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PROFESSIONAL ISSUES

Ethical Considerations in Biobanks: How a Public Health Ethics Perspective Sheds New Light on Old Controversies

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Abstract Biobanks, collections of biospecimens with or without linked medical data, have increased dramatically in number in the last two decades. Their potential power to identify the underlying mechanisms of both rare and common disease has catalyzed their proliferation in the academic, medical, and private sectors. Despite demonstrated public support of biobanks, some within the academic, governmental, and public realms have also expressed cautions associated with the ethical, legal, and social (ELSI) implications of biobanks. These issues include concerns related to the privacy and confidentiality of data; return of results and incidental findings to participants; data sharing and secondary use of samples; informed consent mechanisms; ownership of specimens; and benefit sharing (i.e., the distribution of financial or other assets that result from the research). Such apprehensions become amplified as more researchers seek to pursue national and cross-border collaborations between biobanks. This paper provides an overview of two of the most contentious topics in biobank literature -informed consent and return of individual research results or incidental findings - and explores how a public health ethics lens may help to shed new light on how these issues may be best approached and managed. Doing so also demonstrates the important role that genetic counselors can play in the ongoing discussion of ethically appropriate biobank recruitment and management strategies, as well as identifies important areas of ongoing empirical research on these unresolved topics.

Keywords Biobanks · Bioethics · Incidental findings · Consent

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Introduction

Biobanks, collections of biospecimens with or without linked medical data, have increased dramatically in number in the last two decades (Hawkins 2010). Their potential power to identify the underlying mechanisms of both rare and common disease has catalyzed their proliferation in the academic, medical, and private sectors. One such example, the Kaiser Permanente Biobank, aims to recruit 500,000 members to donate specimens and linked medical data which will allow scientists to gain new insights into how to detect, treat, and prevent illness (Scott et al. 2012).

Despite demonstrated public support of biobanks (O'Doherty et al. 2012; Burgess et al. 2008), some within the academic, governmental, and public realms have also expressed cautions associated with the ethical, legal, and social (ELSI) implications of biobanks. These issues, as outlined in a previous discussion on the topic (Hawkins 2010), include concerns related to the privacy and confidentiality of data; return of results and incidental findings (IFs) to participants; data sharing and secondary use of samples; informed consent mechanisms; ownership of specimens; and benefit sharing (i.e., the distribution of financial or other assets that result from the research). Such apprehensions become amplified as more researchers seek to pursue national and cross-border collaborations between biobanks (Kaye 2011).

This paper aims to provide an overview of two of the most contentious topics in the biobank literature –informed consent and return of individual research results, or IFs. We explore how a public health ethics (PHE) lens may help to shed new light on how these issues may be understood, approached, and managed by genetic counselors. While clinical ethics and genetic counseling focus on the individual or family scale, the primary concern of PHE has been societal scale justice - driven ethical dilemmas concerning social justice, individual autonomy, and resource allocation (Levin and Fleischman

2002). These emerge when trying to influence individual behaviors in order to foster social benefits (Callahan and Jennings 2002). We suggest that genetic counselors can draw from the principles and concepts of PHE when advocating for the best interests of their clients regarding biobank participation. Additionally, research teams would be wise to call on genetics professionals when attempting to construct ethically appropriate biobank recruitment and management strategies.

