that resources must be available both to treat the acute illness and to treat HIV in the long term. Because there is limited utility in stabilizing a critically ill patient with HIV for whom long-term antiretroviral therapy is unavailable, nonconsented HIV testing may not be justifiable in resource-limited settings.

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REFERENCES

1. Pauker SG, Kassirer JP. The threshold approach to clinical decision making. *N Engl J Med*. 1980;302:1109-1117.
2. Akinola NO, Olasode O, Onayemi O, et al. The search for a predictor of CD4 cell count continues: total lymphocyte count is not a substitute for CD4 cell count in the management of HIV-infected individuals in a resource-limited setting. *Clin Infect Dis*. 2004;39:579-581.
3. Aldrich J, Gross R, Adler M, King K, MacGregor RR, Gluckman SJ. The effect of acute severe illness on CD4+ lymphocyte counts in nonimmunocompromised patients. *Arch Intern Med*. 2000;160:715-716.
4. Bayer R. Public health policy and the AIDS epidemic: an end to HIV exceptionalism? *N Engl J Med*. 1991;324:1500-1504.
5. Beauchamp TL, Childress JF. *Respect for Autonomy: Principles of Biomedical Ethics, Fourth Edition*. New York, NY: Oxford University Press; 1994:120-188.
6. Tulane Law School. *Law & Sexuality: A Review of Lesbian, Gay, Bisexual, and Transgender Legal Issues*. 2004;13:5-603.
7. American Medical Association. H-20.920 HIV Testing. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=resultLink&doc=policyfiles/HnE/H-20.920.HTM&s_t=hiv+testing&catg=AMA/HnE&&nth=1&&st_p=0&nth=6&. Accessed June 29, 2005.
8. General Medical Council. *Serious Communicable Diseases*. London, England: General Medical Council; 1997.
9. Ellement J. Patient gets $10,000 in settlement of suit over "secret" HIV test. *The Boston Globe, City Edition*. June 1, 1996:Metro/Region, 13.
10. Dyer C. GP reprimanded for testing patients for HIV without consent. *BMJ*. 2000;320:135.
11. Bayer R, Oppenheimer GM. Toward a more democratic medicine: sharing the burden of ignorance. In: *AIDS Doctors: Voices From the Epidemic*. New York, NY: Oxford University Press; 2000:156-169.
12. Marks H. The dreams of reason: retrospect and prospect. In: *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990*. Cambridge, England: Cambridge University Press; 1997:229-248.
13. Annas GJ. Protecting patients from discrimination: the Americans with Disabilities Act and HIV infection. *N Engl J Med*. 1998;339:1255-1259.
14. Luce JM. Is the concept of informed consent applicable to clinical research involving critically ill subjects? *Crit Care Med*. 2003;31:S153-S160.
15. Bogart LM, Thorburn S. Are HIV/AIDS conspiracy beliefs a barrier to HIV prevention among African Americans? *J Acquir Immune Defic Syndr*. 2005;38:213-218.
16. Burris S. Public health, "AIDS exceptionalism" and the law. *John Marshall Law Rev*. 1994;27:251-272.
17. Turnock BJ, Kelly CJ. Mandatory premarital testing for human immunodeficiency virus: the Illinois experience. *JAMA*. 1989;261:3415-3418.
18. Luce JM, Cook DJ, Martin TR, et al; American Thoracic Society. The ethical conduct of clinical research involving critically ill patients in the United States and Canada: principles and recommendations. *Am J Respir Crit Care Med*. 2004;170:1375-1384.
19. Sommerville A. Commentary: is testing for HIV without consent justifiable? *BMJ*. 2002;325:1226-1227.
20. Domingo P, Guardiola JM, Iranzo A, et al. Remission of progressive multifocal leucoencephalopathy after antiretroviral therapy. *Lancet*. 1997;349:1554.

Disclosing Individual Results of Clinical Research

Implications of Respect for Participants

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CONTROVERSY EXISTS ABOUT THE RESPONSIBILITY OF investigators to communicate the results of research to study participants. These research results may be categorized as either general study results, which represent aggregate data usually published by the research team, or individual results, which are research findings relevant to particular participants. Disclosure of individual research results has become particularly contentious in the context of genetics research, for which genotypes of individual participants often become known to investigators.[1] However, disclosure of individual results should be addressed in all research involving human participants.

