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Biobanks and Electronic Health Records:

Ethical and Policy Challenges in the Genomic Age

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INTRODUCTION

In this paper we discuss the ethical and policy challenges presented by the construction and use of **biobanks** and **electronic health records** systems, with a particular focus on how these resources implicate certain types of security concerns for patients, families, health care providers and institutions. These two technology platforms are selected for special emphasis in this paper for two reasons. First and foremost, there is a close connection between them. Indeed, of the many accepted definitions, this one from the German National Bioethics Commission provides a sense of this close connection and the great power and reflects the great power these two separate platforms provide to probe more deeply the connection between genotype and phenotype:

> "…[B]iobanks are defined as collections of samples of human bodily substances (e.g., cells, tissues, blood or DNA as the physical medium of genetic information) that are or can be associated with personal data and information on their donors."

Second, these two topics implicate both *clinical* ethics issues (those arising at the bedside for health care providers and patients), and *human research* ethics issues (issues arising for scientists, research subjects, ethics review bodies and regulatory authorities). Both of these sub-specialty areas confront similar and complementary ethical issues; for example, issues arising from the nature and adequacy of informed consent, the sufficiency of systems to protect

personal privacy and confidentiality, or the need to balance concerns relating to data security and the need to know. A growing research base supports calls for more attention to these issues, and yet current professional ethics frameworks and policy consultation methods are poorly organized and ill-equipped to anticipate and fully address ethical issues in health information technology generally, or to provide adequate ethical assessment of the tools that elicit these issues.

Our strategy is to orient readers to the history and context of these issues, to frame several key challenges for researchers and policy makers, and then to close with several recommendations for next steps.

BIOBANKS

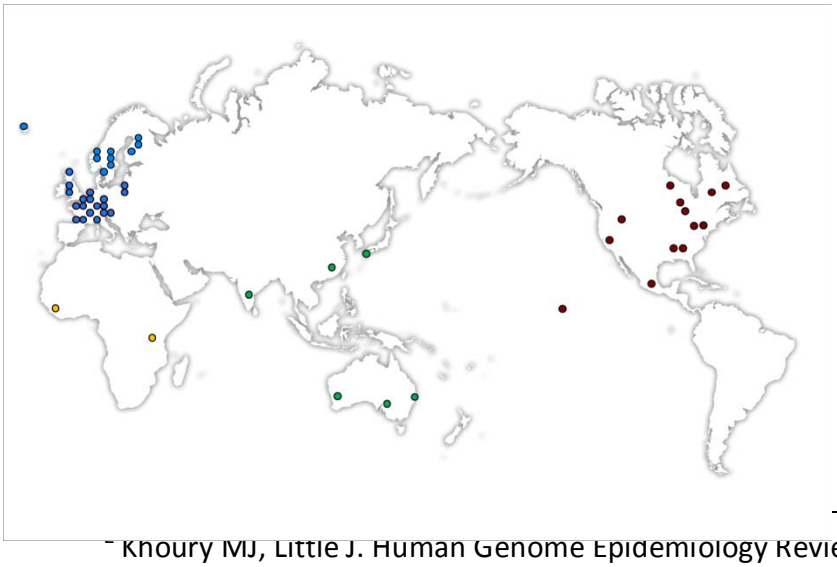
From the very early history of clinical pathology, studies of archived human biological materials (HBMs) including specimens of blood, DNA, but also bone, organs and other tissues have played a prominent role in the diagnosis and treatment of diseases as diverse as cancer, heart disease, diabetes, and stroke,[1] as well as other diseases of significant public health impact.[2] Biobanks

[1] Ackerknecht E. Medicine at the Paris Hospital, 1794–1848 (1967); Baltimore: Johns Hopkins University Press; Korn D. Contribution of the Human Tissue Archive to the advancement of medical knowledge and public health. In: National Bioethics Advisory Commission. Research Involving Human Biological Materials: ethical issues and policy guidance, Vol. II: commissioned papers. Bethesda, MD: US Government Printing Office; 2000: E1–E30.

exists on every continent of the globe, including Antarctica. Figure 1 provides a graphic illustration of many of these repositories, principally those limited to national or other institutional repositories. While no global census of the number of samples and specimens has been undertaken, one of the first domestic U.S. accounting was conducted by the National

Figure 1- Biobanks Around the World

32 million specimens were stored in the nation's pathology laboratories, newborn screening collections, forensic DNA banks, blood banks, umbilical cord banks, organ procurement organizations, tissue banks, and research-related repositories that are maintained for longitudinal studies. [3] This data was later updated by Eiseman, who adjusted the figure upwards to more than



[2] Khoury MJ, Little J. Human Genome Epidemiology Reviews: The beginning of something HuGE. American Journal of Epidemiology 2000;151(1):2-3.

[3] National Bioethics Advisory Commission (2000). Research Involving Human Biological Materials: ethical issues and policy guidance, Vol II: Commissioned papers. Bethesda, MD: US Government Printing Office; Eiseman E. The National Bioethics Advisory Commission: contributing to public policy (MR-1546-STPI). Santa Monica (CA): RAND Corporation; 2003.

350 million.[4] Both figures are likely to be substantial underestimates since they do not include proprietary databases, classified military banks, or privately maintained collections, let alone all the "fridges" maintained in university and hospital laboratories. A conservative estimate of the samples stored in repositories around the world must now exceed one billion. So ubiquitous are these banks, and their potential, that *Time* magazine listed biobanks one of the "Ten Ideas That Are Changing the World Right Now".[5]

Common to the establishment and maintenance of every bank -- domestic or international, public or proprietary -- are a set of ethical and policy issues that must be addressed from the moment the banks are designed through the collection and storage of materials, and which continue when materials are shared and disseminated with others.

