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Exempting All Minimal-Risk Research from IRB Review: Pruning or Poisoning the Regulatory Tree?

In a commentary published in 2009 in *Nature* magazine, Kim and colleagues[1] argued that the federal regulations governing research with humans (known as the Common Rule[2]) should be changed to exempt minimal-risk research from review by an institutional review board (IRB). Among other things, they claim that IRB review of minimal-risk studies leads to a costly human subjects oversight system. Their argument is fairly straightforward: *any* system of oversight ought to be deemed unethical *if* such a system offers no adequate counterbalancing good *when* it simultaneously creates a certain degree of financial, scientific, clinical, and ethical hardships on the activities of those practitioners under scrutiny. Thus, for Kim and colleagues, in order for a regulatory framework to be deemed ethical, its system of rules must reveal adequate compensating benefits in light of the oversight demands placed on those under its umbrella.

In this article, we contend that the argument Kim and colleagues provide as justification for exempting minimal-risk research from IRB review is unsound and caution against embracing their position. Although we agree that reform may be in order for review of minimal-risk research,[3] we think that the approach promoted by Kim and colleagues for pruning the regulatory tree would actually amount to its poisoning.

The Argument for Regulatory Change

To support their argument for deregulating minimal-risk research, Kim and colleagues point to a minimal-risk quality improvement (QI) study that the U.S. Office for Human Research Protections (OHRP) halted because the IRB at the principal investigator's site incorrectly determined that the study met the regulatory standard to be exempt from IRB review.[4] The "Pronovost study" involved implementing a checklist of actions for clinicians in the intensive care unit in order to prevent "hospital-acquired bloodstream infections." The study was performed with the cooperation of the Michigan Health and Hospital Association and carried out in Michigan hospitals. Results were dramatic, showing prevention of numerous deaths, a decrease in the number of days patients were hospitalized, and at least $175 million in savings. The study also was intended to ground scientifically the effectiveness of the checklist in order to encourage its implementation by others. OHRP allowed the hospitals to continue to use the checklist, but halted the effort to demonstrate scientifically its effectiveness. Since the study had been misclassified as exempt from the Common Rule, OHRP called for this evaluation portion of the project to be properly reviewed before the study could continue.[5]

Kim and colleagues claim that the minimal-risk study was subject to unnecessary regulation when OHRP ruled that it should have undergone IRB review. The authors do not view this case as an "abuse" or "misinterpretation" of the regulations, but rather as a case that "illustrates a serious flaw in the regulations."[6] Thus, they propose that minimal-risk research no longer be regulated. Their proposal—especially the cost savings it seems to promise—is prima facie attractive. Even so, the argument that supports this proposal is unsound. Their argument is as follows:

> It is unethical to support a system that creates a significant financial, scientific, clinical and ethical burden with virtually no counterbalancing good [in the case of minimal-risk human subjects research]. . . . Minimal-risk research oversight should be pruned from the federal regulations and made exempt.[7] (Bracketed text is ours.)

Kim and colleagues deny that a counterbalancing/compensating standard can be met for the oversight of minimal-risk research. However, because they offer no

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qualifications to their claim, their exemption request applies to *all* minimal-risk research, as they clearly state in the passage quoted above. To successfully challenge their claim, one must show that enough counterbalancing good is present to insist that oversight of minimal-risk research ought to remain a requirement of the Common Rule. Kim and colleagues seem to think that this challenge cannot be met, paving the way for necessary regulatory change. We beg to differ, primarily because we believe that the cogency of the authors' argument is suspect. Although we agree that IRB review of minimal-risk studies entails additional, albeit necessary, burden on the research enterprise, we argue that compensating goods counterbalance this burden. In other words, we believe that the compensating goods that we defend meet Kim and colleagues' adequacy challenge.

No Counterbalancing Good?