When aggregate results of research correlate with aspects of the health and well-being of participants, disclosing individual results has the potential to significantly affect the lives of participants. Accordingly, investigators and institutional review boards (IRBs) should consider when and how participants should be informed of individual research results. This article reviews previously articulated policies on sharing research data with participants and proposes an alternative ethical approach for communicating individual study results based on respect for research participants. Translating this approach into workable guidelines for investigators and IRBs will require careful thought and discussion, ideally guided by further empirical research assessing the preferences of research participants to receive individual study results and their reactions to such disclosure.

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Existing Standards

Federal regulations governing the conduct of human subjects research provide no guidance on disclosing research results, with the exception of information that may affect a participant's decision to continue enrollment in a study, such as emerging data about adverse effects of study interventions.[2] Perhaps as a consequence, investigators inconsistently communicate research results to participants,[3-5] despite data suggesting that participants are interested in learning study results[6,7] and recent calls for investigators to communicate general research results routinely.[8,9]

Several prominent groups in the United States, including the Office of Protection from Research Risks,[10] the National Bioethics Advisory Commission (NBAC),[11] and the National Heart, Lung, and Blood Institute,[12] have attempted to set policies on sharing study results with research participants. These policies emphasize the possibility that sharing study results may harm participants, causing anxiety and unnecessary medical interventions. The policies further stipulate that research information must be clinically useful before it is shared with participants. For example, the NBAC recommendations are based on "the presumption that the disclosure of research results to subjects represents an exceptional circumstance."[11] Specifically, the NBAC recommends that disclosure of results should occur only when "a) the findings are scientifically valid and confirmed, b) the findings have significant implications for the subject's health concerns, and c) a course of action to ameliorate or treat these concerns is readily available."[11]

Problems With Existing Standards

It is unclear why prevailing policy on disclosure of individual results focuses exclusively on protecting research participants from harm and sharing only results with clinical utility. Regardless, these policies make investigators gatekeepers of research information relating to participants instead of offering participants the opportunity to determine what research information about themselves they wish to know.

The current disclosure policy should be reconsidered in light of data that suggest that the prevalence of distress caused to participants by disclosure is low[13] and that most individuals find disclosure of test results beneficial, regardless of the actual result or accompanying psychic distress.[7,14-16] Additionally, the requirement of clinical utility precludes investigators from sharing individual results that may be personally meaningful to participants even if those results have little or no clinical significance or relate to conditions for which no treatment exists or are late in onset.

Ethical Rationale for Disclosure

Respect for persons is a basic ethical principle that gives rise to obligations regarding how competent adults should be treated. At a minimum, the principle of respect prohibits treating persons as mere means to an end. However, additional specific obligations of respect derive from interpersonal or institutional relationships between persons.

In biomedical research, respect for persons includes investigators' obligations not to coerce or deceive research participants and to obtain informed consent. Respect for persons, including respect for participants' self-determination and a recognition of their integral role in research, underlies investigators' responsibilities to make aggregate research results available to participants.[2,9,17-19] The same considerations that ground making aggregate study conclusions available to participants also oblige researchers to make individual results available to participants upon request. It would be disrespectful to treat research volunteers as conduits for generating scientific data without giving due consideration to their interest in receiving information about themselves derived from their participation in research.

Investigators who share aggregate study results with research participants are likely to receive requests for individual results as participants seek to understand study conclusions that appear relevant to their health or well-being. In disclosing requested individual study results investigators show respect for participants' self-determination, allowing them to incorporate research results into their personal decision making. Furthermore, by providing requested results, investigators acknowledge participants' presumptive entitlement to information about themselves and show gratitude for participants' voluntary participation in research.

However, investigators' prima facie responsibility to respond to participants' requests for individual study results may be overridden in some circumstances. Requested results can be justifiably withheld if disclosing information predictably compromises the safety of a participant or third party; for example, a finding of misattributed paternity in the case of a couple with a history of domestic violence. Knowledge of a threat to participants' safety nevertheless should be distinguished from concerns about possible psychic distress or mistaken medical interventions (for example, related to information about a genetic risk factor) in the absence of data suggesting that these latter harms are likely. In addition, requested individual results may be temporarily withheld until completion of the study if disclosure would compromise scientific validity (eg, would break blinding of a randomized drug trial). An important point is that individual study results should never be withheld when they provide evidence of an immediate risk to individual participants.

Inviting Requests for Individual Results

Respect for persons as research participants requires going beyond providing individual results on request. The same considerations of respect for persons that ground investigators' responsibility to respond to requests from participants for individual research results also ground investigators' responsibility, subject to IRB oversight, to invite such

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requests under certain circumstances. If there is reason to believe that a research result could be significantly meaningful to participants, investigators should make participants aware that this information has been or will be collected and, consequently, invite a request for those individual results.

