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Streamlining Ethical Review

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Abstract

The U.S. review system for human subjects research has been widely criticized in recent years for requirements that delay research without improving human subjects protections. Any major reformulation of regulations may take some time to implement. In the meantime, current regulations often allow for streamlined ethics review without jeopardizing—and possibly improving—protections for research participants. We discuss underutilized options, including research that need not be classified as “human subjects research,” categories of studies that can be exempt from ethical review, and studies that need only undergo expedited review by one IRB member. In addition, we consider ways to simplify review of multi-center research using one institution’s IRB. We speculate on multiple reasons for the underuse of these mechanisms, and exhort IRBs and researchers to take advantage of these important opportunities to improve the review process.

The U.S. review system for human subjects research has been widely criticized in recent years. Many commentators, particularly within the research community, complain of pointless book-keeping requirements that sap the morale of institutional review board (IRB) members,⁽¹⁾ and delay and obstruct life-saving research.⁽²⁾

Various diagnoses of the system’s ills have been given, and corresponding regulatory changes proposed to deal with what Fost and Levine call the “dysregulation of human subjects research.”⁽³⁾ But even if the regulations were substantially reformed, such change would take some time to be implemented. In the meantime, ethics review could be streamlined using the current regulations if institutions, IRBs, and researchers adhered strictly to the definition of human subjects research, and used the available options for exemptions, expedited review, and centralized review.⁽⁴⁾

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These options remain underused in biomedical research. According to Marjorie Speers (President of the Association for the Accreditation of Human Research Protection Programs) many institutions include as “human subjects research” activities that do not fall under the federal definition.⁽⁵⁾ Although much low-risk human subjects research is exempt from review, some institutions insist on having all their research reviewed by IRBs.⁽⁶⁾ A 1998 report found that for each category of exempt or expeditable research 25 to 77 percent of U.S. IRBs “practice some form of review that was more rigorous than specified by the regulations.”⁽⁷⁾ No data appear to be available today that contradict this picture.

There are multiple reasons for the underuse of these options. One key reason is likely a lack of knowledge; but another is fear of the consequences if the regulations are deemed to be violated, since this can entail the complete suspension of an institution’s federally funded research. Our purpose here is to both inform and reassure.

Human subjects research

IRB review is legally required for research conducted or funded by specified U.S. federal agencies,⁽⁸⁾ regulated by the Food and Drug Administration, or carried out at institutions that have elected to subject all their research to the Common Rule requirements. The regulations apply only to “human subjects research.”

In human subjects research investigators obtain data through some “intervention or interaction” with living people, or obtain identifiable private information about them.⁽⁹⁾ Data from people whose identity the investigator cannot “readily ascertain” are not *identifiable* private information.⁽¹⁰⁾ For much medical research, particularly using clinical data, researchers do not need to know the identity of their subjects, and so need not conduct human subjects research. For example, research using data from medical records can be conducted so that the researchers cannot identify the person from whom the data comes. One way to achieve this is for someone not involved in the research to remove identifiers (such as the eighteen specified HIPAA identifiers)⁽¹¹⁾ from the data and agree never to disclose the code linking the data to specific individuals. Researchers can even set up a mechanism to receive future data, without the regulations applying.

Exemptions and expedited review

Even if a proposed research study is human subjects research, it may fall into one of six categories that are exempt from ethical review. Two categories are of particular interest to biomedical researchers. Category 2 exempts research that uses only educational tests, survey procedures, interviews or observation of public behavior, unless the data recorded are *both* identifiable and potentially harmful if disclosed. Consider, for example, a researcher who interviews patients with HIV/AIDS about their medications, and records their names. That study would not be exempt under category 2, since disclosure of the subjects’ HIV/AIDS status could harm them. But if the researcher conducted the interviews anonymously, and never recorded subjects’ names or other identifying information, the study likely would be exempt.

Category 4 exempts research “involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens,” if either the data sources are publicly available or the data recorded are not identifiable.(9) So, for example, a retrospective chart review examining the medications given to the last 50 patients seen at a hospital’s emergency department for suspected cardiac infarction would be exempt (provided the data was recorded without patient identifiers). Decision charts for these exemptions are on OHRP’s website.(12)

If a protocol for conducting human subjects research is not exempt, it may nevertheless be possible to expedite its review. First, initial and continuing review of certain categories of minimal risk research can be expedited, such as research involving only the collection of blood samples, or the non-invasive collection of other biological specimens.(13) Second, expedited review is permitted for “minor changes” in already approved research. Expedited review follows the same standards as full IRB review but it is carried out by just the chairperson or designated experienced IRB members. Use of expedited reviews should speed up the process of review, since it can be conducted on an on-going basis, and it should reduce the time the convened IRB spends reviewing minimal risk research. At present, the sparse available data indicate that for some institutions, expedited reviews save little money(14) and no time,(15) which suggests that some IRB procedures need streamlining, too.