The main problem with the claim of "virtually no counterbalancing good" pertains to the evidence the authors use to make their case.[8] Their only example comes from the specific area of QI in the health care field (the Johns Hopkins study mentioned previously). Although we concede that OHRP may need to provide more guidance about the extent to which the Common Rule's requirements apply to QI research,[9] Kim and colleagues offer no example other than the Pronovost study—and no non-QI example—in support of their claim that the current regulatory framework regarding minimal-risk studies offers "virtually no counterbalancing good." In fact, they push even further their concern about regulation of QI-related minimal-risk studies:

> Patients are affected because of lack of quality-improvement research. A report by an interdisciplinary study group notes that the current system has "generated disincentives to engage in quality improvement" and produces "inconsistent decisions, increases costs, retards improvement, and undermines respect for research review."[10]

QI research is extremely important, but represents just one piece of all research with humans. While there may come a time when regulating minimal-risk QI studies is determined to have "virtually no counterbalancing good," it would not *necessarily* follow that this claim is true for *all* minimal-risk human studies. The concern here is that Kim and colleagues have fallen prey to the *fallacy of composition*. This is an error in reasoning that occurs when one argues that what is true of part of a system is true of the system as a whole.[11] For example, even if it is true that each neuron in the brain is unconscious, it would be an error in reasoning to claim that the brain is necessarily unconscious. Similarly, even if regulation of QI minimal-risk studies reveals no counterbalancing good to the cost of this regulation, it would be an error in reasoning to conclude that regulation across *all* areas of minimal-risk studies reveals no counterbalancing good to the regulation costs.

Presumably, Kim and colleagues have additional resources to combat the fallacy of composition criticism; for without additional justification, it is fallacious reasoning. What additional support, then, could be given to suggest that the current regulatory system offers "virtually no counterbalancing good"? Two distinct resources could prove to be all that is needed in terms of a cogent counterreply. First, utilitarian considerations could justify their claim that there is "virtually no counterbalancing good" in regulating minimal-risk studies. Second, if minimal-risk QI studies were sufficiently similar to minimal-risk non-QI studies, then their claim may be justified as well.

Counterbalancing Good, Utilitarian Considerations, and the Belmont Report

Utilitarian considerations could justify the claim that there is "virtually no counterbalancing good" in regulating minimal-risk studies. As long as the sum of possible benefits of a research project—to individual research subjects and to society—outweighs the costs (e.g., risks), utilitarianism could justify the research. As an (extreme) example, assume that a group of 100 people would die unless one from the group is killed—with or without the consent of the one to be killed. Assuming that the 100 lives are of roughly equivalent value, a strict (act) utilitarian would find it acceptable to kill the one in order to save the other 99. In the much less extreme case of minimal-risk studies, even research with a small expected benefit could be justifiable to an act utilitarian, despite other ethical problems with the research (e.g., problems related to "respect for persons" or to justice). So, if Kim and colleagues are utilitarians, it could explain and perhaps justify their claim that regulation of minimal-risk studies offers virtually no counterbalancing good to the cost of regulation. The question, then, is whether the authors are utilitarians making a utilitarian argument. In order to answer this question, we evaluate their position with respect to the Belmont Report, which provides the ethical foundation

of the current federal regulations governing research with humans.

In contrast to utilitarianism, the Belmont Report specifies that three principles must be collectively satisfied in order for human subjects research—having minimal risk or not—to be permissible. These principles are respect for persons, beneficence, and justice.[12] A strict act utilitarian, seeking only to fulfill "the greatest good for the greatest number," would not necessarily advocate the collective demands of the Belmont Report. For example, the "respect for persons" principle of the Belmont Report entails two requirements: 1) that individuals be treated as autonomous agents and 2) that "persons with diminished autonomy are entitled to protection."[13]

A strict act utilitarian would give little weight to such requirements if their satisfaction meant sacrificing the utilitarian goal of providing "the greatest good for the greatest number." Kim and colleagues clearly do not adhere to a strict act-utilitarian position. With respect to persons of diminished autonomy, they make an exception to their proposal, saying that it is "not meant to apply to minimal-risk research involving direct interactions with people who are incapable of informed consent, because research with such people raises special ethical concerns."[14] Additionally, for fully autonomous persons, they subscribe at least partially to the Belmont Report's prescription of voluntary informed consent, noting that all participants in minimal-risk studies should give "informal" voluntary informed consent for studies in which researchers will have direct interaction with participants.[15] Clearly, then, strict act-utilitarian considerations are not driving their claim of "virtually no counterbalancing good." Yet it is still possible to interpret their argument as a form of rule-utilitarian claim. They could be arguing that "the greatest good for the greatest number" should be pursued, but only if both autonomous agents and those who are incapable of autonomous decision-making (e.g., those who have some sort of cognitive impairment) are protected. Thus, they could insist they are offering a persuasive version of utilitarianism that stands as reasonable support of their position. The problem with this reading is that rule utilitarianism is a rather flimsy position to take in that it can lead to the following dilemma.

