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Applicability of a Function-Based Approach to Informed Consent in International Settings

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Informed Consent; Culture; International Research

The requirement for U.S. investigators to obtain “traditional” in-depth informed consent consisting of the eight “required” elements when performing collaborative research in international settings can present significant cultural challenges to obtaining individual informed consent and hence, preclude the conduct of important research. The Common Rule, however, offer flexibility by specifying four criteria for when a waiver of consent can be approved or when any of the eight required elements of informed consent can be “altered” (the same standards apply to both situations). These criteria include: (1) subjects are exposed to no more than minimal risk; (2) the waiver or alteration does not adversely affect subject rights and welfare; (3) the research could not practicably be carried out without the waiver or alteration; and (4) subjects will be provided with additional pertinent information after participation, when appropriate (U.S. Department of Health and Human Services 1991a). However, IRBs may interpret the “impracticableness” requirement narrowly; use variable concepts of “minimal risks”; and link participants’ “rights” exclusively to autonomy interests, which may not be relevant in other cultural contexts.

Neil Dickert and colleagues reframe the concept of a “valid” consent by detailing other ethical functions that consent promotes, beyond that of an autonomous authorization. Several focused at the participant level include: (a) providing transparency; (b) allowing control and authorization; (c) promoting concordance with participants’ values; and (d) protecting and promoting welfare interests (Dickert and et.al. 2017). Their analysis helps them argue that it would still be ethically meaningful to partially engage potential participants in enrollment decisions with an “altered” consent process rather than a complete waiver in certain types of research. Our agenda is different, as we intend to show how their additional ethical functions can broaden the meaning of “impracticableness” and expand on the concept “rights” to justify an “altered” consent process rather than requiring a traditional in-depth informed consent in international settings where different cultural norms exist.

We anchor our discussion on a case involving a randomized cross-over trial comparing adjuvant treatment surgical oophorectomy and tamoxifen against a placebo group for breast cancer in Vietnam that took place in 1992–3 and represented collaborative research between U.S and local investigators (Love and Fost 1997). Due to lack of resources and systems of care in Vietnam, systemic adjuvant treatments were only occasionally used and when administered, followed regimens unlikely to achieve effectiveness.

The investigators were made aware that it was not customary in Vietnam for patients to participate in their own medical decisions in the way that is normative in Western cultures. Patients expect and look to their physicians to tell them the appropriate treatment; Western notions of informed consent is inconsistent to a paternalistic style that is preferred by Vietnamese patients. While it was believed that it might be technically possible, though difficult to discuss with Vietnamese women about alternative options, an informed consent process that included alternative interventions would not be functionally relevant, as patients would defer to their doctors' decisions regarding treatment decisions. In addition, it is unacceptable for a physician to openly express uncertainty about what is the best intervention (Love and Fost 1997).

As such, the investigators requested from the U.S. institutional review board (IRB) to use an “altered” consent process that would waive elements conveying uncertainty by the treating doctor – not disclosing alternative therapies and not disclosing that the proposed treatment had been determined by the process of randomization. The U.S. IRB disagreed and rejected the request to “alter” the elements of informed consent, although they agreed with including less detailed information.

How might a “function-based approach” of a “valid” consent justify an “altered” consent process? Regarding the “impracticableness” criteria, this usually refers to methodological issues (e.g., consent bias affecting scientific validity) or logistical constraints (e.g., feasibility of contacting patients for their informed consent for retrospective record research). However, the impracticableness of achieving comprehension in other cultural contexts, as demonstrated in the Vietnam study, is rarely considered by Western IRBs due to the prescription to ensure autonomous authorization. Where there are deeply rooted cultural beliefs, such a position can conflict with other values and interests considered culturally important by the participants; consideration of existing cultural norms aligns with the ethical function of “promoting concordance with participants' values”. An “altered” consent would have respected participants' values regarding how they interact with the medical profession and enhance the extent to which their decisions reflected “who they are” and “what they care about” (Brudney 2009). In contrast, efforts at enhancing comprehension maybe met with resistance engendered by fears of cultural imperialism that would result in potential participants being less accepting of the research. Despite extensive efforts to enhance understanding, the monitoring survey performed after trial completion showed it was unclear whether the participants understood that their treatment was determined by randomization.