Consent

Biobank research has posed significant challenges to traditional notions of informed consent, in which competent adults agree to participate in or donate tissues or data to specified research studies for some known purpose. In the case of biobank research involving genetic or other data, future research uses may be unknown and may occur throughout multiple stages of the donor's life, including adulthood, or decades after the adult participant has died. Novel modifications to the consent process have therefore been introduced by the biobanking community in order to uphold and respect a person's autonomous decision-making capacity, while also addressing these future research issues. As a result, some biobanks now obtain broad or blanket consent from participants for all and any future uses of data and specimens (Kegley 2004) while others seek study - by - study consent or the re-consent of participants for specific new studies (Platt et al. 2013). A more recent approach, known as dynamic consent, builds on the authorization model described by Caulfield et al. (2003) by employing an ongoing, interactive process between research participants and researchers. Proponents argue that this offers participants the opportunity to indicate preferences concerning their data and specimen use and the option to change those preferences, including a desire to be re-contacted over time (Kaye et al. 2011; Stein and Terry 2013). To address issues regarding initial access to patients and biobank donation, some groups have demonstrated the success of 'Permission to Contact' models, under which all patients who present for care in a clinical setting are approached to request consent that they be contacted at a later date regarding future research opportunities. This method has the potential to dramatically improve the number of suitable participants available for biobank initiatives (80–94 % of those approached agree to be contacted), while at the same time increasing research potential with improved access to eligible patients, which is essential for the 'big data' science now being demanded to accurately characterize and validate biomarkers (Cheah et al. 2013).

Despite these efforts, many participants find informed consent forms and processes difficult to comprehend and frequently do not understand important aspects of research participation such as risks associated with their involvement and the experimental nature of the biobanking research study (Ormond et al. 2009). For example, a recent study conducted by Kaiser Permanente Colorado found that, while the majority of those approached (69 %) would be willing to participate in a biobank, and 84 % correctly understood that they would not receive personal results from studies, only 32 % of participants correctly understood that their sample would be linked to their medical record. This initial lack of understanding of critical information included in the consent form will likely worsen over time as participants' memories fade and as the privacy, scientific complexity, and other considerations associated with cross border biobank research studies become more complicated. Such issues further question the reality of biobank consent ever truly being informed, as well as the effectiveness and utility of proposed solutions such as broad consent.

Compounding this problem are the questionable practices of some biobanks that have used samples for purposes which the donor population did not intend or approve, such as the Havasupai tribe case in Arizona (Kosseim 2011). A related and well-documented example includes the secondary use of newborn bloodspot specimens in Texas without acquiring informed consent of donors. This eventually led to the destruction of approximately five million samples (Kosseim 2011). Such practices erode public trust in biobanks, potentially undermine the public health benefits of biobank research, and distract public attention away from other risks associated with data-sharing activities. Such data-sharing efforts such as the 2013 Global Alliance to Enable Responsible Sharing of Genomic and Clinical Data (Broad Institute 2013) are intended to foster new medical advances and therapies, and streamline access to scientific tools and clinical trials, among other things (Broad Institute 2013). However, cross-border and cross-agency biobank enterprises also amplify and change risks associated with the confidentiality and privacy of even anonymous donor samples. This is illustrated in a recent study in which researchers were able to breach the anonymity of genetic databases in order to recover participant surnames (Gymrek et al. 2013). Participants must be assured that the laws and guidelines established by each nation will provide adequate and ongoing protection of their personal health information and tissue.

Incidental Findings

IFs, in the research context, are defined as "*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*" (Wolf et al. 2012, p219). Similarly, in the clinical context, an IF is a finding which is unrelated to the initial indication for which testing was ordered (Green et al. 2013).

There has been considerable discussion over the last couple of years regarding whether or not researchers and clinicians have a duty to inform patients or research participants of potentially actionable IFs (Van Ness 2008; Cho 2008; Ravitsky and Wilfond 2006).

In the clinical context, the American College of Medical Genetics advocates an active search for, and reporting of, known mutations in 57 genes when conducting exome or genome sequencing (Green et al. 2013). While the discussion regarding obligatory return of IFs in both clinical and research settings remains contentious (McGuire et al. 2013; Wolf et al. 2013), many insist that it is no longer ethically defensible to deny individuals the opportunity to receive medically actionable IFs under certain conditions (Wolf et al. 2012). For example, the Public Population Project in Genomics and Society International Consortium recommends that researchers should consider returning IFs that are consented to by the participant, analytically valid, have a significant risk of a serious health condition, and are clinically actionable (Knoppers et al. 2013). Wolf et al. (2012) provide specific guidance in the case of biobanks, including four responsibilities with respect to actionable IFs: "(1) clarifying the criteria for evaluating findings and the roster of returnable findings, (2) analyzing a particular finding in relation to this, (3) re-identifying the individual contributor, and (4) recontacting the contributor to offer the finding."

