Title

Communicating results in post-Belmont era biomonitoring studies: Lessons from genetics and neuroimaging research

Authors

Morello-Frosch, Rachel
Varshavsky, Julia
Liboiron, Max
et al.

Publication Date

2015

DOI

10.1016/j.envres.2014.10.001

Peer reviewed

Environmental Research 136 (2015) 363–372

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Review

Communicating results in post-Belmont era biomonitoring studies: Lessons from genetics and neuroimaging research

Rachel Morello-Frosch [a,*], Julia Varshavsky [b], Max Liboiron [c], Phil Brown [d], Julia G. Brody [e]

[a] University of California Berkeley, School of Public Health and Department of Environmental Science, Policy and Management, 130 Mulford Hall, Berkeley, CA 94720-3114, USA
[b] University of California Berkeley, School of Public Health, 50 University Hall, #7360, Berkeley, CA 94720-7360, USA
[c] Memorial University of Newfoundland and Labrador, Department of Sociology, St. John's, NL, Canada A1C 5S7
[d] Northeastern University, Social Science Environmental Health Research Institute, Department of Sociology and Anthropology and Department of Health Sciences, 360 Huntington Avenue, 500 Holmes Hall, Boston, MA 02115, USA
[e] Silent Spring Institute, 29 Crafts St, Newton, MA 02458, USA

ARTICLE INFO

Article history:
Received 25 July 2014
Received in revised form
28 September 2014
Accepted 1 October 2014
Available online 25 November 2014

Keywords:
Bioethics
Biomonitoring
Informed consent
Risk communication

ABSTRACT

Background: Biomonitoring is a critical tool to assess the effects of chemicals on health, as scientists seek to better characterize life-course exposures from diverse environments. This trend, coupled with increased institutional support for community-engaged environmental health research, challenge established ethical norms related to biomonitoring results communication and data sharing between scientists, study participants, and their wider communities.
Methods: Through a literature review, participant observation at workshops, and interviews, we examine ethical tensions related to reporting individual data from chemical biomonitoring studies by drawing relevant lessons from the genetics and neuroimaging fields.
Results: In all three fields ethical debates about whether/how to report-back results to study participants are precipitated by two trends. First, changes in analytical methods have made more data accessible to stakeholders. For biomonitoring, improved techniques enable detection of more chemicals at lower levels, and diverse groups of scientists and health advocates now conduct exposure studies. Similarly, innovations in genetics have catalyzed large-scale projects and broadened the scope of who has access to genetic information. Second, increasing public interest in personal medical information has compelled imaging researchers to address demands by participants to know their personal data, despite uncertainties about their clinical significance. Four ethical arenas relevant to biomonitoring results communication emerged from our review: tensions between participants' right-to-know their personal results versus their ability or right-to-act to protect their health; whether and how to report incidental findings; informed consent in biobanking; and open-access data sharing.
Conclusion: Ethically engaging participants in biomonitoring studies requires consideration of several issues, including scientific uncertainty about health implications and exposure sources, the ability of participants to follow up on potentially problematic results, tensions between individual and community research protections, governance and consent regarding secondary use of tissue samples, and privacy challenges in open access data sharing.

1. Introduction

In the late 1980s, in a remote region of the Canadian Arctic, scientists measured the breast milk of Inuit women for the presence of environmental chemicals, particularly polychlorinated biphenyls (PCBs). At the time, scientists expected that people living far from urban industrial centers would have low levels of these contaminants in their bodies. Shockingly, the levels of PCBs in this group were the highest ever reported in human breast milk (Dewailly et al., 1994). As word spread of the group's unexpectedly high PCB levels due to their consumption of traditional, nutrient rich foods such as marine mammals, fish, and terrestrial wild game, scientists debated whether the risk of eating contaminated food outweighed the risk posed by consuming less healthy alternatives that were difficult to access in the region. Community members, on the other hand, were concerned about the stigmatization of their traditional dietary practices and the inextricable

* Corresponding author.
E-mail addresses: rmf@berkeley.edu (R. Morello-Frosch), juliav@berkeley.edu (J. Varshavsky), mliboiron@mun.ca (M. Liboiron), p.brown@neu.edu (P. Brown), brody@silentspring.org (J.G. Brody).

http://dx.doi.org/10.1016/j.envres.2014.10.001
0013-9351/

role of such food in their survival and cultural identity (Furgal et al., 2005). As a result, they have worked with scientists and public health officials to promote a 'food sovereignty' approach to (re)shaping their diet that reduces contaminant exposures, but without completely doing away with traditional foods that are both "culturally and physiologically nourishing" (Lougheed, 2010).