Ethical Issues in the Collection, Storage and Use of Human Biological Materials

[4] Eiseman, E., and Haga, S.B. (1999) Handbook of Human Tissue Resources: A National Resource of Human Tissue Sample, Santa Monica, CA: RAND, MR-954-OSTP.; Eiseman, E., Bloom, G., Brower, J., Clancy, N., & Olmsted, S.S. (2003a). Case Studies of Existing Human Tissue Repositories: "Best Practices" for a Biospecimen Resource for the Genomic and Proteomic Era, Santa Monica, CA: RAND, MG-120-NDC/NCI.

[5] *Time,* March 16, 2009. The other nine: Jobs Are the New Assets; Recycling the Suburbs; The New Calvinism; Reinstating The Interstate; Amortality; Africa: Open for Business; The Rent-a-Country; Survival Stores; and Ecological Intelligence.

The 'standard' clinical paradigm describing the nature of the encounter between a patient and her physician may be summed up as follows: the virtuous physician, respectful of individual patients, will seek permission to undertake interventions (treatment, surgery, etc.) that are jointly believed to be in the particular patient's best interest. In so doing, the respectful clinician provides sufficient information to allow an informed choice by the patient to be treated, while at the same time protecting certain information from the gaze of those who have no need to know (or see) it.[6]

Similarly, the "standard' *research"* paradigm describing the nature of the relationship between an investigator and prospective research subject may be described as follows: the virtuous researcher is one who designs studies that answer valuable and valid questions, avoids conflicts of interest that compromise scientific objectivity and bias, submits protocols for prior scientific and ethics review and approval by an Institutional Review Board that includes clearly written consent forms and descriptions of how consent will be sought, recruits participants while protecting vulnerable populations from exploitation, and conducts the study according to accepted scientific standards of rigor, analysis and reporting.[7]

[6] A voluminous literature exists on these topics. See for example, Pellegrino ED and Thomasma DC (1984) For the Patient's Good. New York: Oxford; Ramsey, P. For the Patient's Good (1960) Princeton University Press; Veatch RM. A Theory of Medical Ethics (1981), New York: Basic Books.

[7] An equally voluminous literature exists on this topic, but one paper in particular is highlighted because of its enduring impact. Beecher, HK. Ethics in Clinical Research. (1966):

These two "paradigms" may only be ideals, but whatever the valence we give to them, they are both being subjected to challenges arising from genomic science. The esteemed Canadian physician, William Osler wrote in 1892: "*If it were not for the great variability among individuals, medicine might as well be a science and not an art."* This statement was prescient in many ways. Little did he know that a little more than a century later, researchers with the complete sequence of the human genome would turn their attention to the minute but important differences between people at the level of the individual letters of the genetic alphabet – A,C,T,G. These differences, called single nucleotide polymorphisms (SNPs) help to explain why some people respond to drugs and other do not, why some are at increased risk of succumbing to certain diseases while other are not. Many of the issues arising from these developments were first outlined by NBAC in 2000,[8] and others are found more extensively in the Appendices to this report. We review and update some of these, as they relate to the focus of this conference.

New England Journal of Medicine 274(24):1354-1360. In a memorable quotation, Beecher described the most reliable safeguard for ensuring ethical experimentation is: "…the presence of an intelligent, informed, conscientious, compassionate, responsible investigator."

[8]National Bioethics Advisory Commission (2000). Research Involving Human Biological Materials: ethical issues and policy guidance, Vol. II: Commissioned papers. Bethesda, MD: U.S. Government Printing Office.

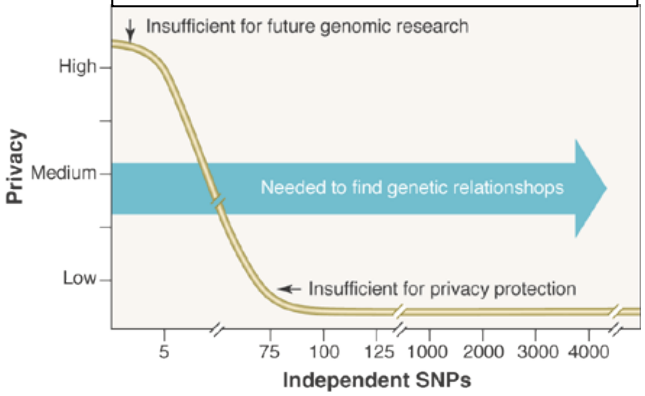
Identifiability. A key consideration in determining the extent to which ethical concern is implicated in the collection and use of HBM bears on the degree to which a human subject is involved in the research, and particularly whether the biological material can be linked to the person from whom it was obtained. [9] The debate about research use of human biological materials has been at times complicated by the fact that the language that is used varies and often is at odds with the categories used in the applicable federal regulations. To the extent that individuals can be identified, they can be harmed either directly or indirectly. Stanford bioinformaticist Russ Altman and colleagues helpfully framed the dilemma facing genomic scientists and privacy advocates. [10] Put simply, the more SNPs that are identified, the more an individual person can be identified and, therefore, the less privacy protection that can be assured. The converse of this relationship holds as well: the fewer SNPs identified, the less one is able to make meaningful associations of genotype and phenotype. At the extremes, one can imagine two undesirable outcomes of this relationship: absolute privacy protection dramatically inhibits research; complete access to SNP information dramatically inhibits privacy protection.

[9] The relevant regulatory provision is found at 45 CFR 46.102(f), referring to identifiable private information.

[10] Lin Z, Owen AB, Altman RB. Genetics, Genomic Research Human Subject Privacy. (2004) Science Jul 9;305(5681):183

The challenge is in identifying the optimal balance between the two concerns – bearing in mind that the electronic health record of the near future will come to serve as a favored repository or source of genomic information for both clinical and research purposes. Still, "Altman's Curve" (as we have chosen to call it, see Figure 2), is only a heuristic device to capture the real dilemma between the need to find genetic relationships of significance and the need to ensure adequate protection of private information. One of the approaches to resolving this dilemma has come from empirical research conducted on public attitudes about and willingness to participate in biobanking.