Providing such information, which may include provisions for genetic counseling, could cost an estimated $1,322 for each disclosure (US Presidential Bioethics Commission Report, 2013), making this obligation difficult, if not impossible, for many biobanks to meet. In addition, while returning these results may be beneficial in some cases, it may also lead to unnecessary worry and distress for participants, especially if this prospect is not anticipated and carefully addressed during the informed consent process. The possibility of receiving research results also has the potential to influence the expectations of research participants in substantive ways (Greely 2007). For example, participants who view genetic information as qualitatively different from other types of biological information are more likely to donate and desire re-contact if they believe that genetic research results will be helpful at the individual level in predicting or avoiding future health conditions (Ruiz-Canela et al. 2011).

Discussion: Forging a Relationship Between Public Health Ethics and Genetic Counseling Regarding Biobanks

Issues associated with consent and the return of IFs in biobank research are the subject of heated and ongoing debate and certainly raise many ethical questions of relevance to genetics professionals. While bioethical principles of autonomy, beneficence, non-maleficence, and justice should be necessary components of any discussion in the biobanking field, it is essential not to view these principles as barriers to potentially life changing progress for those suffering from genetic disease. While biobanks have important public health implications, broader contemplation of the public implications of research through a PHE lens is important when considering issues such as consent and IFs in biobanks. Utilizing a PHE lens also helps to shed new light on how these issues may be understood, approached, and managed by genetic counselors. In addition, we suggest that in certain situations, genetic counselors may find it useful to draw on concepts from PHE to serve the best interests of their clients who wish to donate samples and data to biobanks.

Concern for social justice forms the moral foundation of public health and, by extension, the PHE approach. As such, respect for an individual's autonomy is rooted within a broader commitment to improving public health equality and maximizing collective good (Childress et al. 2002). PHE approaches already play a significant role in other areas of novel thinking concerning biobanks, such as trustworthy and participatory governance structures for biobanks, patient group initiatives, and deliberation (e.g., the Mayo Clinic Biobank's Community Advisory Board (Mayo Clinic Community Advisory Board 2013)). These strategies, by introducing a social component to discussions, represent mechanisms by which to raise and address issues of collective public interest that are not adequately dealt with through more traditional, individualist approaches to ethics. In this sense, the evolving field of PHE offers an important, and perhaps more appropriate perspective to some of the ethical considerations which arise in biobank - related research. After all, biobanks represent a shift in thinking from individual to population - based understandings of health and, as such, public health frameworks are applicable.

Genetic counselors already steer away from strictly individualistic notions of autonomy in their practice, instead taking a more relational approach (Hawkins and Ho 2012; Sherwin 1998) which emphasizes autonomous decision making within an individual's specific familial, psychosocial, and cultural context (NSGC 2006; Burgess and d'Agincourt-Canning 2001). This relational versus individualistic approach is of particular relevance in a field such as genetics, where decisions regarding testing and research may have broader familial impacts to past, present, and future biological relatives compared to other areas of medicine. However, in select cases such as large - scale biobanks, an even broader PHE approach would explore public considerations in addition to individual and familial issues. This may prove to be the appropriate lens with which to view and provide counseling and consent for the complexities associated with biobank participation. In this sense, the PHE lens encourages a broader orientation to considerations of individual risks and benefits than afforded by the traditional family-oriented approach.