Cases such as this one highlight how research on environmental chemicals has shifted dramatically in the past two decades, driven largely by affected communities and innovative scientists who increasingly collaborate to explore novel lines of scientific inquiry and leverage exposure data to protect public health (Balazs and Morello-Frosch, 2013; Brody et al., 2014, 2009b, 2007; Brown et al., 2012; Frickel, 2004; Morello-Frosch et al., 2012, 2006; Shostak, 2013). As exposure science shifts from measuring chemicals outside the body (in media such as air, water, and food) toward characterizing exposures inside the body (in human tissues such as blood, urine, or breast milk), biomonitoring has quickly become a tool to examine the human health impacts of environmental chemicals and other exposures. Indeed, scientists seek to better understand the "exposome," a compliment to the genome that encompasses the totality of life-course exposures from physical and social environments (Rappaport and Smith, 2010; Wild, 2005). As biomonitoring methods become increasingly sensitive – capable of detecting more chemical analytes at increasingly lower levels – as well as less expensive and more widely available, diverse groups of scientists, regulators, and environmental health advocates are conducting biomonitoring research. Moreover, mounting public interest in learning about human exposures to environmental chemicals from industrial sources and consumer products has led communities to marshal their own scientific resources and expertise to conduct research, and to develop strategies for communicating results to individual participants and the broader public (Adams et al., 2011; Altman et al., 2008; Brody et al., 2009a,b; Brown et al., 2012; Emmett et al., 2009; Hernick et al., 2010; Morello-Frosch et al., 2012). For example, environmental health advocates successfully advocated for a communication requirement in California's Biomonitoring Program that mandates individual data be made available to study participants who want them (California Environmental Contaminant Biomonitoring Program, 2006).

These transformations in exposure assessment science, coupled with increased institutional support for community-engaged environmental health research, challenge established institutional norms related to study results communication and data sharing between scientists, study participants, and their wider communities. Further, Institutional Review Boards (IRBs) face emerging bioethical questions associated with research projects that entail the sharing of biomonitoring data in the context of scientific uncertainties about exposure sources and health effects, while balancing competing demands of community-level and individual-level research protections. The Belmont Report, which provides IRBs within the United States guidance for human subjects protection oversight, does not directly address these emerging ethical tensions in exposure science research (U.S. Department of Health and Human Services, 1979).

Technological advances are raising similar ethical issues in other scientific fields, particularly genetics and medical imaging. In the 1990s, the Human Genome Project sequenced a composite human genome from individual DNA and demonstrated that individual genomes were very similar, with less than a 0.5% difference (Levy et al., 2007). Some researchers argue that even a small difference is significant, as heritable variations in the human genome, such as single-nucleotide polymorphisms (SNPs, pronounced 'snips'), small deletions, insertions, and other structural differences in genomes might partially explain variation in human susceptibility to certain diseases. Genome mapping has spawned a new field of 'risk genomics' in which large-scale statistical analyses involving genome-wide association studies (GWAS) seek to identify SNPs potentially involved in human variation of disease susceptibility (Fujimura et al., 2008). These data have been used by scientists as well as private companies to derive individualized disease risk estimates before the extent to which SNPs are linked to disease causation is fully understood and before treatments are available (Fujimura et al., 2008; Goetz, 2007). This is evidenced by the proliferation of direct-to-consumer marketing of genetic disease risk and ancestry tests (Bloss et al., 2013; Bolnick et al., 2007). The launching of large-scale GWAS projects has also broadened the scope of who has access to and uses genetic information. For example, the Personal Genome Project based at Harvard University seeks to put 100,000 individual genomes online in an open-access database (http://www.personalgenomes.org) to facilitate global data sharing among researchers to advance understanding of human health and disease (Ball et al., 2012).