Figure 2- Altman's Curve



Informed Consent. The obligation to seek permission to obtain and use parts of an individual, whether for research or treatment purposes is among the most settled issues in bioethics and law. At issue in biobanking is not whether to obtain consent, but when, under what conditions and with what degree of specificity.[11]

[11] An equally exhaustive literature exists on consent. See for example, Sass, H. M. (1998). Genotyping in clinical trials: towards a principle of informed request. J Med Philos **23**(3): 288-96; Shickle, D. (2006) The consent problem within DNA biobanks. Stud Hist Philos Biol Biomed Sci **37**(3): 503-19; Skolbekken, J.-A., L. Ã. y. Ursin, et al. Not worth the paper it's written on? Informed consent and biobank research in a Norwegian context.Critical Public Health **15**(4): 335-347; Stegmayr, B. and K. Asplund (2002). Informed consent for genetic research on blood

Public Attitudes. A growing body of evidence exists regarding the public's willingness to donate tissue or other biological material to science in general, and to biobanks in particular. A review of the empirical literature conducted on PubMed in early 2009 found no fewer than 60 studies, with at least 20 surveys published between February 2008 and January 2009. [See Appendices]. Space does not permit a thorough review of these analyses, but at the risk of simplifying a very robust set of studies undertaken on different groups of people, in different countries, under different conditions, being asked different questions, it would appear that in recent years there has been a gradual *increase* in the public's expression of willingness to participate in biobanks.

Our own studies in Indiana are consistent with this general claim. Several of these surveys are briefly described. In 2006 and 2007 we surveyed cancer patients who contributed leftover tissue to the Indiana University Cancer Center Tissue Bank and found that a clear majority of subjects would permit unlimited future research on stored human biological materials without re-contact and re-consent, and, further, that a significant minority appear to

stored for more than a decade: a population based study. BMJ **325**(7365): 634-5. Wendler, D. (2006). One-time general consent for research on biological samples. BMJ 332(7540): 544-7. Williams, G. and D. Schroeder (2004). Human genetic banking: altruism, benefit and consent. New Genet Soc 23(1): 89-103.

desire ongoing control over future research uses of their tissue. [12] In 2007-2008 when we surveyed women in community health clinics to estimate their willingness to donate specimens for DNA analysis by needle stick as compared with collection of saliva, the majority of the 279 women surveyed would do both in high numbers (needle stick: 68.3%; saliva: 75.7%).[13] In both of these surveys, we learned that *support* for biobanking was modulated by certain factors. For example, in our study of cancer patients about two-thirds (62.6%) of respondents agreed or strongly agreed that it was "all right" for researchers to use their donated tissue to develop a new tool or treatment for profit though support for "for profit" biobanking varied somewhat with this population depending on age, education and other demographic factors. In our study involving women in the community health clinic, we found a number of reasons why they indicated an unwillingness to participate, including worries about the use of the specimens, violations of privacy, the potential for future discrimination, and the fear surrounding unfavorable results.

We also undertook a more comprehensive telephone survey of more than 1,000 Indiana adults in 2007 and 2008, one of the aims of which was to assess public confidence in medical

[12] Helft PR, Champion VL, Eckles R, Johnson CS, Meslin EM: Cancer patients' attitudes toward future research uses of stored human biological materials. J Empir Res Hum Res Ethics 2007;2:15-22.

[13] Haas DM, Renbarger JL, Meslin EM, Drabiak K, Flockhart D: Patient attitudes toward genotyping in an urban women's health clinic. Obstet Gynecol 2008;112:1023-1028.

and genetic research.[14] Respondents were asked five questions relating to privacy, answering each using a scale of 1-10 with 1 being 'not at all concerned' and 10 being 'extremely concerned':

- How concerned are you that genetic research is carried out by pharmaceutical, biotechnology and other for-profit businesses?
- How concerned are you that information collected in the course of genetic research might be used by people other than the researchers?
- Specifically, how concerned are you that this information might be used by employers?
- How concerned are you that this information might be used by health insurance companies?
- How concerned are you that this information might be used by schools?

Table 1 (opposite) provides the demographic data relating to each of these questions. In general, the highest level of concern among the public is related to the use of genetic

Table 1- Concerns About Privacy

	Business	Non-Science	Employers	Insurance Companies	Schools
TOTAL	6.47	6.78	6.47	7.70	5.76
Gender					
Male	***6.13***	6.73	6.56	7.56	***5.55***
Female	***6.80***	6.83	6.39	7.83	***5.95***
Race					
White	6.44	***6.72***	6.43	7.71	***5.67***
Minority	6.55	***7.24***	6.71	7.61	***6.24***
Age					
18-24	***6.36***	***6.38***	***6.05***	***6.93***	***5.25***
25-44	***6.34***	***6.77***	***6.31***	***7.67***	***5.59***
45-64	***6.57***	***7.04***	***6.85***	***8.10***	***6.00***
65 +	***6.62***	***6.51***	***6.40***	***7.59***	***6.04***
Education					
HS or less	6.65	6.87	6.58	7.59	***5.89***
Some College	6.48	6.91	6.55	7.76	***5.93***
4yr Degree	6.21	6.50	6.23	7.75	***5.33***

[14] IUPUI Survey Research Center. Public attitudes regarding genetic research: Survey methods and findings: IU Center for Bioethics, 2009 available at www. bioethics.iu.edu

information by insurance companies. The group with the highest level of concern comprised those approaching retirement (45-64-year-olds) who reported among the highest levels of concern over all five of the issues presented.