Employing Public Health Ethics to Address the Complexities of Consent and Incidental Findings

More than ever, genetic counselors are expected to play a central role in the evolving biobank discussion, especially as it relates to consent and IFs. For example, the 2013 US Presidential Bioethics Commission Report on IFs in genomic research provides 17 recommendations, including crucial ways in which genetic counselors could potentially address and mitigate risks and harms that participants may encounter when receiving IFs. Specifically, Recommendation 13 advises that "*researchers should develop a process for evaluating and managing unanticipatable findings*." It is suggested that methods of disclosure should be established, which may include assistance from genetic counselors who can help communicate the significance of findings to participants. The report appendices also highlight the ways in which genetic counselors have been included in other important guidance documents on similar topics.

In an era of heated discussion regarding the ethical obligation to return some IFs, genetic counselors can provide important input to the IF discussion on both an individual and public health level, addressing questions as to if and how IFs are disclosed, complexities in counseling, and risks and benefits of IF disclosure policies. Not only may genetic counselors contribute to informed decisions in this regard, they can also serve as a key resource in the appropriate dissemination and counseling of IFs for highly penetrant genetic conditions, including providing support, advice, and follow-up guidance. Their input into IF discussions can also clarify their role in the dissemination of results for common complex diseases, which may be more appropriately managed by other sectors of the public health system. While there is some data to suggest that participants would like to be informed of medically actionable IFs (Meulenkamp et al. 2011; Bollinger et al. 2012), there is also a need for ongoing empirical research to determine the real impacts of returning IFs. As genetic counselors may be involved in IF counseling, they are in a key position to conduct essential research into the short and long term outcomes of receiving IFs. Finally, given the rapid expansion, availability, and decreased cost of whole genome sequencing (Scott et al. 2012) and the increasingly realistic possibility of population based whole genome sequencing, IFs are likely to become a significant public health issue. Considerations of social justice and resource allocation will be paramount. Input from genetic counselors as to their appropriate role in this arena is critical, especially considering their already stretched capacity, licensure, and billing capabilities.

In regards to informed consent for biobank participation, genetic counselors, with their intimate understanding of how to obtain informed consent for complex issues such as genomics, could also have an essential role in rethinking and re-evaluating traditional consent methods for biobank participants. Genetic counselors could contribute to the development of online educational consent tools, or pictorial representations of biobanks and the risks, benefits, and limitations of donating a specimen or data, including the possibility of IFs. By invoking a PHE lens, genetic counselors may open up novel consent and recruitment strategies, whereby specimens are collected when most clinically appropriate and retrospective consent is sought when a patient is not under medical stress, time constraints, or duress, and thus able to make a fully informed, considered, uncoerced, and thoughtful decision. In addition, genetic counselors may provide a connection to certain rare disease groups where novel consent strategies, such as community consent for novel lines of research, are sought via appropriate community engagement mechanisms. Similarly, they can provide insight into public or community engagement strategies regarding whether or not research results or IFs should be returned based on consideration of factors such as public resources, possible group stigmatization, as well as individual issues. While new to the area of biobank research, such approaches are considered ethically defensible strategies currently employed in other areas of public health research such as disaster and emergency studies (Gibbs et al. 2013; Norris et al. 2006).

Finally, genetic counselors have a central role in advocating for patients who may benefit, directly or indirectly, from donating a specimen or data to a biobank. For example, families of children with rare genetic conditions may receive therapeutic emotional benefit from being connected, and perhaps donating a specimen and/or data, to a biobank for researchers examining the genetic basis of their child's disease. This again speaks to a PHE, rather than an individualistic ethic approach.

The above discussion has illustrated how a PHE lens sheds different light on how issues of informed consent and return of individual results in biobanks may be approached and managed. In addition, we have argued that genetic counselors play a crucial role in the ongoing discussion of ethically appropriate biobank recruitment and management strategies, as well as involvement in ongoing empirical research on these unresolved topics.

Conflict of Interest Alice Hawkins Virani and Holly Longstaff declare that they have no conflict of interest.

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