In the realm of neuroimaging research, there has been an exponential increase in the use of imaging technologies, especially functional magnetic resonance imaging (fMRI) (Smith, 2012). One survey of the literature found that in 1991, there were 15 published studies that used fMRI, in 2001 there were 865, and in 2003, 2,224 articles reported using this imaging technology (Illes et al., 2006b). Applications of neuroimaging technology have extended beyond brain science to include research on economic behavior, religious experiences, personality types, lie detection, and other forensic applications used in court (known as neurolaw) (Harris et al., 2009; Koelsch et al., 2013; Logothetis, 2008; Rosen and Savoy, 2012; Rosen, 2007). These novel applications of neuroimaging technology have raised ethical questions about the significance and potential application of study results, particularly in reporting individual results and incidental findings to study participants (Illes et al., 2003; Wolf et al., 2008).

We examine ethical tensions related to reporting individual data from biomonitoring studies in environmental health research by drawing on relevant lessons from genetics and neuroimaging, both of which have grappled with similar ethical and scientific challenges related to results communication. In all three research arenas, such ethical debates have been precipitated by rapid technological innovation and broader public interest in and use of the data generated by these fields. In contrast to genomic and imaging findings, biomonitoring results are more likely to lend themselves to prevention-oriented strategies that reduce human health risks associated with environmental exposures. Moreover, increasing public interest and engagement in the scientific enterprise has compelled IRBs, researchers, and regulatory scientists in all three fields to grapple with the challenges of balancing informed consent, privacy protections, and demands by study participants to know their personal data, despite scientific uncertainties regarding the implications of results for human health. We engage four ethical areas of relevance to results communication: tensions between participants' right-to-know their personal data versus their ability or right-to-act to protect their health; incidental findings; biobanking; and open-access data sharing. We begin with a description of our research methods and then discuss the four themes outlined above in the context of scientific uncertainty, balancing individual autonomy and community decision-making, challenges in IRB oversight of research, and logistical constraints faced by researchers as they try to nimbly and ethically engage diverse communities in biomonitoring projects.

2. Materials and methods

For our analysis, we reviewed literature from the biomonitoring, neuroimaging, and genetics fields. Sources included peer-reviewed journal articles, secondary

references from our initial search, published consensus recommendations from professional meetings, as well as other relevant workshop findings, websites, books, and news articles. We focused primarily on ethical questions related to whether and how to report individual and aggregate results to study participants and the broader study community; how to address incidental, or unanticipated, findings in the study design process; the potential ethical pitfalls of long-term storage of biological samples for future research; and procedures for informed consent in recruitment of participants for personal exposure assessment research. We used PubMed to search for keywords, including "incidental findings", "results communication", "results return", "incidental results return", "individual results return", "biobanking", "biorepositories", and "communication" in "imaging" and "genetics" fields, and limited our search to the most recent guidance (post-2000). We targeted our attention to high impact journals and prolific authors, and identified a national consensus process currently underway to address ethical issues in both the imaging and genetics fields. This consensus process has included several workshops and subsequent manuscripts deliberating relevant ethical challenges ("2011-12 Annual Report," 2012; "Special Issue on the ethical, legal and social implications of genetics and genomics," 2012; "Special 'Themed issue' on incidental findings," 2013; Illes et al., 2006a), one of which took place in May 2011 in Bethesda, MD, called "Should We Return Individual Research Results and Incidental Findings from Genomic Biobanks & Archives?" ("Special Issue on the ethical, legal and social implications of genetics and genomics," 2012), that was attended by one of the authors of this paper. We also drew from relevant environmental health case studies, existing biomonitoring "best practice" guidance, past report-back interviews with scientists and community member stakeholders, ethical discussions from biomonitoring workshops, and experiences from our own relevant research projects. Study protocols were approved by the Institutional Review Boards of the University of California, Berkeley (#2010-07-1959) and Northeastern University (#12-08-03).