Finally, we recently completed a national telephone survey in September 2009 which we sought the opinions of close to 400 people about genetic research and the use of personal information, including specific questions about identifiability.[15] For example, we asked respondents to consider the following question:

> **Q2: If I were asked to provide access to my medical records to obtain information that could be used for genetic research, I would be willing to give permission for use of my records.**

On a scale of 1-5, where 1 signified that they "strongly agreed", and 5 that they "strongly disagreed", the responses from 397 respondents were as follows: (1) 19.8%; (2) 8.10%; (3) 19.5%; (4) 16.3%; (5) 36.6%. We also asked this question:

> **Q5: How confident are you that genetic research is generally carried out in ways that protect the privacy and confidentiality of the research subjects involved?**

On the same scale (1 = not at all, 5 = extremely concerned), the public sample (N = 397) responded as follows: (1) 8.40% ; (2) 14.10%; (3) 27.20%; (4) 24.60%; (5) 25.70%. We also asked a series of questions designed to elicit attitudes about the possibility that researchers

[15] We are still analyzing the survey results. Data presented in this paper are for illustrative purposes only.

might be able to identify individuals in published studies with increasing certainty, using attacks" such as those proposed by Homer[16] and more recently by colleagues from Indiana University-Bloomington.[17] We first gave an introduction:

> Now I would like for you to imagine that you are invited to participate in a genetic research study where you will be asked to give a blood sample that will be analyzed in a laboratory. When the study is completed, the results will be published. While you will not be personally identified by name, address, or any of the other usual ways, there are now sophisticated statistical techniques under development that might be able to identify you as a participant in the study. These techniques involve looking at DNA of all the people in the study, and then examining the blood samples. It is possible, therefore, to identify you, even though your name was not mentioned in the published article. Since the article will be read by other scientists and many other people, it is possible that they too might be able to identify you as a participant in the genetics study.

We then asked the following question:

> **Q7: Knowing this, how concerned would you be in being identified in this way? Please select a number between 1 and 5, with 1 being not at all concerned and 5 being extremely concerned.**

[16] N. Homer, S. Szelinger, M. Redman, D. Duggan, W. Tembe, J. Muehling, J. V. Pearson, D. A. Stephan, S. F. Nelson, and D. W.Craig. Resolving individuals contributing trace amounts of dna to highly complex mixtures using high-density snp genotyping microarrays. *PLoS Genet*, 4(8):e1000167+, 2008.

[17] Wang R, Li Y, Wang XF, Tang H, Zhou X. Learning Your Identity and Disease from Research Papers: Information Leaks in Genome Wide Association Study. Technical Report TR680. http://ns2.lam-mpi.org/cgi-bin/techreports/TRNNN.cgi?trnum=TR680. Accessed. October 1, 2009.

Of the 398 people who responded, answers were as follows: (1) 22.40%; (2) 16.10%; (3) 23.60%; (4) 13.40; (5) 24.50%. Given these responses, we then probed further to determine whether the likelihood of identifying individual persons affected their level of concern. Four questions were asked, providing respondents with different probabilities of being identified, ranging from < 5% to 95% or more. The Table below lists the responses to the interviewer's question when different probabilities of identifying the individual were given.

Q8A: What if the probability of identifying you is <5% ?		**Q8B: What if the probability of identifying you is between 5 and 20%?**		**Q8C: What if the probability of identifying you is about 50%?**		**Q8D: What if the probability of identifying you is 95% or more?**	
Yes	71.20		79.60		72.10		86.50
No	28.80		20.40		27.90		13.50
N = 391		N = 283		N = 226		N = 161	

It is tempting to accept data of the kind presented above as dispositive – and conclude that the public's opinions ought to guide public policy. We would, however, urge caution in drawing such premature conclusions. The first reason for this caution is reflected in the data above – we are not at all clear about the explanation for why a *greater* percentage of people would agree to participate in a study where there is a greater (rather than lesser) chance of their being identified.[18] A second reason for being cautious is explained by a counter-example from Australia.

[18] As noted above, these data have not been fully analyzed.

The Experience of the Western Australia Data Linkage Unit. For more than three decades, the state government of Western Australia has been collecting one of the world's largest administrative health datasets, including birth records, midwives' notifications, cancer registrations, inpatient hospital morbidity, in-patient and public out-patient, mental health services data and death records.[19] Used in combination with medical record audits, the WA Dataset provides a platform for comprehensive evaluation of health system performance. Moreover, investigators have developed a system for linkage which is aimed at meeting the dual goals of protecting privacy and enabling health systems research.[20] This "win-win" approach results from keeping any identifiable information from the researchers, who only need the linked data on exposures and outcomes for their analyses. Of note, since this program has been in place, general requests for access to identifiable data have declined markedly.[21] Indeed, when people in the general community were asked if they approved of

[19] Hobbs MS, McCall MG. Health statistics and record linkage in Australia. J Chronic Dis 1970;23(5):375-381; Stanley FJ, Croft ML, Gibbins J, et al. A population database for maternal and child health research in Western Australia using record linkage. Paediatr Perinat Epidemiol 1994;8:433-447;Holman CDJ, Bass AJ, Rouse IL, et al. Population-based linkage of health records in Western Australia: development of a health services research linked database. Aust N Z J Public Health 1999;23:453-459

[20] Kelman CW, Bass AJ, Holman CD. Research use of linked health data--a best practice protocol. Aust N Z J Public Health 2002;26:251-255.

