Published in final edited form as:

J Med Ethics. 2017 February ; 43(2): 132–133. doi:10.1136/medethics-2016-103429.

Afterword: Returning to philosophical foundations in research ethics

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Abstract

This is an afterword to the JME symposium on the benefit/risk ratio challenge in clinical research, and the case of HIV cure. It notes implications of the symposium for research ethics in general.

The contributions to this symposium addressed what we have called the benefit/risk ratio challenge in some early-phase studies of strategies for HIV cure or durable remission. Our team has a wide range of views on which candidate solutions would be ethical and practical and which would not. Together, these candidate solutions form a far wider range of possibilities than research ethicists usually consider, including currently-neglected approaches that may nonetheless chime in with insights in other areas of practical ethics. That suggests future agendas for inquiry in research ethics.

One lesson of the symposium is that more dialogue between research ethics and general philosophy could be fruitful. Rahul Kumar's piece suggests that central positions in research ethics contradict paradigm consequentialist and paradigm nonconsequentialist ethical theory. A possible interpretation is that research ethics is mistaken, and ought to be revised, perhaps radically. Of course there are other possibilities. Perhaps foundational ethics is mistaken and should be revised with implications in many areas of practical ethics. Either way, that dialogue needs to happen.

A further lesson concerns the structure of research ethics. That ethics has usually been understood as a collection of requirements, all of which must be met by investigators so that studies remain ethical (or approvable). In that view, an ethical study involves both informed consent and a favourable benefit/risk ratio and scientific validity and independent review, and so forth. In this vein, a paramount article summarizing seven alleged requirements of research ethics concludes, 'Fulfilling all⁷ requirements is necessary and sufficient to make clinical research ethical.'¹ In legal documents on research participant rights, the different articles are nearly always understood as a list of necessary conditions, violating any of which is impermissible. In fact, however, large parts of research ethics may be best understood as disjunctive: we are obligated to either let volunteers consent to take on risks, or, if we are doubtful of the quality of their consent, protect them independently;² to either assign their protection to the independent review, or protect them through robustly informed consent, or... A further possibility is that research ethics has a probabilistic structure, akin to that of the Diagnostic and Statistical Manual of Mental Disorders (the DSM). Many

problems in a study protocol (and especially ones that matter a lot) sink its ethics; many resolutions save it. For example, if the point of study regulation is to treat study participants with respect, is any one act really conclusive that the package deal takes the person too lightly or contemptuously, or does the overall package matter too?

Finally, and returning to early-phase HIV cure and remission studies, if the concern about the risk-benefit ratio is resolvable in this or in that way, high-risk studies may yet raise other ethical concerns as such—because they are high-risk. A very different ground for concern about the high risk in some cure studies has to do with the preservation of public trust in the research enterprise. Unexpected and serious harms to study participants can trigger crises of confidence in a research program.^{3–7} Moreover, in past eras, harm to participants undermined trust in researchers and care providers, particularly among underrepresented populations, contributing to lower participation in trials and lower medical adherence.^{8–11} Risky HIV cure trials have the potential to result in severe adverse events that could affect public trust and set back research and care. What forms of HIV cure trials would minimize that hazard? This argument for radically decreasing risks to participants (even if there are ample benefits to participants!) is potentially consequentialist, since it is concerned about adverse future outcomes. If so, it also needs to be balanced against the societal benefits from the potential success of the investigation.² Still, if a cure or durable remission strategy were scalable and could make a dramatic difference to the lives of millions around the world, and an ethical solution were found to the alleged inherent concern about the net risks to individual participants, perhaps the challenge of societal distrust could be resolved? Perhaps we could hope to convince society that some risks, and even some adverse events, are the flip sides of appropriate scientific pursuits to reduce human morbidity and mortality?

Acknowledgments

This article has been accepted for publication in The Journal of Medical Ethics following peer review. The definitive copyedited, typeset version, J Med Ethics medethics-2016-103429, is available online at: <http://jme.bmj.com/content/early/2016/06/27/medethics-2016-103429.full.pdf+html>.

Funding

This work was funded by NIAID grants 1 R01 AI114617-01A1 and 1 R56 AI114617-01, both titled ‘HIV cure studies: risk, risk perception, and ethics.’ The study sponsor had no role in the study design; in the collection, analysis and interpretation of the data; in the writing of the report; and in the decision to submit the paper for publication.

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