instead, we believe the common assumption that all clinical interventions should be medically indicated or part of a formal research study is mistaken. The scan represents a third type of activity—an information-gathering intervention—which can be hugely valuable as an adjunct to responsible innovative practice. When they also pose sufficiently low risks to patients, information-gathering interventions can be ethically appropriate. We call, then, for the recognition of information-gathering interventions and their inclusion in innovative practice guidelines to encourage their use and ensure their ethical appropriateness.

***The Need for Guidance on Information-Gathering Interventions***

Administering the second PET scan to gather information about the DBS treatment’s mechanism of action was valuable in two ways. First, it provided information about the extent to which the DBS device successfully activated the target area of the brain. This information was useful for determining whether any adjustments might be needed to make the treatment more effective for future patients. Second, gathering information about the DBS treatment’s mechanism of action helped to screen out alternative mechanisms of action and identify potential confounders. This kind of information can be crucial for identifying appropriate hypotheses and methods for a rigorous research study of an innovation, as well as the appropriate timing for such a study. For example, if the second scan had been unable to detect whether the target area had been activated, this would have revealed the need to develop different data collection strategies before initiating a formal trial of the novel DBS treatment.

These considerations reveal that using information-gathering interventions as an adjunct to innovative practice can have significant social value. At the same time, they impose risks and burdens on patients for the benefit of others. While this raises important ethical concerns, imposing risks on patients for the benefit of others can be ethically appropriate in some circumstances. Quality assessment and quality improvement (QA/QI) activities impose additional risks and burdens on current patients to improve medical practice for subsequent patients at a given health care institution.[[14]](#endnote-15) Similarly, it is widely accepted that investigators can expose research participants to some risks in order to collect data that has the potential to improve care for future patients. These examples show that exposing patients to certain risks for the benefit of future patients can be acceptable when it is consistent with appropriate guidelines which ensure that the risks are low and the information to be collected is valuable.

This conclusion suggests that the problem with information-gathering interventions is not that they expose patients to added risks and burdens for the benefit of future patients. The problem is that clinicians who engage in innovative practice lack adequate guidance to determine when it is appropriate to add information-gathering interventions. Developing specific guidance encouraging the use of appropriate information-gathering interventions as part of comprehensive guidelines for innovative practice therefore should be a priority.

***Should Information-Gathering Interventions Be Subject to Research Oversight?***

Like research interventions, information-gathering interventions are not medically indicated care and impose risks and burdens on patients for the benefit of others. Without adequate oversight, information-gathering interventions might be performed when they are unnecessary, excessively risky, collect only low-value information, or proceed without patients’ informed consent.[[15]](#endnote-16),[[16]](#endnote-17) This suggests that, although information-gathering interventions technically are not research interventions, it might make sense to subject them to national and international requirements for clinical research oversight, including review and approval by institutional research ethics committees.[[17]](#endnote-18),[[18]](#endnote-19)

Developing a proposal for and approval by institutional research ethics committees can take months, which might prevent clinicians from using information-gathering interventions in the context of urgent innovative treatments. And because they are not engaged in research, clinicians engaged in innovative practice would often be unable to meet research ethics committees’ demands for a formal protocol, refined scientific hypotheses, and plans for systematic data collection and statistical analysis.6,[[19]](#endnote-20) These concerns suggest that information-gathering interventions in innovative practice should be subjected to research oversight only if there are no better alternatives for protecting patients.

Some commentators have argued to the contrary that publishing or otherwise sharing information gleaned from innovative practice constitutes that activity as research, and therefore it must meet ethical and regulatory requirements for research.17,[[20]](#endnote-21) However, intending to publish or share information about a clinical activity does not magically transform it into clinical research. Absent the possibility of generating generalizable health knowledge, innovative practice does not constitute research. Of course, clinicians should proceed with caution when communicating about innovative practice, with or without information-gathering interventions, and avoid making claims about safety or efficacy that are not supported by the available evidence.

***Ethical Considerations for the Use of Information-Gathering Interventions***

Information-gathering interventions in innovative practice are not inherently unethical care or research, but they nonetheless can raise important ethical concerns. For example, it would be unethical for a clinician to conduct multiple lumbar punctures on a patient to satisfy her academic curiosity about an innovative treatment’s effects on the central nervous system. It would also be unethical for a clinician to conduct an information-gathering psychological evaluation that she has misled her patient into believing is medically indicated care. To protect patients and avoid subjecting information-gathering interventions to inappropriate research oversight, guidelines for innovative practice need to include specific guidance on the use of information-gathering interventions (see Table 1).

Existing proposals state that ad hoc or standing committees in health care institutions should prospectively review plans for innovative practice.7­­–10 These reviews should evaluate whether the proposed innovative practice offers patients a reasonable chance of benefit and should require enhanced informed consent procedures to ensure patients understand the treatment’s innovative nature. We argue that clinicians also should be required to gather and share valuable information about innovative practice whenever feasible, potentially by adding information-gathering interventions.

Engaging in innovative practice without using appropriate information-gathering interventions can contribute to the widespread adoption of ineffective medical innovations.6,[[21]](#endnote-22),[[22]](#endnote-23) Prominent examples of heralded innovative treatments that later proved ineffective include high-dose chemotherapy plus autologous bone marrow transplant for breast cancer and percutaneous coronary intervention for stable coronary artery disease[[23]](#endnote-24),[[24]](#endnote-25) Information-gathering interventions are a powerful tool for gaining the kind of early insights that can be crucial for preventing the spread of harmful and ineffective clinical interventions.9,10

Innovative practice should be subjected to prospective review, and reviewers should ensure that clinicians use information-gathering interventions when they can collect information that is valuable for determining how best to treat subsequent patients or how best to design future research studies. As with innovative practice more broadly, oversight of information-gathering interventions can help address potential ethical concerns. Clinicians should minimize the risks and burdens of information-gathering interventions, and generally they should involve only minimal risk. Information-gathering interventions that pose greater than minimal risk should be considered only in exceptional circumstances, should face more stringent review, and should be permitted only when they promise significant social value. Clinicians should also prospectively inform patients that the information-gathering interventions are not intended for their benefit, but rather to help future patients who might receive the innovative treatment.

Should patients ever be required to accept information-gathering interventions as a condition of receiving innovative treatment?[[25]](#endnote-26) It seems appropriate to require patients to agree to information-gathering interventions that collect valuable information and pose minimal risk, such as an extra blood-draw or survey. Information-gathering interventions that pose greater than minimal risk, however, should be optional for patients. In either case, patients should give their informed consent to all information-gathering interventions, and this requires clinicians to clearly explain that they are not medically indicated for the patient’s health.

Innovative practice has yielded both important medical advances as well as harmful failures. The appropriate oversight and use of information-gathering interventions can help clinicians improve future clinical care and prepare for clinical research while minimizing the potential harms of innovative practice.

*Table 1: Ethical Guidance for Information-Gathering in Innovative Practice*

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| --- | --- | --- |
| ***Guidance*** | ***Justification*** | ***Implementation*** |
| Gather important information | Reduce risks for future patients and/or prepare for future research | Identify, plan, and execute interventions to gather valuable information |
| Prospective, independent review | Protect against clinician bias; identify ways to improve information-gathering | Seek critical evaluation of plans from peers and institutional officials and address any concerns |
| Minimize risks and burdens for patients | Nonmaleficence | Use the least risky intervention necessary to gather desired information |
| Fully inform patients | Respect for autonomy; reinforce patients’ understanding of risks of innovative practice | Explain innovative nature of activity, risks of information-gathering and lack of clinical indication |

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