[21] Trutwein B, Holman CD, Rosman DL. Health data linkage conserves privacy in a research-rich environment. Ann Epidemiol 2006;16(4):279-280.

their information being used in this way, they were found not only to be supportive of it, but they questioned why it was not already being done.[22]

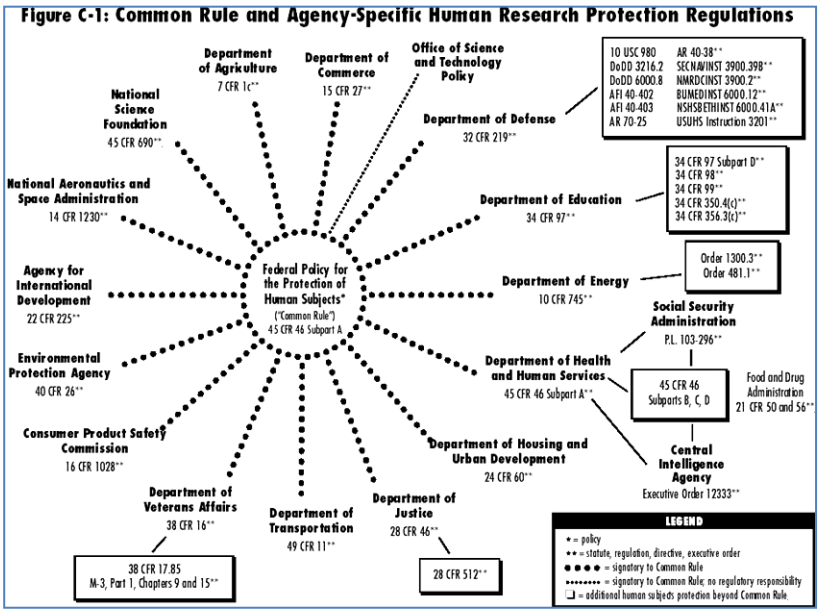
Our conclusion from this empirical data is that it is not enough to know *that* the public has concerns (as evinced by the public opinion data above). Instead, it is critical to appreciate that the context for these concerns inform the type of tradeoffs between protecting privacy and permitting access to information to advance research on human health.

Governance and Regulatory Issues. With the domestic and international proliferation of obanks and their associated connections to health information databases, scholarly attention has been turning from the ethical issues arising from the *construction* of biobanks to the ethical issues that emerge in their *operation and management.* In the years since there has been no shortage of guidance documents on these topics. A search of the authoritative *HumGen* database listed 52 international, 38 regional and 204 national guidance documents on the topic of biobanks alone.[23] In the United States, a set of federal regulations governs the oversight of

[22] Stanley FJ, Meslin EM Australia Needs a Better System for Health Care Evaluation, *Medical Journal of Australia* (2007); 186: 220-221

[23] http://www.humgen.org/int/GB2_p.cfm?mod=1. Accessed October 1, 2009.

research involving human subjects, and it is within this regulatory structure that the research uses of human biological materials is assessed.[24]



Many commentators have observed that there are significant ambiguities in the regulations for the protection of human subjects.[25] This situation can be partly explained by simply referring to a pictorial representation of the Common Rule (see opposite) that resembles a "hub and spoke" prepared by NBAC in 2001 to show how 16 federal agencies and

[24] This set of regulations includes but is not limited to the Common Rule (45 CFR 46 Subpart A); relevant FDA regulations at 21 CFR 50/56; the HIPAA Privacy Rule 45 CFR 160, 164; and the *Genetic Information and Non-Discrimination Act.*

[25] National Bioethics Advisory Commission: Research involving human biological materials: Ethical issues and policy guidance, volume i : Report and recommendations of the national bioethics advisory commission. Bethesda, MD, National Bioethics Advisory Commission, 1999; Evans BJ: Inconsistent regulatory protection under the u.S. Common rule. Camb Q Healthc Ethics 2004;13:366-379; Evans BJ: Finding a liability-free space in which personalized medicine can bloom. Clin Pharmacol Ther 2007;82:461-465.Evans BJ: Seven pillars of a new evidentiary paradigm: The food, drug, and cosmetic act enters the genomic era. Notre Dame Law Review 2009.

offices agreed to be bound by the same "common" set of rules (45 CFR 46, Subpart A), leaving more than 50 other agencies to fend for themselves. But this does not explain why, for example, the FDA's regulations differed in critical ways from those of the *Common Rule*.[26] Still, sufficient clarity is evident within the regulatory space provided by existing guidance documents to permit considerable local discretion by IRBs.[27] In other words, U.S. regulations already provide IRBs with the authority they need to make determinations about whether consent forms could be constructed to permit blanket consent, and about the adequacy privacy and confidentiality protections.

ELECTRONIC HEALTH RECORDS

The practice of medicine and nursing necessarily (though not of course sufficiently) require the keeping of records. Biobanks are in many respects records, albeit organic ones. More familiarly,

[26] Evans BJ, Meslin EM: Encouraging translational research through harmonization of FDA and Common Rule informed consent requirements for research with banked specimens. J Leg Med 2006;27:119-166

[27] Office for Protection from Research Risks: Issues to consider in the research use of stored data or tissues, 1997 www.ohrp.gov ; Drabiak-Syed K: State codification of federal regulatory ambiguities in biobanking and genetic research. J Leg Med 2009;30:299-327; Wolf LE, Lo B: Untapped potential: Irb guidance for the ethical research use of stored biological materials. IRB: Ethics & Human Research 2004;26:1.

physicians' notes about signs and symptoms, treatment decisions and outcomes serve as reminders, to guide the care of individual patients; and as a source of information for research, to shape the care of all patients. Without stored accounts about what is seen, felt, heard, measured and done, there can be no effective medical practice, no sharing, teaching learning of any substance or consequence.

The practice of making notes about patient encounters is ancient and has been attributed to Hippocrates, though what survive are case histories intended to be used for teaching. Garrison's 1913 classic, *An Introduction to the History of Medicine,* notes that in 25 of the 42 cases in the Hippocratic corpus, the patients died – and were therefore especially instructive; he compares these to the records of Galen, which are boastful and limited to remarkable cures and the errors of other practitioners. Hippocrates: *" I have written this down deliberately believing it is valuable to learn of unsuccessful experiments and to know the causes of their failure."*[28]

More than a millennium later, the Syrian physician Ishap bin Ali Al Rahwi (CE 854–931) suggests in *Ethics of the Physician* that clinicians had a duty to make two sets of notes with one copy to be assessed by a council of physicians to determine if the standard of care had been