If a utilitarian is wedded to securing actions that either support or do not hinder a set of rules—regardless of the consequences—then they would be considered "rule-worshippers" in the light of consequences suggesting that a particular rule be violated. Alternatively, if they abandon the rule in the light of pressing consequences, then they are really act utilitarians when push comes to shove. In the light of either scenario, rule utilitarianism is not a very stable position to endorse. For example, consider a social psychologist who wishes to answer some important question about a particular type of group influence on individual human behavior. Assume the social psychologist needs to use a deception research paradigm because if a subject were to know the true nature of the experiment, it would influence his or her behavior, thereby obscuring the effect of the group's influence on his or her individual behavior. Assume the researcher really wants to study group bullying in the workplace, but informs the subject that the purpose of the research is to learn more about group cooperation in the pursuit of a common goal. Further assume that the "group" exerting influence on the individual is not a group of other research participants, but rather a group of actors working in concert with the researcher to deceive the real subject about the true nature of the experiment. Then the individual subject would not be fully informed at the time of making the decision of whether to participate in the research. The Common Rule permits IRBs to waive the regulatory requirement for informed consent if four criteria are satisfied: the research must be minimal risk, a subject's "rights and welfare" must not be "adversely affected" by granting the waiver, the research could not be carried out otherwise, and subjects are debriefed at some point, when appropriate.

Kim and colleagues contend that regulating minimal-risk research creates a significant financial, scientific, clinical, and ethical burden with virtually no counterbalancing good.

Assume an IRB waives the consent requirement. Now, enter the rule utilitarian. Assume the rule utilitarian has a rule prohibiting any form of deception, whether in the context of human subjects research or not. If the rule utilitarian insists that the deception not be approved with a waiver of consent, no matter what the Common Rule may allow and in spite of the possibility that the research could shed light on a serious social problem, then this utilitarian is more interested in not violating one of his or her rules than being sensitive to relevant consequences.

Alternatively, if the rule utilitarian abandons the "no deception" rule in the light of overall beneficial consequences, then he or she really is an act utilitarian. For instance, if the rule utilitarian is quick to abandon the no deception rule in the light of the considerable benefit for society to learn more about workplace bullying, then it is unclear what work the no deception rule is doing in his or her overall moral calculus. Either way, if they do not address this objection, rule utilitarians are in the unenviable position of being morally obtuse or disingenuous. Thus, since Kim and colleagues do not pursue this line of discussion, we surmise that rule utilitarianism is not (or should not be) their overarching normative foundation. The overall implication of these arguments is that utilitarian considerations are not motivating the authors' defense in any substantive way.

Beneficence and Justice

If minimal-risk QI studies are sufficiently similar to minimal-risk non-QI studies, then Kim and colleagues' claim may still be salvaged. In order to assess the similarity of QI to non-QI research, we will evaluate the consequences of not regulating minimal-risk research for each type. These consequences will be evaluated in terms of how the Belmont Report principles of respect for persons, beneficence, and justice might be affected in unregulated minimal-risk human subjects research.

The Belmont Report's principle of beneficence has two requirements: "do not harm" and "maximize possible benefits and minimize possible harms." Given that Kim and colleagues propose exempting only minimal-risk research from regulation,[16] the principle of beneficence would probably be undisturbed for both QI and non-QI studies.[17] In other words, with respect to beneficence, consequences of not regulating minimal-risk QI and non-QI studies would probably be similar.

