Updating Research Oversight for the 21st Century

Digital data offer exciting potential for improving health outcomes. Researchers can evaluate the effectiveness and safety of therapies in real-world settings and develop personalized health promotion interventions using routinely collected personal data from mobile devices, the Internet and cell phones, mobile applications, and electronic health records. Such data could include physical activity, food and restaurant purchases, and geolocation. Companies already use these data to develop products and services and send individualized advertisements and offers. However, as the articles in this issue by Grande and colleagues and Simon remind us (1, 2), in addition to potential health benefits, research using digital data raises ethical concerns.

Clinical research poses a fundamental ethical dilemma: Participants face risk to benefit future patients and society but generally not themselves. Federal regulations for human subjects research developed in the 1970s require that an independent institutional review board (IRB) judge a study’s level of acceptable risk in light of the anticipated benefits and that participants give informed, voluntary consent. Certain “minimal-risk” research is permitted without full IRB review or consent. However, revisions to federal research guidelines are anticipated (3), in part because of concerns that regulatory oversight stifles important low-risk research, such as secondary studies using existing specimens or digital data (3) and social and behavioral research. It is thus timely to address several ethical questions.

**What Risks Should Be Considered in Assessing Research?**

The concept of “minimal risk,” permitting certain research to receive less oversight, needs to be reconsidered. A risk that is no greater than risks in daily life is not necessarily ethically acceptable in research. For example, although huge breaches of digital data at retailers and banks are common, lapses in the protection of research subjects’ data are unacceptable, and security in research must be continuously updated.

Furthermore, current regulations do not consider the risks of not doing research. A lack of rigorous research on the efficacy and safety of many therapies in actual clinical settings may doom many patients to ineffective care and poorer health outcomes. For patients treated for serious illness, the risks of a research study should be framed as those beyond the risks faced in standard treatments (4).

**What Constitutes Ethically Valid Permission for Research?**

Informed consent for research is the default ethical requirement. However, consent is impractical in many quality improvement studies, comparative effectiveness research, and analyses of existing specimens or digital data. Furthermore, consent requirements introduce selection bias (5). For society to gain the benefits of such research, exceptions to specific consent are needed. One-time permission for unspecified future research with specimens and data has been proposed (3). This can be done in several ways. Digital companies, such as Facebook, require users to click “I agree” to conditions of data use, allowing the company to study how to present services, information, advertisements, and prices to attract more users and increase revenue. Such an agreement is ethically problematic because few consumers read the small print presenting the conditions of use.

Broad permission for unspecified future research with specimens and data collected during clinical care makes intuitive sense for the vast majority of secondary research. However, patients seeking care may not read the permission request or appreciate its implications. Another ethical concern is that a considerable minority of persons would object to the use of their data or specimens for certain secondary research, even if deidentified. For example, a considerable percentage of people would object to their specimens being used for derivation of human gametes from induced pluripotent stem cell lines, transplantation of human stem cells into animals (6), or research on biological weapons. Many might object to use of their data to study human evolution or the genetic basis of criminal behavior (7). Empirical research using vignettes, as in Grande and colleagues’ study, could show what percentage of the population would consider a study objectionable. Such objectionable research should be allowed only if donors give specific consent for it, just as frozen embryos may not be used to derive human embryonic stem cells unless the donors give specific consent (8). Broad consent for unspecified future research should not suffice for objectionable research.

**What Is Appropriate Research Oversight?**

Four reforms could strengthen research oversight without unduly burdening minimal-risk research. First, the same ethical standards should apply regardless of the funding or site of research (9). Currently, companies like Facebook that receive no federal research funding need not follow federal regulations on human subjects research, and indeed they did not, as Simon emphasizes (2). Equivalent ethical standards for all research would require congressional action, unless companies agree to comply with these standards voluntarily. Second, IRB membership needs to be broadened. Facebook’s plans for an in-house IRB have been criticized as lacking independence. However, the same criticism holds for IRBs at universities, which primarily comprise employees. To better ensure independent review, the number of lay and community members of ethics boards should be increased.

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review boards needs to be increased so that they are not
token members (9). They also need better training in re-
search design and research ethics. Third, a proposed new
category of “excused” research would include interviews
and secondary studies of existing data and materials, pro-
vided that confidentiality is appropriately protected. Risk-
based oversight is sensible. However, studies should not be
excused by investigators themselves. The IRB staff should
screen for uncommon but higher-risk or potentially objection-
able studies. This triage should be timely so that the
vast majority of excused studies could begin in 2 or 3 days.
Fourth, research oversight should learn from experience.
In the judicial system, rulings by appellate judges are pub-
dished so that judges in future cases can build on or dis-
agree with their reasoning. In contrast, the reasoning of
IRBs in difficult cases is not shared with other IRBs or the
public (10).

In summary, revisions to the federal regulations for
human subjects research and rethinking the ethical frame-
work supporting them will better protect participants, fa-
cilitate research to improve clinical care, and increase pub-
lic trust that research ethics keeps pace with cutting-edge
science and information technology.

Bernard Lo, MD
The Greenwall Foundation
New York, New York

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Requests for Single Reprints: Bernard Lo, MD, The Greenwall Founda-
tion, One Penn Plaza, 47th Floor, New York, NY 10119; e-mail,
bernardlo@greenwall.org.


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