[28] Garrison FH. *An Introduction to the History of Medicine*, Philadelphia: W.B. Saunders Company, 2nd Ed., 1917, p. 88. Note that the Hippocratic corpus is likely a composite, drawn from several sources, and there is disagreement among some historians about the very existence of a man, Hippocrates, as the author of documents attributed to him.

followed. It is apparently the first documented instance of peer review. (The council's reports could later be used in malpractice suits.)[29] Even the most rudimentary data can be of use: John Snow's famous analyses of case reports and maps contributed to halting a cholera epidemic in London in 1854.[30]

The clearest early modern statement of the utter necessity of complete and easily accessible medical records is arguably made by Abraham Flexner in his analysis of U.S. medical education. The medical record is seen as essential for quality care and the education of those who would provide it – in ways not dissimilar to contemporary claims for the utility of biobanks for translational medicine and pharmacogenomics:

> Pupils are more apt to disappoint than to astonish their teachers; they do not generally better their instruction. In consequence hospital records made by internes [sic] graduated by these schools are scant and unsystematic … whoever is responsible, poorly kept records are very apt to denote inferior bedside instruction. The situation is this: there lies the patient; teacher, interne, and students surround the bed. The case is up for discussion. A question arises that requires for its settlement now a detail of the patient's previous history, now a point covered by the original physical examination, now something brought out by microscopic examination at some time in the course of the disease. If complete, accurate, and systematic records hang at the bedside, there is an inducement to ask questions; doubtful matters can be cleared up as fast as they are suggested. That, then, is

[29] Spier R. The history of the peer-review process. *Trends in Biotechnology* 2002;20(8):357-358; Al Kawi MZ. History of medical records and peer review. *Ann. Saudi. Med*. 1997;17:277–278; Ajlouni KM, Al-Khalidi U. Medical records, patient outcome, and peer review in eleventh-century Arab medicine. *Ann. Saudi Med*. 1997;17:326–327.

[30] Koch T, Denike K. Crediting his critics' concerns: Remaking John Snow's map of Broad Street cholera, 1854. *Social Science & Medicine* 2009;69(8):1246-1251.

> the place for the records – full records, at that. In few instances are the records full; in still fewer are they, full or meager, in easy reach.[31]

The 1940s saw the invention of the first programmable electronic computing machines (developed in secret as tools of warcraft) and, in temporal coincidence, the policy decision that properly maintained medical records should be a requirement for hospital accreditation. Within a generation, physicians were experimenting with, developing and, well, fooling around with computers as storage devices for those records. There are many reasons why it made sense to explore the utility of information technology. They include:

- Human memory is fallible, variable and, for certain complex information, short. The clinical encounter generates too much information to recall accurately. This was, in one degree or another, always a challenge, but given the amount of clinical information generated by the modern clinician it became clear that storing this information on paper is feckless and perhaps even futile.
- Even if one could easily and swiftly find the information needed for patient care, it was difficult to analyze. Computers make it easy to track and compare lab values, diagnoses and prescriptions, say, over time.
- Information technology enables analyses that bear on change, quality, error and other phenomena. A computer lets one compare the patients on Ward A (or Hospital X) to those on Ward B (or Hospital Y), for instance. Simple reminder and alert systems run on quotidian clinical data.
- Computers support research which would otherwise be impossible, or at least impossibly tedious.
- Information technology supports the kinds of analyses and assessments that now go by the names of "comparative effectiveness research" and "meaningful use."

[31] Flexner A. Medical Education in the United States and Canada, Bulletin Number Four (The Flexner Report). New York: The Carnegie Foundation for the Advancement of Teaching, 1910.

Here is the case, made more than two decades ago, for "Fully operational computer-stored medical record systems" –

> These systems have demonstrated three kinds of benefits: (1) Computer-stored medical records can solve many of the logistic problems of finding, organizing, and reporting patient information that occur with purely paper systems. (2) They can improve the efficiency and accuracy of physicians' decisions by performing calculations and by identifying clinical events that need attention. (3) They can guide future policies and practices by analyzing past clinical experience within a hospital or a physician's office.[32]

If this is true, then something remarkable has happened, or is happening. Consider that contemporary bioethics has in some key respects been about the appropriate use of (new) technology. Generally, scholars have tried to determine whether a tool or device should be used at all and, if so, which constraints should be in place. Put differently, bioethics has been about finding arguments to support the recommendations to *stop, slow down, beware*. Organ transplantation, the use of machines in end-of-life care, gene therapy, stem cell research and so on and on were about controversy and the need to determine the scope of appropriate use. But what if there were machines which, it could be argued, were essential or necessary for high quality care of all patients? Were that the case, it would be blameworthy *not* to use the

[32] McDonald CJ, Tierney WM. Computer-stored medical records: their future role in medical practice. *JAMA* 1988;259(23):3433-40.

machines – for all patients.[33] It is only in epidemiology and public health that we see such strong imperatives to study and use certain tools for the benefit of all. It might be that the use of biobanks will constitute another such imperative.

More than two decades of research have demonstrated that the establishment, implementation and dissemination of health information technologies (HIT) raise profound ethical, legal and social issues for patients, clinicians, researchers and society.[34] With the passage of the American Recovery and Reinvestment Act of 2009 (ARRA) comes the promise of a profound and comprehensive expansion of the use of health information technology in health care and society, and with it a commensurate set of ethical and policy issues. Developments in health information technology are sufficiently challenging to occupy ethical and policy analysis, but when coupled with parallel and interconnected developments in the life sciences – mapping and sequencing the human genome, the proliferation of electronic health records and the advent of real-time research data sharing and exchange – HIT generates issues that extend well beyond concerns about privacy protection and confidentiality of medical information:

[33] Miller RA, Schaffner KF, Meisel A. Ethical and Legal Issues Related to the Use of Computer Programs in Clinical Medicine. *Annals of Internal Medicine* 1985;102:529-537.