3. Results

3.1. Report-back: Scientific uncertainty and research right-to-know

Since World War II, over 83,000 chemicals have been registered for commercial use in the United States, 3000 of which are produced or imported at one million pounds or more per year (Environmental Protection Agency, 2011). Most of these chemicals have little to no toxicity testing data (Environmental Protection Agency, 2010), and information on exposure sources, mitigation strategies, and health implications remain elusive in many cases (Morello-Frosch et al., 2009). Although we increasingly know more about the effects of chemicals on health, significant data gaps remain and raise ethical and scientific challenges for whether and how to report biomonitoring results to study participants. As our analytic capacity to detect chemicals in humans surpasses our ability to interpret results, scientists and IRB members have raised the question of whether it may be detrimental to share individual biomonitoring results with study participants. Tensions between participants' right-to-know their exposure results and their capacity or right-to-act to reduce those exposures can raise ethical challenges when developing results communication protocols. For example, in some occupations (e.g. farm workers or custodians) study participants may not be able to take action to reduce their chemical exposures, either through the use of personal protective equipment or the substitution, reformulation, and purchasing of products used at the workplace (Holmes, 2013; Senier et al., 2007).

Although debates about report-back of personal exposure results in environmental health research are relatively new, the neuroimaging and genetics fields have addressed similar questions related to individual results communication in the face of scientific uncertainty (Wolf et al., 2012, 2008). For example, genetic studies have fairly poor predictive value in terms of health outcomes, particularly for complex and common diseases (Burke and Psaty, 2007; Topol et al., 2007). Although research may indicate candidate genes that may have a role in the etiology of diseases like Type 2 diabetes, researchers caution that such genetic traits are likely to account for a small portion of population attributable risk (Janssens et al., 2006). In addition, genetic alterations may indicate susceptibility to or elevated risk of developing a disease, but not the certainty of having it. Therefore, there is concern that reporting such genetic information may cause undue anxiety to participants, particularly when there is a paucity of effective preventive or therapeutic interventions. Additionally, while incidental findings are prevalent in studies involving fMRIs, many detected abnormalities ultimately prove to be inconsequential (Hartwigsen et al., 2010; Illes et al., 2004, 2002; Katzman et al., 1999; Kim et al., 2002; Morris et al., 2009; Seki et al., 2010; Vernooij et al., 2007). The relatively common occurrence of such false positives in medical imaging research has prompted ethical discourse about whether and how neuroimaging researchers should manage incidental findings report-back, mirroring similar discussions about uncertain implications of many genetic testing results.

Traditionally, individual imaging and genetic results have not been returned to study participants under a "research-focused" approach, in which it is assumed that research is intended to benefit society as a whole rather than individual participants (Ravitsky and Wilfond, 2006). Conversely, some geneticists believe that findings should generally be communicated to participants because of their fundamental right to receive results under an "autonomy-focused" approach (Ravitsky and Wilfond, 2006). Others also argue that providing individual results encourages more people to support and engage in genetic studies (Fernandez and Weijer, 2006; Kohane et al., 2007). Some genetics and brain imaging researchers remain hesitant to report all results and argue that report-back of individual data should occur, but only if the health consequences are well understood and actionable steps can be taken to treat or prevent identified clinical problems (Ravitsky and Wilfond, 2006; Rothstein, 2006; Wolf et al., 2012). This approach is based on the analytic validity and clinical utility of a particular result, determining whether or not it should be reported (Ravitsky and Wilfond, 2006). For example, some forms of genetic testing can encourage appropriate clinical measures, such as enhanced breast cancer screening among known BRCA mutation carriers (Burke and Psaty, 2007). In fact, the American College of Medical Genetics and Genomics (ACMG) recently acknowledged the need to report incidental genomic findings to patients of medical genetic services for a defined set of mutations like BRCA that have "medical value" (Green et al., 2013). However, the policy statement is controversial in the medical community (Evans, 2013) with some arguing that the predictive value of genetic testing is too low to provide this kind of guidance to health professionals (Burke et al., 2013) and that patient preferences are not taken into account since the recommendations do not give patients a choice as to whether they want to receive their results (Vayena and Tasioulas, 2013). Another alternative is a "tiered disclosure" approach, in which participant preferences are incorporated into the report-back decision-making process at the beginning of the study (Rothstein, 2006). For example, participants could select during the consent phase what results they would like to be notified about and they could also choose how they would like to be notified (in person by a physician, for example).