The criteria involving “rights” is usually interpreted as reflecting important autonomy interests that should not be adversely affected by an altered consent. But cultures may differ on the weight they place on the value of self-determination as being instrumentally valuable

in promoting a person's well-being. Rather than determining whether an "altered" consent might hinder a narrow concept of "rights", Western IRBs should instead determine whether an "altered" consent would better respect relational concepts of persons and permit "high social value" research that advances the common good (Wertheimer 2015). Such research would promote "concordance with individual participants' values", especially in settings where community and solidarity represent fundamental cultural values, as opposed to the emphasis on individualism that exist in Western settings.

The criteria that a waiver or an "altered" consent be restricted to research that presents no more than minimal risks (i.e., research without appreciable net risks) serves to advance the ethical function of "protecting participants' welfare interests". Dickert and colleagues agree with this viewpoint when they state that when research "intrudes on bodily integrity or privacy", then authorization of enrollment by participants becomes important (Dickert and et.al. 2017). Other authors also agree that the function of autonomous authorization should vary depending on the risk-benefit profiles of the research (Miller and Wertheimer 2011).

While the minimal risk standard should serve as a threshold for a waiver of consent, we question whether this standard should be normative for an "altered" consent. There are several reasons to maintain that an altered consent can be approved in greater than minimal risk research (i.e. net risk research), particular in international settings under certain conditions.¹

First, we look towards the federal regulations involving children (Subpart D) where non-beneficial research is permitted when the net risks are greater than minimal risk (specifically, no more than a minor increment above minimal risk) and "likely to yield generalizable knowledge...which is of vital importance for the understanding or amelioration of the subjects' disorder or condition" (U.S. Department of Health and Human Services 1991b). In such situations, the child's assent, if appropriate, serves as an important protection safeguard. The ethical function of "control", however, represents a greater safeguard than mere assent. That participants in the Vietnam study exerted such "control" was confirmed by the monitoring performed in the Vietnam study that suggested the participants understood they could refuse to be in the study². Dickert and colleagues do recommend additional mechanisms to "advance other consent-related functions that cannot be realized by consent". Accordingly, in the Vietnam study, "surrogate" groups were established to ensure that participants' interests would not be violated by their participation in the study.

Second, net risk research can be permitted, as explained in Subpart D, when justified by the "vital importance" of the research, which was explained by the National Commission as holding "the promise of significant benefit" that may require "the advice of scientific consultants" (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979). Research of "vital importance" can be interpreted as being analogous to "high" social value research mentioned previously that would "promote concordance with participants' values".

¹ One could argue that the Vietnam study presented net risks equal to zero, as both arms of the trial were conceivably in equipoise with alternatives in clinical care, but further analysis is beyond the scope of this commentary.

² There was a concern, however, that maybe some refusals resulted from physician directives.

In international settings, a traditional in-depth consent process may not be able to realize all of the ethical functions of a “valid” consent, as explained by Dickert and colleagues. Also, several of these functions may conflict with each other, in which case tradeoffs between competing values must be made (Dickert and et.al. 2017). We believe that an “altered” consent process should be considered in international settings when a) comprehension of certain concepts is largely unachievable; b) the research “promotes concordance with participants’ values and interests” that justifies any significant net risks; and c) participants’ “control” of their decisions coupled with additional mechanisms ensure their “welfare interests”. The local community should be largely responsible for how the competing ethical functions should be balanced.

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REFERENCES

- Brudney D 2009 “Choosing for another: beyond autonomy and best interests.” *Hastings Cent Rep* 39 (2):31–7. [PubMed: 19388384]
- Dickert N, and et al. 2017 “Re-Framing Consent for Clinical Research: A Function-Based Approach” *Am J Bioeth* In Press.
- Love RR, and Fost NC. 1997 “Ethical and regulatory challenges in a randomized control trial of adjuvant treatment for breast cancer in Vietnam.” *J Investig Med* 45 (8):423–31.
- Miller FG, and Wertheimer A. 2011 “The fair transaction model of informed consent: an alternative to autonomous authorization.” *Kennedy Inst Ethics J* 21 (3):201–18. [PubMed: 22073815]
- The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. 1979 *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Available at: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>.
- U.S. Department of Health and Human Services. 1991a. “Code of Federal Regulations. 45 CFR 46 subpart A.”.
- U.S. Department of Health and Human Services. 1991b. “Code of Federal Regulations. 45 CFR 46 Subpart D. 46.406
- Wertheimer A 2015 “The social value requirement reconsidered.” *Bioethics* 29 (5):301–8. doi: 10.1111/bioe.12128. [PubMed: 25470450]