Existing disclosure policies limit the scope of "meaningful information" to data that have clear, direct implications for participants' clinical treatment.[11] However, research participants have been shown to be interested in using test results for other important aspects of their lives, such as the decision to have children or, in the case of late-onset disease, to make appropriate educational or career plans.[20] Information generated in research might also be relevant to understanding potential vulnerability to disease conditions and participants' personal identities. Thus, investigators and IRBs should consider the broader context of potentially meaningful information a study might uncover and include provisions in the study design for proactively alerting participants to the availability of this information. The informed consent process offers an opportunity for investigators to alert participants about the future existence of results about them and also allows participants the chance to request those results. Future empirical research will aid investigators and IRBs in determining which results will be meaningful to participants.

It is critical to take the reliability and accuracy of study information into account when considering inviting requests for individual results. Research findings may not be replicated. Accordingly, it may be wise to refrain from inviting requests for results that are preliminary until the reliability of the information has been adequately established. When requested, however, investigators should disclose preliminary results, ensuring that adequate emphasis is placed on any uncertainty as to the reliability or implications of the information communicated.

Objections to Disclosure

There are at least 2 objections to a policy requiring disclosure of requested individual research results. First, some may argue that if investigators clearly state during the informed consent process that results will not be available to individual study participants, the investigators have no obligation to do so. However, even though informed consent is generally a necessary component of ethical research with human participants, it is not sufficient. Respect for participants operates independently from the informed consent process, as do fair subject selection and independent review of protocols.[18] Investigators cannot use informed consent to waive participants' rights and should not use informed consent to disclaim ethical responsibilities.[21]

Second, US investigators and research administrators may be concerned that the Clinical Laboratory Improvement Act of 1988 (CLIA)[22] prevents disclosure of research results if the data were obtained in a research laboratory that is not CLIA-compliant. CLIA delineates quality control standards for laboratories performing tests for the purpose of "providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings." When potentially clinically relevant research results have been obtained in a non–CLIA-compliant laboratory, investigators must balance their responsibility to notify participants of these meaningful results with the potential added burden of retesting samples in a CLIA-compliant laboratory to ensure analytic validity. Importantly, CLIA does not restrict the communication of non–clinically relevant research results to participants, which may include some reproductively relevant results such as genetic carrier status, results important to participants' social or personal identity, or communication of other requested results. Nevertheless, investigators should be candid with participants about the reliability of any disclosed information.

Method of Disclosure

Much of the controversy about disclosing individual research results stems from the uncertainty inherent in the interpretation of research data. This uncertainty could be problematic in 2 ways. First, investigators may not be able to interpret confidently the meaning of particular research results; for example, those generated in early development or application of a test for a genetic marker, as in the case of *APOE* genotyping for Alzheimer disease. Second, participants may have difficulty understanding complex or probabilistic interpretations of research results and may consequently pursue harmful or unnecessary medical interventions, a concern, for example, accompanying the communication of results of *BRCA1/2* genotyping.[23] Investigators therefore may be hesitant to disclose research results if they doubt their own ability, or that of their participants, to understand and interpret research results. However, these problems can be addressed. If the investigator is unable to interpret results in the context of the study goals, he or she should be willing to explain this uncertainty to participants. Furthermore, if requested individual results are to be meaningful and useful to participants' personal decision making, they must be disclosed in a manner that is as understandable as possible. Investigators should rely on plain language[24] and use established counseling methods to communicate complicated or uncertain results requested by participants.

Some object that the costs and burdens of disclosing study results to participants, including contacting participants and maintaining trained counselors on staff, will tax already strained research budgets and make future studies more difficult.[25] This is an important concern but should not obviate investigators' obligation, based on respect for persons, to communicate requested individual results to participants. The actual costs of disclosure are likely to be small for most studies. For example, ancillary counselors may only

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be needed to communicate information relevant to specialty health care or reproductive decisions and will not be needed for the disclosure of most research results. Additionally, providing requested results to participants will make the process of research more transparent and may increase participants' willingness to enroll, thereby facilitating future studies.

Conclusions

Respect for participants in research underlies the responsibilities of investigators to communicate the aggregate conclusions of clinical research to participants. As investigators increasingly provide these results to participants, they are likely to receive more requests from participants for individual-level results. Respect for research participants requires investigators to meet these requests in all but a few circumstances, and the burden is on the investigators to justify nondisclosure. Additionally, information that can be predicted to be meaningful to participants should be identified by investigators and IRBs in the design phase of the study and highlighted to participants during the informed consent process or after the completion of the study, as appropriate. Adoption of these guidelines is likely to expand respectful communication between investigators and participants in research, enhance the transparency of clinical research, and improve public perception of the biomedical research enterprise.