Research on report-back in biomonitoring, genetics, and neuroimaging research has also explored study participant perspectives and expectations. These studies indicate that in general, participants want their individual results regardless of scientific uncertainty, and that learning results does not necessarily cause undue worry or stress. In biomonitoring research, evidence suggests that while some participants might personally opt out of learning their results, the vast majority believe they have a right-to-know (Brody et al., 2007; Morello-Frosch et al., 2009; Nelson et al., 2009a; Sly et al., 2009; Wu et al., 2009). One study reported that 97% of participants wanted their personal exposure results even if the health implications of the data were not clear (Brody et al., 2007), mirroring the strong desire of study participants in other environmental health studies to receive results (Brown-

Williams, 2009; Nelson et al., 2009a; Quandt et al., 2004; Wu et al., 2009). As in biomonitoring studies, participants in neuroimaging and genetics research are increasingly requesting their personal results. One imaging study revealed that most participants believed researchers would detect a brain abnormality if one existed, even if they were not looking for one (Kirschen et al., 2006). Although less than 10% of such abnormalities are ultimately deemed clinically significant, 97% of participants wanted their results disclosed to them regardless of their clinical significance (Kirschen et al., 2006). Public attitudes about genetic research also support the return of individual results. A recent poll concluded that for many study participants, learning their results was a large motivating factor for enrolling in such studies, with 75% of 4500 respondents in one study indicating they would be less likely to volunteer if individual results were not provided (Kaufman et al., 2008).

Despite this evidence, individualized report-back remains controversial as many IRBs question whether scientific uncertainty regarding health implications of genetic, biomonitoring, or neuroimaging results can cause undue stress among study participants. This concern may not be warranted. A randomized study investigating the psychological effects of disclosure of an apolipoprotein E (APOE) allele associated with Alzheimer's disease revealed that participants who were informed that they had a genetic predisposition did not show more symptoms of anxiety or depression (Green et al., 2009) compared to participants who did not get their screening results. Similarly, evaluation of report-back in chemical biomonitoring studies indicates that participants generally want to know their personal data (Altman et al., 2008) and that learning about their chemical exposures enhanced their knowledge about environmental health, stimulated behavioral changes (e.g. in purchasing decisions), and catalyzed their engagement in the policy process (e.g. public testimony to influence industrial permitting decisions) to reduce exposures (Adams et al., 2011).

While there is so far little guidance for environmental health researchers on whether and how to report results to study participants (Dunagan et al., 2013), two frameworks have traditionally guided decisions about report back in personal exposure studies. The first is *clinical ethics*, a biomedically-driven approach emphasizing report back only when health implications are clear and/or clinically actionable. The second is *community-based participatory research* (*CBPR*) that emphasizes individual and community level report back to: empower study participants with knowledge, address community-level concerns like stigmatization, and promote policy change. While the latter framework has a strong emphasis on the right-to-know, the clinical ethics framework does not. Additionally, clinical ethics narrows participation in the development of consent protocols to researchers, whereas the CBPR framework encourages community or individual participation in this process. Proponents of the latter framework generally share the belief that returning study results with participants not only elucidates potentially novel exposure reduction strategies, but democratizes knowledge production by engaging groups traditionally marginalized by the scientific process (Morello-Frosch et al., 2009). Using methods such as usability testing and focus groups, study participants can give researchers valuable input into the development of report-back materials to enhance their understandability and relevance (Health Research for Action, 2011). This work has contributed to the development of guidance for researchers seeking to report-back biomonitoring results to their study participants (Brody et al., 2014; Dunagan et al., 2013).

