HeLEX Seminars

'Talking Law & Ethics'

Feeding results back to research participants

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Talking Law and Ethics

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overview

background

ethical justification

to feedback

state of science

core problems

way forward

open discussion

background

- trend to feed research results back
    * **terminology** (disclose, return, feedback, notify)
- genomic accumulation & sophistication
    * rapid accumulation of massive amounts of information
    * exponential sophistication of research technologies
- social context, expectations of access

justification

- standard of non disclosure
- **AGAINST disclosure**
  * nature of research
  * therapeutic misconception
  * harm
  * right not to know
- **PRO disclosure**
  * autonomy, self-determination
  * no means to an end
  * reciprocity
  * trust, communication

nature and extent of duty

- general routine duty v 'some' duty (obligation v consideration) to disclose
- proactive (offer) v passive (request)
- ethical v legal
- confusion
- focus on 'offer'

types of results

- **aggregate** (wide dissemination)
- **individual** (narrowly qualified duty)
  * **beyond traditional boundaries?**

    Lumley T, Rice, K. 'Potential for Revealing Individual-Level Information in Genome-wide Association Studies' 2010 JAMA 303(7) 659-660
- **research findings (RF) v incidental findings (IF)**
  * **raw data**
  * **high or low penetrance**
  * **treatable or non-treatable**
  * **common complex disease**

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incidental finding

- "… incidental finding (IF) is a finding concerning an individual research participant that has potential health or reproductive importance and is discovered **in the course** of conducting research but is **beyond the aims** of the study…"

  Van Ness, B. 'Genomic Research and Incidental Findings' 2008 JLME 36(2) 361

- the guidelines developed for RF are relevant to IF

  Wolf, S.M. et al 'Managing Incidental Findings in Human Subjects Research' 2008 JLME 36(2) 219

Table 3
Comparison of Recommendations on Returning Individual Research Results

National Bioethics Advisory Commission (NBAC)*	Return results only if: (a) "the findings are scientifically valid and confirmed" (b) "the findings have significant implications for the subjects' health concerns" and (c) "a course of action to ameliorate or treat these concerns is readily available."
Centers for Disease Control (CDC)**	Criteria for returning individual results in population-based genetic research: "When the risks identified in the study are both valid and associated with a proven intervention for risk reduction, disclosure may be appropriate."
National Heart, Lung, and Blood Institute (NHLBI)***	Criteria for returning individual genetic results: (1) "The risk for the disease should be significant, i.e. relative risk>2.0. Variants with greater penetrance or associated with younger age of onset should receive priority." Note: "Genetic test results should not be reported to study participants and their physicians as clinically valid tests unless the test(s) was performed in a CLIA certified laboratory. If the test was performed in a non-CLIA certified laboratory, a CLIA certified laboratory should be sought to confirm results by redrawing a sample and performing the test within the CLIA certified laboratory. Results reported by a research laboratory should be identified as 'research' results." (2) "The disease should have important health implications, i.e. fatal or substantial morbidity or should have significant reproductive implications" and (3) "Proven therapeutic or preventive interventions should be available."
National Research Council & Institute of Medicine (NRC & IOM)****	In human embryonic stem cell research, the duty to report individual research results "depends in large part on the reliability of the findings and the significance of the information to human health." "CLIA regulations do not permit the return of research results to patients or subjects if the test were not conducted in a CLIA-approved laboratory."
National Human Genome Research Institute (NHGRI)*****	Upon their request, "[r]esearch participants should have access to experimental research data except when . . . [t]he research results are of unproven clinical validity, and the IRB has judged that there is no benefit to the research subjects."

* National Bioethics Advisory Commission (NBAC), *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance* (Rockville, MD: 1999), 1: at 72.

** L. M. Beskow et al., "Informed Consent for Population-Based Research Involving Genetics," *JAMA* 286, no. 18 (2001): 2315-2321, at 2320.

*** National Heart, Lung, and Blood Institute, *NHLBI Working Group on Reporting Genetic Results in Research Studies, Meeting Summary*, Bethesda, MD, July 12, 2004, *available at* <http://www.nhlbi.nih.gov/meetings/workshops/gene-results.htm> (last visited January 8, 2008).