[34] Goodman KW., ed., Ethics*, Computing and Medicine: Informatics and the Transformation of Health Care.* New York: Cambridge University Press, 1998; Goodman KW, Miller R. Ethics and Health Informatics: Users, Standards and Outcomes. In EH Shortliffe et al., eds., *Medical Informatics: Computer Applications in Health Care and Biomedicine*, 3rd ed. New York: Springer-Verlag, 2006: 379-402.

access to and control of personal health records by patients, health care providers, community service organizations; data identification and de-identification in biobanks; dissemination of risk information for use in all-hazards preparation and response; emergency public health informatics (EPHI); bioinformatics; computational decision support; open source/intellectual property; secondary use of information by government and industry; and the growth of telemedicine and telehealth.

Ethical Issues in the Development and Use of Electronic Health Records

The paper-based medical record, which continues to predominate in U.S. practices, clinics and hospitals, raises ethical and security issues insofar as:

- Someone not authorized or supposed to view them might do so at their points of use or storage. Consider a passerby, a family member, an orderly deciding to have a peek at a patient's chart.
- Records might be improperly transported or discarded. Patient charts have been found in the street, in dumpsters and in other places not connected to patient care.
- Paper charts might be used inappropriately, as for instance when they are removed from clinic or hospital and taken to a clinician's home for review or research, say, and are overseen by family members, for instance.

In fact, one could argue, privacy and confidentiality are more at risk when people speak carelessly about a patient than they are when patient information is stored in paper records. At any rate, the evolution and spread of electronic health records (EHR) and, more recently,

personal health records (PHR)[35] have changed the way we (need to) think about information privacy and security – even as it agreed that paper records are too inefficient, clumsy and difficult to access and learn from.

The challenge posed by any system of record retention for medical information is simply stated: How do we make information about patients easily available to those who need it for patient care and other legitimate uses, and unavailable – difficult or impossible to access – for all others? Among the corollaries:

- Will electronic records alter privacy and confidentiality breach risks?
- What happens when records are shared or distributed across data bases? What security risks arise when digitized health data and information are stored, replicated and transmitted?
- How will personal health records – electronic tools with which patients view and manage their own health information – alter the privacy landscape?
- What will be the effects on health care and information security when, in a pharmacogenomic world, EHRs are linked to biobanks (and, for that matter, when some of the information contained in biological material becomes an integral part of the EHR)?
- What is the relationship between information security practices developed to safeguard data from corruption and inadvertent and intentional alteration and practices developed to protect privacy and confidentiality?

[35] The first study of ethical, legal and social issues raised by PHRs was Project HealthDesign, Robert-Wood Johnson Foundation-funded initiative begun in 2007. Among findings by a University of Miami team is that in an era of social networking and other on-line interactions, traditional conceptions of privacy are shifting, and that privacy itself is a somewhat vaguer concept than customarily thought. For instance, young people especially are far more inclined than expected to allow medical information to be shared by others who are not health professionals. See http://www.projecthealthdesign.org/overview-phr/ELSIgroupresources for a list of ethics reports from Project HealthDesign.

It has, further, been argued for some time that the electronic health record is or can be *more* secure than paper records, in part because, unlike paper, an electronic record can be sculpted, structured or secured to impede or prevent inappropriate access.[36] Many of the mechanisms to achieve this security have already been put in place and, indeed, have become the standard for health care organizations: password and login requirements to access records; audit trails, which record the identity of all those who have viewed a record; encryption standards for data transmission; etc. Indeed, there is a growing body of professional and regulatory oversight addressing the security of records, including FDA requirements for audit trails (21 CFR Part 11).[37] In fact, evolving security standards have identified the "trusted insider" as among the most insidious sources of inappropriate access.[38] A trusted insider has a login and perhaps even some plausible (but not actual) need to access a record; consider the hospital clinician who wants to find out why his sister's partner is visiting the infectious disease

[36] Barrows R, Clayton P. Privacy, confidentiality and electronic medical records. J Am Med Inform Assoc 1996;3:139-48.

[37] The U.S. National Institute of Standards and Technology is a key source of guidance on a variety of information technology standards. See "NIST Special Publication 800-12: An Introduction to Computer Security - The NIST Handbook," Chapter 8, for an analysis of audit trails. Available at http://csrc.nist.gov/publications/nistpubs/800-12/800-12-html/.

[38] Office of Technology Assessment. *Report Brief: Protecting Privacy in Computerized Medical Information*. Washington, D.C.: U.S. Government Printing Office, 1993.

clinic ….).[39] This means that one of the greatest sources of concern for EHRs is of remote or offsite access.

More than a decade and a half ago, in a report to the Secretary of the U.S. Department of Health and Human Services, the Workgroup for Electronic Data Interchange, a public-private task force, noted,

> Historically, providers have stored medical information and filed health insurance claims on paper. The paper medium is cumbersome and expensive, two factors that led to the call for the use of EDI [electronic data interchange]. Ironically, it is this "negative" aspect of the paper medium (its cumbersome nature) that has minimized the risk of breaches of confidentiality. Although a breach could occur if someone gained access to health records or insurance claim forms, the magnitude of the breach was limited by the sheer difficulty of unobtrusively reviewing large numbers of records or claim forms. … From the provider perspective, EDI changes the environment dramatically. … Stringent security protocols may make it more difficult for intruders to access patient-identifiable data. If the security measures are overcome and access is attained, however, the electronic medium will potentially allow for remote and unauthorized review of unlimited health information. It will greatly increase the dimension of inadvertent and intentional breaches of confidentiality.[40]

Now, the adoption of various mechanisms of encryption and firewall protection can address these concerns in varying degrees, but there has been for some time generally broad

[39] For an overview of security and privacy ethics and standards, see Cushman R, *Privacy / Data Protection Project*, University of Miami, available at http://privacy.med.miami.edu/index.htm. The "Encyclopedia" entries under "security" give synopses of core requirements of HIPAA's Security Standard and Rule.