Moreover, biomedical ethics are evolving in ways that promote more open communication between patients and health care providers. This trend could influence results communication strategies in environmental health science. As information technology makes medical records more accessible, patients' interest in reading their doctors' visit notes can promote more transparency in health care. The Open Notes project has experimented with ways to invite patients to review doctor visit notes online with the goal of improving patients' understanding of diverse indicators of their health status, fostering more productive communication, and encouraging shared decision-making (Delbanco et al., 2010). Patients who had electronic access to doctors' notes reported feeling more informed and in control of their health care, and were more likely to adhere to medication regimens. Equally important, the Open Notes experiment led to few privacy concerns, worry or confusion among patients (Delbanco et al., 2012). Digital communication interfaces tested in the clinical setting could be adapted for applications to report back individual results to participants in personal exposure studies. Such a strategy could be enhanced using a community-engaged approach to develop digital interfaces that ensure respect for cultural and individual differences by providing options for receiving results, including views using text or graphs, in different languages, and aimed at diverse literacy levels.

These challenges can be proactively addressed if researchers purposefully develop protocols and communication strategies in partnership with study communities (Brown et al., 2010). Key to this process is a collective understanding about who represents the interests of study communities and how their issues can be effectively incorporated into protocol development. For example, the Navajo Nation maintains its own IRB to oversee human subjects protection in research (Sharp and Foster, 2002). Indeed, most tribal research ethics codes, rules of conduct, and reviews strongly encourage report-back of findings to individual research participants and/or the tribe (American Indian Law Center, 1999; Freeman, 2004). Report back is viewed as a continuous process rather than something that occurs only at the conclusion of a research project. The American Indian Law Center developed a *Model Tribal Research Code* that requires researchers to create "opportunities for the tribe, communities, and individuals, as appropriate, to receive periodic reports on the progress of the research and to comment on periodic and draft final reports, the burden under this code being on the researcher to show that tribal, community, or individual input would be inappropriate" (American Indian Law Center, 1999). Similarly, the Indigenous Rights Protection Act (Indigenous Peoples Council on Biocolonialism, 2000) stipulates that researchers must provide a detailed plan on how they will communicate personal results to individual participants and how the community at large will be educated or empowered by their proposed study. A description of the frequency and manner by which the aggregate data and progress reports will be shared with research review committees along with a communication plan for presenting aggregate results to the community at large must be included in study protocols. These requirements affirm the notion of community-engagement in the development of results communication protocols and the report-back of results as an ongoing, reflexive, and iterative process (Cordner et al., 2012).

3.2. Addressing incidental findings

Although the prevalence of incidental findings in personal exposure assessment studies is unknown, ethical issues arise regarding whether and how to communicate incidental findings, for example in situations when chemical levels in some participants in biomonitoring studies are elevated compared to a regulatory benchmark or a representative sample of the U.S. population, such as the National Health Assessment and Nutrition Examination Survey (NHANES). Furthermore, researchers may be asked by IRBs to clarify what follow-up steps they would take in cases where chemical levels are considered to be elevated.

Incidental findings are a common occurrence in neuroimaging studies, particularly those involving fMRIs. Imaging researchers estimate that incidental findings, defined as any structural abnormality detected by a scanner (with or without the potential to be clinically significant), are found in 10–40% of healthy, asymptomatic study participants. A small portion of these abnormalities (about 1–8%) either requires routine or, in very rare cases, immediate follow-up with a health provider (Hartwigsen et al., 2010; Illes et al., 2004, 2002; Katzman et al., 1999; Kim et al., 2002; Morris et al., 2009; Seki et al., 2010). Thus far, efforts to address incidental findings among imaging researchers vary widely (Booth et al., 2010; Illes et al., 2004). One study investigated the differences in study protocols for dealing with incidental findings in MRI research by surveying authors of peer-reviewed publications between 1991 and 2002. Out of 74 responses, 82% of the authors reported having incidental findings in their research, yet there was wide variability with regard to their procedures for dealing with such situations, specifically how they communicated unexpected findings to study participants (Illes et al., 2004).

