POLICY FORUM

BIOETHICS

Return of results and data to study participants

A recent report urges progress but builds barriers to research participants' access

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Researchers conducting imaging, environmental health, and genetics studies have offered participants their research findings for years, publishing data on this experience and producing consensus guidelines (*1*–*5*). Research participants have articulated the value in the return of results and data (*6*). The National Academies recently issued a report at the request of the National Institutes of Health (NIH), the Centers for Medicare and Medicaid Services (CMS), and the Food and Drug Administration (*7*) that focuses on the return of results in studies with human biospecimens. It proclaims support for the interests of research participants, endorses the importance of offering participants their individual-specific results, and advocates assessing the value of results from the standpoint of participants. Unfortunately, in our view, the report's announced commitment to participant-centered progress is undercut by its actual recommendations. We believe the report creates major roadblocks to the return of data and results and would constrict participants' existing rights of access.

Some research results will meet clinical standards for quality, but many will not, because research seeks to advance understanding. Participants may value results related to themselves for a wide range of reasons (see the figure). As the report notes, empirical studies show that most participants want the option of return, and results are valued even when uncertain.

Researchers, in close consultation with ethicists and legal scholars, have developed three pathways for returning results when those results raise potential clinical concerns. The first is to perform research analyses in laboratories that comply with the Clinical Laboratory Improvement Amendments of 1988 (CLIA)—a federal statute that aims to ensure the safety and analytic quality of laboratory tests conducted for health care purposes—so that research results can be freely used in clinical care. A second pathway, for results from non-CLIA research laboratories, is for researchers to confirm results that raise clinical concerns in a CLIA laboratory before return. A third option for results from non-CLIA research laboratories is a clinical hand-off: return research results while advising the participant that clinical confirmation and follow-up are needed before clinical use. In this option, researchers maintain the line between research and clinical care by making a referral for clinical workup rather than venturing a diagnosis based on potentially uncertain research results (*8*). All three paths protect participants by requiring CLIA confirmation before clinical use of results and preserve participants' access.

Reasons for access to personal research results and data

- Preserve health (through diagnosis, treatment, and prevention)
- Seek clinical confirmation and follow-up (for the participant and possibly family members)
- Monitor developing scientific understanding of the results
- Form social networks with people who have similar test results
- Contribute data for other research uses, including citizen science
- Assess privacy risks posed by the collection and circulation of personal data

The Academies' report rejects this widely supported, legally sound approach. Although the report correctly states that research protocols planning to produce results for clinical use should use a CLIA laboratory, the report casts doubt on the feasibility of the accepted practice of seeking CLIA confirmation only for a subset of results to be returned. When protocols do not plan return of results for clinical use, the report recognizes that requiring CLIA compliance is unrealistic, as research laboratories may find the cost and regulatory burdens prohibitive, CLIA analytic requirements may not fit some research testing, and CLIA has not kept pace with rapid developments in advanced testing technologies. As an alternative, the report allows return from research laboratories approved under a "quality management system" (QMS) that does not yet exist. In the report, the NIH is urged to lead the massive effort required to develop the QMS. Unfortunately, the report counts on the success of that effort for return of non-CLIA results, although success is far from assured and such a system will take years to develop. As a last resort, the report allows Institutional Review Boards (IRBs) to approve return of results, but only after extensive and restrictive vetting.

The report thus constricts participant access to results, while providing no greater protection in clinical care, as accepted approaches already call for CLIA confirmation before using research results for diagnosis or treatment. The report expresses concern about possible sample mix-up in returning results but notes that research laboratories may have sound tracking systems (even better in some cases than CLIA laboratories) and details how researchers can communicate any uncertainty. The report's retreat from robust return of results is puzzling, given the report's acknowledgment that the risks of return have been overstated and the benefits underestimated.

Efforts to turn back the clock on return of results appear rooted in confusion about the law. The Academies' report states that CLIA "bars laboratories that are not CLIA certified from reporting individual research results" (*7*). However, neither the CLIA statute nor regulations impose this ban. They only prevent non-CLIA laboratories from reporting results "for the diagnosis, prevention or treatment of any disease or impairment of, or the assessment of…health"—that is, for clinical uses (*9*, *10*). When the purpose for return of results is to recommend that the participant seek clinical confirmation and evaluation, rather than for direct use in clinical care, CLIA does not apply (*8*). Nor does it apply when the goal of returning results is to respect the many non-

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clinical reasons why participants want their results and data.