[40] Workgroup for Electronic Data Interchange. *Report to the Secretary of the U.S. Department of Health and Human Services.* Washington, D.C.: Workgroup for Electronic Data Interchange, 1992: appendix 4, pp. 3-4.

agreement that security mechanisms alone are just inadequate to the task of confidentiality protection. They are necessary but inadequate:

> There is a tendency to focus on technical measures, such as encryption, when discussing information security. Relatively simple physical protections, such as restricting access to areas with computers, fax machines, etc., can be just as important. … Most important are the "administrative" (policy and procedural) efforts, from the rules about "who may see what" to details such as how userids and passwords are disseminated. *Even the most sophisticated technical and physical measures will be defeated by bad practices.*[41]

This insight is captured in many respects by the Security Rule under the Health Insurance Portability and Accountability Act – HIPAA:

> The general requirement of the Security Rule can be simply stated: covered entities that "collect, maintain, use or transmit" PHI in electronic form must construct "reasonable and appropriate administrative, physical and technical safeguards" that ensure integrity, availability and confidentiality. Such measures – notably in the form of policies and procedures – must provide protection against "any reasonably anticipated threats or hazards."
>
> That construction of administrative, physical and technical safeguards can be described as including three major steps for the covered entity:
>
> - "assess potential risks and vulnerabilities" to electronic PHI that it maintains or transmits;
> - "develop, implement and maintain appropriate security measures" given those anticipated risks; and
> - document those measures and keep them current.

[41] Cushman R, *Privacy / Data Protection Project*, University of Miami, Encyclopedia entry "Security and Data Protection," available at http://privacy.med.miami.edu/glossary/xd_security_basicdef.htm. Emphasis added.

> Safeguards must also "ensure compliance" with the requirements by the covered entity's officers and employees – hence this Rule, like the Privacy Rule, has a training component.[42]

Aspects of these requirements have been known for some time, and they point to what should be regarded as a suite of best practices for applied ethics in the domain of electronic health records and perhaps especially so when those records are merged with or linked to biobanks. Generally, there are recognized to be three intertwined approaches: public policy initiatives, including laws that penalize egregious abuses; technological standards, including the likes of audit trails and encryption; and education and training.[43] This last is too often overlooked and, in consequence, too infrequently embraced. Health professionals and others who are entrusted with patient information have ancient duties to safeguard that information. The *moral* obligations to protect privacy and confidentiality are uncontroversial, but the foundations of privacy rights are obscure to some. This is a teaching moment. The easy cases (don't sell patient data to businesses without patient consent) might require little exegesis, but more difficult cases (what if EHR information can be used to warn third parties of health risks? how should biobanks data about an individual be communicated to a potentially affected family

[42] Ibid., "Security Standard/Rule (HIPAA)," http://privacy.med.miami.edu/glossary/xd_security_stds.htm

[43] Alpert SA, Health care information: access, confidentiality, and good practice, in Goodman KW, ed., *Ethics, Computing, and Medicine: Informatics and the Transformation of Health Care*, Cambridge: Cambridge University Press, 1998, pp. 75-101.

member?) require some grounding in the processes for balancing competing values. This, too, is fertile ground for educators.

The relationship between privacy and consent, considered earlier, points to the importance of sharing with learners empirical data that bears on the question of secondary, tertiary and *n*-ary use of health information stored in EHRs. A growing body of research parallels the Western Australian experience and "suggests that patients are in fact willing to share their information and, indeed, that privacy concerns do not necessarily pose the kinds of constraints and inhibitions customarily invoked to limit information sharing."[44] In addition to being rich in potential applications to public policy, studies about patient preferences (a key component of most definitions of evidence-based practice) can inform curricula that provide guidance and standards for developing public policy when values are in (potential) conflict.

This is rarely as important as it is when considering the utility of EHRs and PHRs for public health and epidemiology:

> … patients, clinicians and society have generally uncontroversial duties to support civil society's public health mission, information technology supports this mission, and the effects of automated and computerized public health surveillance are likely to have little if any effect on the clinician-patient relationship. … nevertheless … electronic public health surveillance raises interesting and important ethical issues, some of which can be addressed if not resolved by empirical research, especially regarding patient preferences

[44] Goodman KW. Ethics, information technology and public health: New challenges for the clinician-patient relationship, *Journal of Law, Medicine and Ethics*, in press, citing Marquard JL, Brennan PF. Crying wolf: Consumers may be more willing to share medication information than policymakers think. *Journal of Health Information Management* 2009;23: 26-32.

about secondary use of health data and their moral obligation to contribute to population-based health.[45]

Ongoing Challenges

We have outlined a set of ethical and policy challenges raised by both repositories of human biological material and electronic health records. It is or should be uncontroversial that the future will see genomic data and information become an integral part of the patient record, with potentially great changes to and challenges for clinical and research practice and ethics. Thus, while no list of continuing challenges can be exhaustive, we note for further discussion the following set of questions:

- How should the current system for the protection of human subjects, which may still be ill-equipped to address the ethical issues arising from studies involving HBMs or EHRs, be modified to adapt to these new technologies?
- When should individual research results be returned to subjects?
- How should harms be assessed when results are of unknown clinical significance?
- What clinical, scientific and ethical challenges are raised when genomic information becomes a component of records which for thousands of years have been restricted to accounts of somewhat more pedestrian observations, data and actions?
- As the need for greater access to identifiable health information collides with the opportunity for undertaking studies that require greater access to genotypic information, how will prevailing clinical and research paradigms adapt?

Recommendations

[45] Goodman, ibid.

- Detailed investigators are necessary to explore current and potential links between biobanks and EHRs and PHRs.
- There should be more and better research on patient preferences regarding secondary use of information in electronic records.
- Increased attention should be devoted to ethical analyses of the consequences of digitizing parts of biobank contents.
- Development of curricula for health professionals, researchers, patients, patients as potential subjects (or sources of biological material for research) and others must be regarded as socially, morally and political urgent.