**** National Research Council and Institute of Medicine Committee on Guidelines for Human Embryonic Stem Cell Research, *Guidelines for Human Embryonic Stem Cell Research* (Washington, D.C.: National Academies Press, 2005): at 89-90.

***** National Human Genome Research Institute, *Federal Policy Recommendations Including HIPAA, available at* <http://www.genome.gov/11510216> (last visited January 8, 2008).

researcher will have access to less information than the physician providing patient care, a more limited set of obligations that are grounded in averting harm in the research process, and usually a participant less dependent than is a patient relying on a physician for health care. This suggests that researcher obligations will be more limited, but that researchers do shoulder obligations that include the proper handling of unexpected information of potential health or reproductive importance, including disclosure to participants when potential harm may be averted.

Specifying how researchers should handle IFs to meet these obligations is challenging. It is instructive to compare the literature on offering individual research results to participants (as opposed to offering aggregate research results to a study population, as in

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reliability of results

- **significance of findings**
  * serious / relevant / other
  * available medical intervention
  * benefit to patient
- **standards for evaluation**
  * research v clinical care / validity, utility, accreditation

Kohane, I. et al 'The Incidentalome: A Threat to Genomic Medicine' 2006 JAMA 296(2) 212

- **expectations of access?**

McGuire A.L. et al 'Research Ethics and the Challenge of Whole-genome sequencing' 2008 Nat Rev Genet 9(2) 152

responsibility

- who is responsible to disclose findings?
  - researcher
  - clinician
  - counselor
- to whom to disclose?
  - individual
  - third parties e.g. family
  - clinician

core issues

- 1. What should a researcher do when they uncover a research finding that may have health implications for the participant and her family members?
- 2. What if the finding is unrelated to the research to which the research participant has consented?
- 3. What are the researcher's responsibilities to communicate this information to the research participant or clinician?
- 4. What guidance is available when planning for these situations and/or making such decisions?

Dressler, L.G. 'Disclosure of Research Results from Cancer Genomic Studies: State of the Science' (2009) Clin Cancer Res 15(13) 4275

steps forward

- ***establish a management pathway***
  * e.g. develop guidelines for researchers to assess the likelihood that the study will reveal clinically relevant information
  * e.g. develop policies to guide how these findings should be validated, and returned to research participants