The report's error stems from giving credence to a highly restrictive CMS position that a laboratory reporting an individual's research results for any reason is doing so for clinical use and thus needs CLIA certification: "[T]he committee was advised that making any comments, analysis, or conclusions regarding the appropriateness of that interpretation would be beyond what is intended in the statement of task" (*7*). However, both the CLIA statute and regulations are clear—only laboratories that are reporting results for clinical use require CLIA certification. The mere act of reporting individual-specific results is not enough. CMS has no power to revise the statute, creating new rules and presumptions that would demand CLIA compliance by additional laboratories—only Congress can do that (*11*). Although the report ultimately recommends that CMS should allow somewhat broader return (under CLIA, the proposed QMS, or with IRB approval), the report impedes current return by wrongly assuming a CLIA laboratory is required by existing law.

The report restricts access to research results and raw data, even when participants themselves request it. Under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, research participants have a legally protected right of access to their data and results in the "designated record set" (DRS) at HIPAA-covered clinical and research laboratories (*12*). HIPAA ensures a person's right of access to their information so that they can assess the level of privacy risk that circulation of that information entails.

In the Genetic Information Nondiscrimination Act (GINA), Congress made clear that these HIPAA access rights include genetic information. GINA recognizes that people can suffer invasion of privacy, discrimination, stigmatization, and other harms based on erroneous, low-quality genetic information, including information that is wrongly attributed to them. Accordingly, Congress placed genetic information under the protections of the HIPAA Privacy Rule, including HIPAA's access right (*13*).

The report advocates restricting these federal access rights. It calls on the HIPAA regulator (the Office of Civil Rights) to revise its definition of the DRS to exclude research data and results unless they meet the CLIA and QMS quality standards recommended by the report. Again, the report fails to trust participants with research data and results while misunderstanding the law. The report ignores a longstanding Congressional determination, reflected in privacy statutes for nearly 50 years [for example, (*14*)], that broad individual access is essential to privacy protection.

Given the problems in requiring compliance with CLIA or the proposed QMS, the report creates one last option—researchers may offer results if approved by an IRB. Here the report reverts to an old strategy with recognized drawbacks, by loading return-of-results decisions on IRBs to be made on a "study-by-study" basis. Although IRBs already play a role in return of results, the report goes further and calls on IRBs to decide with researchers "whether and how" to return results in each study; to determine whether the quality of results supports return through CLIA-certification, a QMS, or IRB approval; and to "develop policies and procedures that support the assessment of plans for…return" (*7*). This places substantial new burdens on IRBs, despite extensive literature on the limits of IRB decision-making and inconsistency in decisions across IRBs (*15*).

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The report then maximizes the burden on IRBs by mischaracterizing existing consensus guidelines (*1*–*4*) and suggesting that IRBs start over. Those guidelines already embrace values endorsed by the report—assessing the value of results from the participant's perspective and "defin[ing] 'utility' to include information that a research participant is likely to find important," rather than focusing merely on what clinicians find actionable (*1*, *2*). These published guidelines distinguish results that should be returned, may be returned, and should not be returned and have offered a starting point for researchers and participants. Yet instead of building on that literature, the report repeatedly misstates the content of these guidelines, eroding progress already made.

The report ultimately recommends that IRBs reject return of results that current guidelines allow. The report urges returning only those results that have "high quality," calling on IRBs to evaluate the analytic validity, clinical validity, and value of the results, with in-depth review of laboratory quality. The report advocates that IRBs permit return only when "the probability of value to the participant is sufficiently high and the risks of harm are sufficiently low" and "the quality of laboratory analysis… provide[s] confidence in the result, as determined by a review process independent of the laboratory" (*7*). This contrasts with current guidelines that allow return when sufficiently important to participants, even when return may involve risks (*1*–*4*). Moreover, current guidelines would allow more generous return of results, based on the researcher's efforts to ensure the result's analytic validity and an assessment of the result's value—including its value in triggering clinical confirmation and follow-up—without insisting on the extensive review required by the report.

The Academies' report endorses the idea of participant access to results and data, but then builds daunting barriers. The report rejects established legal rights of access, two decades of consensus guidelines, and abundant data showing that participants benefit from access while incurring little risk. The report too often prefers paternalistic silence over partnership. Although the report acknowledges that research is transitioning to models involving participant engagement and leadership, the report creates roadblocks to this partnership.

True progress on return of results requires accepting participants' established rights of access and respecting the value that participants place on broad access to their data and results. The next step is not to build barriers but to promote transparency. Access is central to advancing participant-centered research practices and building successful collaboration with research participants. ■

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