Multi-center research

Since the regulations were established, the number of collaborative studies taking place at multiple institutions has greatly increased. Because responsibility for ethical review rests with institutions, multi-center research frequently results in the same protocol being reviewed by each institution’s IRB.(16) Not only does this involve duplication of work, it also increases the time and resources spent getting research projects approved, as different IRBs mandate different, often minor, changes to consent documents or the protocol, and researchers go back and forth between them.

Again there are already regulatory resources for addressing this problem. According to the Common Rule, when a research project involves more than one institution, “an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.”(9) This arrangement is underutilized not for legal reasons but because of institutional reluctance to cede control and underlying liability concerns. The Office for Human Research Protections recently published a request for public comments on an amendment to the regulations that would allow it to hold IRBs and the organizations operating them directly responsible for meeting some regulatory requirements, rather than always enforcing compliance through the institutions engaged in the research.(17) For example, if an independent IRB reviewed a particular study and incorrectly approved it using expedited review when it should have undergone review by the convened IRB, any compliance action would fault the IRB, rather than the institution that hired it to review this study. It is hoped that this would encourage more institutions to rely on review by an external IRB by reducing their liability concerns.

One existing “joint review” arrangement is the National Cancer Institute-sponsored Central Institutional Review Board (CIRB) Initiative, which covers certain NCI-sponsored multi-center adult and pediatric cancer studies.⁽¹⁸⁾ For studies in the initiative the CIRB performs a single review of the protocol and then local IRBs may defer to the CIRB and themselves perform only a “facilitated review” of ethical issues that arise because of the local context. The CIRB generally performs the continuing reviews, amendment reviews and reviews of serious adverse events for the protocol.

Ethical concerns

Medical research pursues the ethically important goal of developing interventions to improve human health. It does so under the constraint of another goal—protecting research participants. The measures that can speed up ethics review clearly help with the first goal. They can reduce the time that it takes to develop healthcare interventions, and allow resources that would otherwise be taken up by ethical review to be directed towards beneficial research. Expending excessive resources on reviewing studies that pose minimal risks, or replicating other IRBs’ review is ethically troubling. One concern, however, might be that speeding up ethical review will compromise the welfare of people it is designed to protect.

It is unlikely that following these measures would reduce human subjects protections. First, the categories of research that are exempt or eligible for expedited review are unlikely to include highly unethical studies. For example, these studies will almost always pose no more than minimal risk to participants, which should ameliorate concerns about participant harm. Thus, the absolute probability of increased use of these measures leading to more unethical research is low.

Second, there are always constraints on IRBs’ time and resources. Time spent reviewing one protocol takes away time from reviewing others. IRBs should prioritize their time to focus on protocols that are more likely to generate ethical issues. Of course, they need a way to determine whether a study will raise ethical issues without actually reviewing the full protocol. The regulatory measures explained above seek to do just that: they identify categories of research which are very unlikely to be ethically problematic. Using them therefore frees up resources for reviewing more risky research.

Action

This article has two main goals. First, to inform biomedical researchers about the measures through which the ethical review of low-risk and multi-center research could be made more efficient under the existing regulations. Second, to extol their use to researchers, IRBs, and institutional officials: there are good reasons for thinking that we *ought* to make use of these measures. Not only might they allow valuable research to be carried out more rapidly, and reduce the cost of protocol review, they allow IRBs to focus on research that is more likely to be ethically challenging.

Researchers cannot act alone. IRB offices, and the officials that oversee them, need to be willing to prioritize time and resources by allowing exemptions and developing efficient

procedures to expedite reviews. Moreover, the institutions that host research need to be willing to trust the ethical review systems at other institutions. That trust needs to be built. Finally, regulatory bodies need to reassure the research community that their primary concerns lie not with meeting bureaucratic requirements but with genuinely protecting human subjects. That is a message that will help encourage institutions to undertaking appropriate streamlining changes to their policies and procedures, since it should minimize concerns about being subject to inappropriate regulatory responses.

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