The large variability in how imaging researchers address incidental findings raises ethical questions about what responsibility researchers have for follow-up. In 2005, the National Institutes of Health (NIH) and Stanford University convened neuroimaging scientists, bioethicists, health professionals, and legal experts to develop basic consensus guidelines with respect to the management of incidental findings in neuroimaging studies (Fernandez and Weijer, 2006; Illes et al., 2006a; Magnus et al., 2009; Shalowitz and Miller, 2005). These deliberations pointed to inherent tensions between several functions: ensure the scientific integrity of research; protect the welfare of participants and understand their expectations regarding results communication; and clearly convey responsibilities for following up on incidental findings while acknowledging potential logistical and financial constraints faced by researchers and study participants. Ultimately, workshop attendees agreed that neuroimaging investigators should anticipate as much as possible potential incidental findings and design protocols for addressing them in a timely manner in terms of whether, how, and who will evaluate and follow up. This includes deciding whether a neuro-radiologist or qualified physician will be consulted, whether and at what point study participants will be informed of any abnormality detected, what constitutes an incidental finding, what kind of consultation and referral participants should expect, and within what time time-frame follow-up would take place. While workshop participants agreed that a clear procedure for dealing with incidental findings is vital to ethical brain imaging research, they also placed responsibility on IRBs to ensure that researchers have established proper protocols for handling incidental findings. Ultimately, no consensus was reached regarding specific guidelines for handling incidental findings, but all participants agreed that a clear, transparent process for how unanticipated findings will be dealt with should be outlined by researchers *a priori* and that the approach should be clearly articulated to study participants during the consent phase. Additionally, all researchers agreed that participants should be allowed to opt-out of learning about incidental findings if they so wish. However, concern remained about a scenario in which a participant has opted out of disclosure and an investigator finds a life-threatening and treatable condition (Illes et al., 2006a).

Researchers have further refined these 2005 workshop recommendations and proposed models for ethical research protocols for addressing incidental findings that are integrated into the informed consent process (Hoggard et al., 2009; Illes et al., 2008; Miller et al., 2008; Seki et al., 2010; Wolf et al., 2008). Wolf et al. evaluated how 100 different universities that receive NIH funding deal with incidental findings. The scope of the survey included genomic studies in addition to imaging studies and yielded three categories for determining whether to report-back incidental findings: (1) Strong net benefit: a grave or life threatening finding that can be treated; (2) Possible net benefit: a grave but non-fatal finding that cannot be treated; and (3) Unlikely benefit: a non-serious or unknown risk. A strong net benefit coincides with an ethical obligation to disclose. If the study participant asserted their right not to know about incidental findings, this should be reconfirmed if a strong net benefit is found. Disclosure of a possible net benefit would depend on the study volunteer's preferences, confirmed during the consent process. An unlikely benefit coincides with an ethical obligation not to disclose in order to protect the study participant from unnecessary anxiety and potential financial burden (Wolf et al., 2008). This classification scheme does not acknowledge the inherent difficulty in judging which category to assign incidental findings in order to determine whether and how to follow-up, and it may contradict the desire of study participants to know about incidental findings regardless of their clinical significance (Seki et al., 2010).

Similar ethical challenges regarding incidental finding management have emerged in biomonitoring and personal exposure studies. For example, researchers conducting air sampling for chemicals in the homes of a community in Cape Cod, Massachusetts detected polychlorinated biphenyls (PCBs) in the indoor air of almost one third of 120 homes tested. However, two of the homes had much higher concentrations of PCBs than the rest, and the scientists followed up to investigate potential sources of exposure by retesting the homes to verify the initial results and by further biomonitoring the participants. Biomonitoring results revealed that participants had elevated levels of PCBs in their blood—higher than 95% of the national population. Further investigation identified some wood floor finishes as a likely source of PCB exposure. This case study highlights how reporting to participants incidental findings can reveal novel and potentially significant sources of exposure to environmental chemicals (Rudel et al., 2008).