With regard to justice, the spirit of this principle as described in the Belmont Report is that both the burdens of research participation and the benefits of research should be distributed fairly:

> whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.[18]

How would implementing the justice principle be affected if QI and non-QI minimal-risk studies were exempt from the provisions of the Common Rule? In the case of QI research, there may be little or no effect. If, as many commentators contend, QI is part of the clinical experience for all patients, then when any patient shows up at a clinic seeking care, he/she should expect to be included in ongoing QI activities at that clinic because the goal of those activities is to improve patient care at that clinic. Therefore, eliminating regulation of minimal-risk QI research may have little impact with respect to the justice principle. This could explain why Kim and colleagues were mute on this point.

Eliminating regulation of minimal-risk non-QI studies, however, may lead to violations of the justice principle. The case of Henrietta Lacks and establishment of the HeLa cell line, which occurred prior to implementation of the Common Rule, illustrates this point. This example has the characteristics necessary for our analysis: the research likely posed minimal risk for the subject, and there was no informed consent process. The tissue was just taken while the subject was on the operating table.[19] Note that this example differs from present-day tissue collection, storage, and research, where tissue may be voluntarily donated or obtained from medical waste and where the researcher may not be able to readily identify the individual from whom tissue was obtained. By contrast, what happened in the Lacks case would probably not be legal today for research subject to the Common Rule. In the absence of regulation, it seems that the justice principle was violated in the Lacks case, even though the research itself posed little risk to the subject. At that time, scientists considered it fair to conduct research using indigent patients unable to pay; moreover, Lacks's children have had difficulty obtaining health care in spite of the advances in health care made possible by their mother's cell line.[20] As the quote from the Belmont Report above suggests, it is unjust for one segment of the population to bear the brunt of research, while a different segment receives the bulk of its benefits.

We are not claiming that cases similar on their surface to the Lacks example would necessarily happen as a result of deregulation. Our point is that violations of the justice principle could occur when minimal-risk non-QI research is unregulated, even if such violations would not occur when minimal-risk QI research is unregulated.

Respect for Persons and Informed Consent

As described previously, the "respect for persons" principle in the Belmont Report requires that persons be treated as autonomous agents and that there should be protection for persons of diminished autonomy. Because Kim and colleagues' proposal seems not to apply to persons of diminished autonomy,[21] respect for persons would probably be undisturbed for both QI and non-QI minimal-risk studies. However, would fully autonomous persons in QI and non-QI minimal-risk research be differentially affected with regard to the principle of respect for persons by exempting minimal-risk research from IRB review? Because voluntary informed consent is the main application of the "respect for persons" principle in the case of fully autonomous persons,[22] the effect of deregulating both types of research must be considered.

In the case of minimal-risk QI studies, one could argue that no IRB oversight would have little impact on the matter of consent. For example, some commentators claim that whether a research component is present or not, a "patient's consent to receive treatment" entails "consent to inclusion in minimal-risk QI activities."[23] Although this claim requires separate argument, assume for present purposes that it is justified—that voluntary informed consent to treatment is sufficient for participation in minimal-risk QI activities. Then, even when a research component accompanies such activities, a lack of IRB review for this research component may not matter. The point is that some form of voluntary consent will have occurred.

For minimal-risk non-QI studies, however, who would ensure that researchers obtain informed voluntary consent from individuals in the absence of a regulatory requirement for IRB review of such minimal-risk studies? Consider sociobehavioral research, which tends to pose minimal risk. Would professors engaged in this type of research obtain informed consent from students who depend on them for a grade knowing that their research is not subject to IRB review? Moreover, sociobehavioral research has very diverse goals and methodologies and is by no means limited to participants from the population of college students. Sociobehavioral research includes ethnographic studies of certain populations, domestic or international; psychological laboratory research on cognition and perception; certain types of oral history; user evaluation of Web sites and software interfaces; mental health studies that may have both a treatment and a research component; and community activism studies that may include a research component intertwined with activism. This heterogeneous list of sociobehavioral research paradigms is by no means exhaustive. In each of these research paradigms there may be power dynamics between the researchers and the participants that raise issues about adequate voluntary informed consent. With no IRB review of these studies, it is unclear what oversight mechanism would be used to deter researchers from unduly inducing or coercing individuals to participate in their studies. Those who believe that risk is the only issue to consider with regard to deregulating some human subjects research may not be swayed by this concern. But it is one that should be acknowledged and openly discussed.