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REFERENCES

1. Fuller BP, Kahn MJ, Barr PA, et al. Privacy in genetics research. *Science*. 1999; 285:1359-1361.
2. Office for Human Research Protections. Protection of human subjects (2001) (codified at 45 CFR §46). Available at: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm. Accessed July 15, 2005.
3. Fernandez CV, Kodish E, Taweel S, Shurin S, Weijer C. Disclosure of the right of research participants to receive research results: an analysis of consent forms in the Children's Oncology Group. *Cancer*. 2003;97:2904-2909.
4. Fernandez CV, Kodish E, Shurin S, Weijer C. Offering to return results to research participants: attitudes and needs of principal investigators in the Children's Oncology Group. *J Pediatr Hematol Oncol*. 2003;25:704-708.
5. Partridge AH, Hackett N, Blood E, et al. Oncology physician and nurse practices and attitudes regarding offering clinical trial results to study participants. *J Natl Cancer Inst*. 2004;96:629-632.
6. Partridge AH, Burstein HJ, Gelman RS, Marcom PK, Winer EP. Do patients participating in clinical trials want to know study results? *J Natl Cancer Inst*. 2003;95: 491-492.
7. Partridge AH, Wong JS, Knudsen K, et al. Offering participants results of a clinical trial: sharing results of a negative study. *Lancet*. 2005;365:963-964.
8. Partridge AH, Winer EP. Informing clinical trial participants about study results. *JAMA*. 2002;288:363-365.
9. Fernandez CV, Kodish E, Weijer C. Informing study participants of research results: an ethical imperative. *IRB*. 2003;25:12-19.
10. Office for Protection From Research Risks. *Protecting Human Research Subjects: Institutional Review Board Guidebook*. Bethesda, Md: National Institutes of Health; 1993.
11. National Bioethics Advisory Commission. *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance.* Rockville, Md: National Bioethics Advisory Commission; August 1999.
12. National Heart, Lung, and Blood Institute. Working Group on Reporting Genetic Results in Research Studies meeting summary. Available at: http://www.nhlbi.nih.gov/meetings/workshops/gene-results.htm. July 12, 2004 (updated September 30, 2004). Accessed July 15, 2005.
13. Broadstock M, Michie S, Marteau T. Psychological consequences of predictive genetic testing: a systematic review. *Eur J Hum Genet*. 2000;8:731-738.
14. Smith CO, Lipe HP, Bird TD. Impact of presymptomatic genetic testing for hereditary ataxia and neuromuscular disorders. *Arch Neurol*. 2004;61:875-880.
15. Steinbart EJ, Smith CO, Poorkaj P, Bird TD. Impact of DNA testing for early-onset familial Alzheimer disease and frontotemporal dementia. *Arch Neurol*. 2001; 58:1828-1831.
16. Schulz CJ, Riddle MP, Valdimirsdottir HB, Abramson DH, Sklar CA. Impact on survivors of retinoblastoma when informed of study results on risk of second cancers. *Med Pediatr Oncol*. 2003;41:36-43.
17. Council for International Organizations of Medical Sciences; World Health Organization. *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Geneva, Switzerland: World Health Organization; 2002.
18. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *JAMA*. 2000;283:2701-2711.
19. 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: Department of Health, Education, and Welfare; 1979.
20. Fanos JH, Gelinas DF, Miller RG. "You have shown me my end": attitudes toward presymptomatic testing for familial amyotrophic lateral sclerosis. *Am J Med Genet A*. 2004;129:248-253.
21. Banks TM. Misusing informed consent: a critique of limitations on research subjects' access to genetic research results. *Sask Law Rev*. 2000;63:539-580.
22. Centers for Medicare and Medicaid Services. Laboratory requirements, 42 *Federal Register 493* (2003).
23. van Dijk S, van Asperen CJ, Jacobi CE, et al. Variants of uncertain clinical significance as a result of *BRCA1/2* testing: impact of an ambiguous breast cancer risk message. *Genet Test*. 2004;8:235-239.
24. Executive Secretariat, National Institutes of Health. The Plain Language Initiative. Available at: http://execsec.od.nih.gov/plainlang/index.html. 2003. Accessed July 15, 2005.
25. Lawrence WF, Peshkin BN, Liang W, Isaacs C, Lerman C, Mandelblatt JS. Cost of genetic counseling and testing for BRCA1 and BRCA2 breast cancer susceptibility mutations. *Cancer Epidemiol Biomarkers Prev*. 2001;10:475-481.

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