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Ethical Rules for Human Subjects Research: A Case Where the “Is” Must Inform the “Ought”

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In response to recurrent reports of human rights abuses in the name of medical research, the United States has created a system of local oversight of research to ensure compliance with accepted ethical standards. In the United States, all federally funded research must be approved by an Institutional Review Board (IRB), and federal regulations specify under what circumstances an IRB may approve research.(2005) Under the regulations, the IRB must ensure valid study design, minimization of risk to subjects, the right of subjects to withdraw from participation, no undue inducement of subjects, and other ethical aspects of research involving human subjects. The regulations pertain only to federally funded research, however many institutions have chosen to require IRB approval for all research involving humans, and most journals will not publish reports of research that was not IRB approved.(Council of Science Editors 2009) Although there is no data regarding the number of studies conducted in the United States without IRB approval, because results of any such research cannot be published in leading journals I expect that most human subjects research in the United States is reviewed by an IRB.

In his analysis, Sachs argues eloquently that such regulations represent “rules of policy” rather than “ethical rules.”(Sachs 2010) This argument is based on the assertion that these rules are not ends unto themselves, but rather are means to attain ends consistent with ethical principles. That is, if we hold x to be ethically imperative, and we believe that y subverts x , then creating a policy that investigators cannot do y will further our objective of ensuring ethical research, or so we think. Indeed, what if we are mistaken and y does not subvert x ? In such a case, prohibiting y may not further our goals of ensuring ethical practices in research and may actually facilitate unethical research practices if in fact doing y supports x .

Let us take as an example the rule of forbidding undue inducement. As Sachs notes, undue inducement is prohibited in the rules set forth by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research,(1979) the Council for International Organizations of Medical Science,(2002) and the National Bioethics Advisory Commission.(2001) Indeed, this proscription is codified in the federal code §46.116. Sachs notes that the most compelling argument in favor of this rule is that if potential subjects are offered very large sums of money to volunteer, such an offer subverts the individual's ability to make a rational choice. Since we accept the ethical rule of respect for personal autonomy, and because subverting the individual's ability to make well-reasoned choices diminishes his personal autonomy, we must therefore forbid undue inducements.

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Such an argument is compelling, and has resulted in IRBs carefully considering the remuneration volunteers receive to ensure that such funds do not constitute undue inducement. This argument, however, is predicated on the assumption that offering a potential subject a large sum of money negates his ability to make well-reasoned choices. Further, this argument assumes that subjects use logical reasoning when deciding whether they should enroll in research. If in fact subjects rely on a general sense of what they should do, on the counsel of their physician, or on a “gut feeling” when deciding to enroll in research, perhaps the promise of a large monetary payment for participation would not undermine their decision-making ability—or perhaps it would.

What is clear is that we need more data. How do potential subjects view their decision-making process? Do they want to make such choices in solitude so that they can best exercise their personal autonomy, or would they prefer a more robust decision-making process? What effect does money have on decision-making? Does offering large sums of money subvert the subject's ability to make a “good” choice?¹ If so, how much money would it take to unduly influence a potential subject's choice? Without these data, we cannot adequately assess the utility of the ban on undue inducement in human subject research.

As I have argued previously, empirical research can, and should, inform our ethical norms. (Kon 2009) Indeed, since we hold that potential subjects ought to be allowed to make “good” choices, it would be helpful to generate data illuminating whether a large monetary inducement actually is a barrier to “good” decision-making. Such a study would be an example of Ideal vs. Reality research. If we find that large sums of money compromises choice-making, then Improving Care studies would be helpful if designed to test the hypothesis that offering less money leads to “better” decision-making.² Finally, once we have amassed sufficient data, likely from multiple studies, we would be poised to alter our rules in accordance with our underlying ethical principles and the data generated by investigators. As such, I applaud Sachs' analysis and hope that this work is a call to bioethicists and others to design and conduct research on this and other important topics.

Since it would be helpful to generate robust data, it would likely be important for such research to be conducted at multiple sites, however most bioethics research tends to be single-center work. The Clinical and Translational Science Award Consortium's Clinical Research Ethics Key Function Committee has developed a working group specifically to consider and conduct multicentered research on clinical and translational research ethics (information available at <http://www.ctsaweb.org>). Perhaps others will consider this model as well and move from single-center studies to multicentered research in bioethics. Such endeavors cannot succeed, however, without increased support from the NIH and other funding agencies. While the Greenwall Foundation has been leading the charge to fund creative work in bioethics, other must join in this effort. The NIH and other non-governmental organizations need to realize the importance of this research and increase funding opportunities.

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REFERENCES

1. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.. The Belmont Report. 1979. Available at <http://ohsr.od.nih.gov/guidelines/belmont.html>

¹How one defines “good” in such a circumstance is certainly debatable.

²How one defines “better” in this circumstance would again be debatable.

2. Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries.. Report and Recommendations of the National Bioethics Advisory Commission. 2001. Available at http://www.bioethics.gov/reports/past_commissions/nbac_international.pdf
3. International Ethical Guidelines for Biomedical Research Involving Human Subjects. World Health Organization; 2002. Council for International Organizations of Medical Sciences..
4. Basic Policy for Protection of Human Research Subjects.. 45 Code of Federal Regulations 46. 2005. Available at <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>
5. CSE. Council of Science Editors' White Paper on Promoting Integrity in Scientific Journal Publications. 2009. Available at http://www.councilscienceeditors.org/editorial_policies/whitepaper/2-2_authorship.cfm
6. Kon AA. The role of empirical research in bioethics. *Am J Bioeth* 2009;9(6-7):59–65. [PubMed: 19998120]
7. Sachs. The Case for Evidenced-Based Rulemaking in Human Subjects Research. *American Journal of Bioethics* 2010;x(x):xx–xx.
8. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.. The Belmont Report. 1979. Available at <http://ohsr.od.nih.gov/guidelines/belmont.html>
9. Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries.. Report and Recommendations of the National Bioethics Advisory Commission. 2001. Available at http://www.bioethics.gov/reports/past_commissions/nbac_international.pdf
10. International Ethical Guidelines for Biomedical Research Involving Human Subjects. World Health Organization; 2002. Council for International Organizations of Medical Sciences..
11. Basic Policy for Protection of Human Research Subjects.. 45 Code of Federal Regulations 46. 2005. Available at <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>
12. Kon AA. The role of empirical research in bioethics. *Am J Bioeth* 2009;9(6-7):59–65. [PubMed: 19998120]
13. Sachs. The Case for Evidenced-Based Rulemaking in Human Subjects Research. *American Journal of Bioethics* 2010;x(x):xx–xx.