steps forward

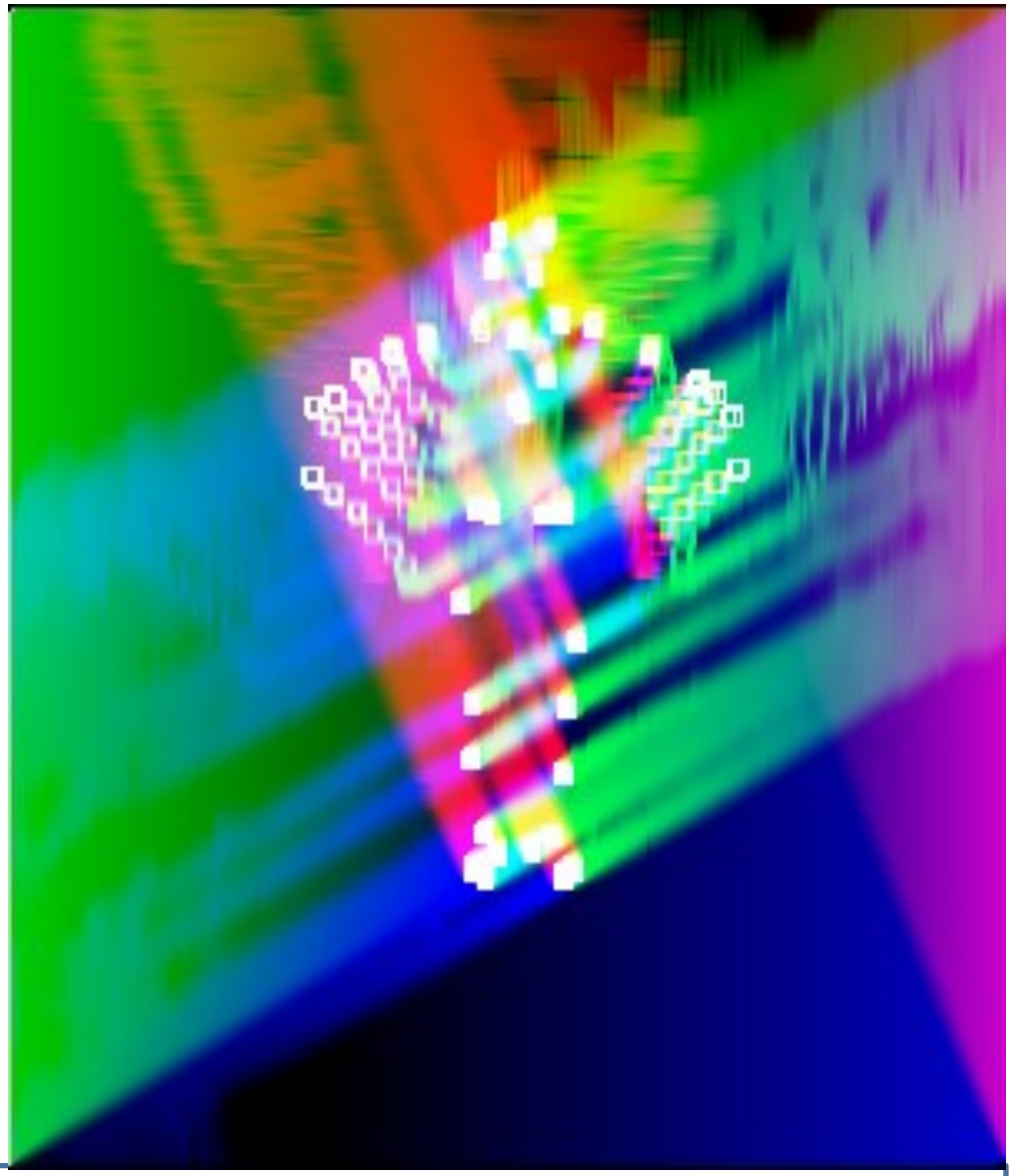
- ***build opportunities for participants to know or not to know the findings***
  * e.g. indicate and justify in the informed consent process whether or not individual RF or IF will be disclosed to the participant
  * e.g. plan for the release of aggregate data in plain language

steps forward

- ensure that medical professionals who are trained in genetic counseling communicate the results to participants
- ***set up national task forces and/or working groups to develop policy about feedback***

sum up

- variation of opinion
- ethical duty
- research results
- incidental findings
- reliability
- responsibility
- guidance
- ethics ≠ law



legal considerations

- common law duty of care in research
  * same standard as in clinical context (equivalence)
  * close relationship (akin to doctor - patient)

Creutzfeldt-Jakob Disease litigation (1996) QB 54 BMLR 8:9

- therapeutic v more removed research
- establish proximity: ***grey area!***
- no case law, no statute, no guidelines

legal considerations

- ECHR Art 2 ‘positive obligation to take steps to avoid risk of loss of life or serious harm’

  Osman v UK [1998] 29 ECHR 245

- ECHR Art 8 and subject access request

  K.H. and others v Slovakia App 32881/04 [2009] ECHR 709

- Identifiable third parties / family relatives
  - (UK) no duty of care (sufficiently identifiable, facts of case)
  - (US) limited duty to warn patient (of risk, and for patient to inform others)

discussion

- difficulties in current work
- existing guidance
- solutions in current work
- other issues?

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recommended reading

- *Journal of Law, Medicine and Ethics* 36 (2) 2008

  Special Issue, Symposium on Incidental Findings

  http://www.jlme.org/content/vol36/issue2/index.dtl
- Kaye J. et al 'Ethical, Legal and Social Issues Arising from the use of GWAS in Medical Research', HeLEX/Ethox Wellcome Trust Report 2009

  http://helex.medsci.ox.ac.uk
- Bovenberg J. et al, 'Always Expect the Unexpected', Center for Society and Genomics Report 2009

  http://www.society-genomics.nl

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