The recent lawsuit by a Native American tribe is an example of how, even when research poses minimal risks, an inadequate consent process can weaken the public's trust in the research enterprise. Some members of the Havasupai Tribe, which has long occupied portions of the Grand Canyon, alleged that researchers failed to disclose adequately in the consent process how they would use blood samples collected from some tribal members.[24] Although the consent form specified that the blood samples might be used to "study the causes of behavioral/medical disorders," tribal members who gave blood samples to the researchers claimed their understanding was that the blood samples would be used specifically for the purpose of trying to determine why the Havasupai suffered from a high rate of Type 2 diabetes.[25] In addition to studying diabetes, researchers used the blood samples to study other topics, such as schizophrenia and the origin of the Havasupai tribe. Their finding that the Havasupai originated in Asia contradicted a cherished belief that the tribe originated in the Grand Canyon. Even though the additional research not related to diabetes apparently did not pose additional risks to the biospecimen contributors, the "respect for persons" criterion and respect for the tribe itself were violated, resulting in an out-of-court settlement in favor of the tribe. (Part of the settlement included returning all existing blood

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samples to the tribe.)

Conclusion

Kim and colleagues' claim that there is "virtually no counterbalancing good" in regulating minimal-risk human subjects research assumes that the consequences of not regulating QI and non-QI minimal-risk studies would be identical. As we have argued, though, this assumption is unwarranted. The "counterbalancing good" of regulating minimal-risk studies is that oversight exists to ensure that respect for persons and justice requirements are satisfied when they otherwise might not be. Although we concur that IRB review should not be disproportional to a study's risk level, we believe that the correct approach to "easing the regulatory burden" is in the proper application of the flexibility that already exists in the Common Rule—for example, recognition of current exemption categories, appropriate use of an expedited procedure, and appropriate use of the provision to waive documentation of informed consent.

Because the claim that the current regulatory system offers "virtually no counterbalancing good" is false, Kim and colleagues' argument is unsound. Thus, federal regulators should not explicitly exempt *all* minimal-risk research from IRB oversight, even if it turns out that *some* additional categories of research should be exempted. To stop regulating all minimal-risk human subjects research would be to poison the regulatory tree.

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References

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11. For more on the fallacy of composition, see Codell Carter K. *A First Course in Logic, Gold Edition*. New York: Pearson/Longman, 2005, pp. 88-89.

12. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Washington, DC: Government Printing Office, 1979.

13. See ref. 12, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979.

14. See ref. 1, Kim et al. 2009, p. 534.

15. See ref. 1, Kim et al. 2009, p. 534.

16. See ref. 1, Kim et al. 2009.

17. Without regulation of minimal-risk human subjects research, a researcher would face less pressure to "maximize possible benefits" of his or her research. In our experience, however, it is not uncommon for an IRB to fail to press this issue anyway, when research clearly poses minimal risk.

18. See ref. 12 , National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979.

19. Skloot R. *The Immortal Life of Henrietta Lacks*. New York: Crown Publishers, 2010.

20. See ref. 19, Skloot 2010.

21. See ref. 1, Kim et al. 2009, p. 534. But note that their exception is stated as follows: "our proposal is not meant to apply to minimal-risk research involving direct interactions with people who are incapable of informed consent." It is not perfectly clear that they intend for *all* research involving persons of diminished autonomy to be excepted from their proposal (e.g., consider research not involving "direct interactions"), but we will assume here that they do.

22. See. ref. 12, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979. Informed consent is best understood as autonomous authorization: (i) a patient substantially understands the proposal, options, and issues; (ii) the patient's decision is substantially free (there's a substantial absence of control by others); (iii) the patient acts intentionally; and (iv) the patient authorizes the intervention. See Faden RR, Beauchamp TL. The concept of informed consent. In: Beauchamp TL and Walters L, eds., *Contemporary Issues in Bioethics*, 5th ed. Belmont, CA: Wadsworth, 1999, pp. 139-143.

23. See ref. 9, Lynn et al. 2007.

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25. See ref. 24, Rubin 2004.