In another study, researchers in Ohio sought to evaluate the potential impact of environmental chemicals on puberty and the risk of breast cancer later in life among girls ages 6–8 years old residing in two communities in the greater Cincinnati area. Researchers analyzed blood and urine samples for a number of contaminants. In the pilot precursor to the larger study, researchers unexpectedly found that more than 90% of the girls in one community had blood levels of perfluorooctanoate (PFOA) that were significantly greater than the national median for young adolescents in the United States. Further study of 30 additional girls from the same community revealed that blood levels of 88% of the participants were above the 95th percentile nationally. Although language in the informed consent documents indicated that participants would be notified if researchers discovered a finding that might impact their health, PFOA exposure was not originally included as one of the original aims of the study, but was added later for Centers for Disease Control (CDC) analysis. Moreover, the health impacts of PFOA were largely unknown, interventions for reducing PFOA exposures were not clear, and there was ongoing litigation and regulatory review regarding PFOA contamination of drinking water in the surrounding community (Hernick et al., 2010).

Because the Ohio study entailed a collaboration with breast cancer advocates in protocol development and implementation, they deliberated together about whether and how to inform the families about the elevated PFOA levels. Ultimately, the research team chose to disclose the incidental findings to the local community. The team noted that modern advances in environmental biomarker technology precede the collective knowledge of how to address unexpected findings, and hence researchers should design a thoughtful communication plan at the outset of a study and

clearly articulate it in the informed consent process. This approach mirrors strategies put forth by researchers in the brain imaging and genetics fields (Hernick et al., 2010; Wolf et al., 2012, 2008). However, unlike the genetics and imaging fields that are closely integrated with medical infrastructure and health insurance, the public health and regulatory infrastructure of biomonitoring research may not provide as clear an avenue for addressing incidental findings. For example, if an individual's chemical levels are found to be very high, reducing sources of exposure may require significant resources (e.g. removing lead paint in homes).

3.3. Biobanking

Both genetics research and biomonitoring entail long-term storage of human tissue samples with possible future secondary uses that are not known or specified at the time of consent. Large population-based biobanks that entail mass collection of biological samples with associated human data, known as Human Biobanks and Genetic Research Databases (HBGRDs), have become increasingly common over the last 10–15 years due to advancements in gene testing technology, the increased reliance on biobanks by new and growing fields like genetic epidemiology, the expansion of diverse biomedical applications, and increased government funding (Cambon-Thomsen, 2007, 2004). It is conservatively estimated that over 1 billion biological samples are now stored worldwide, and *Time* magazine called biobanks one of the "ten ideas that are changing the world right now" (Lasso, 2010; Park, 2009). The expanding infrastructure for large genetic biobanks mirrors the increasing trend of storing of human tissues for future use in biomonitoring studies, albeit on a smaller scale; for example, the Environmental Polymorphisms Registry (EPR) is a long-term research project sponsored by the National Institute of Environmental Health Sciences that is collecting DNA from up to 20,000 North Carolinians in a biobank ("North Carolina DNA Bank," 2014). The focus of the registry is on the study of environmental response genes that may increase the risk of human disease when combined with environmental exposures. The EPR is a linked DNA registry where samples are coded with identification numbers that can be traced to participants' contact information. This system enables scientists to conduct follow-up studies with those donors who choose to participate.

Biobanks in genomics and biomonitoring projects raise similar ethical issues regarding unknown future secondary studies, and how to disclose this information to participants during the consent process. Traditionally, research involving human subjects has been defined by specific aims or hypotheses and a delimited timeframe. However, tissue biobanking extends the time-scale and openness of research use almost indefinitely and therefore poses problems for achieving meaningful informed consent from potential participants (National Bioethics Advisory Commission, 1999). Furthermore, research on biobanked tissue from a particular community or ethnic group – such as the chemical biomonitoring of the Inuit or haplotype projects that focus on specific populations of common geographical ancestry – can have implications for all members of that group regardless of whether or not they participate directly in the research (Hoover et al., 2012; Knoppers and Chadwick, 2005; Reardon, 2001; Sharp and Foster, 2002). This situation challenges traditional ethical paradigms of study participants as autonomous individuals by introducing important notions of group autonomy and rights, which have emerged in population genomics and biomonitoring projects.

In 1999, the National Bioethics Advisory Commission (NBAC) proposed a framework governing the use of biobanked human samples in unforeseen research (National Bioethics Advisory Commission, 1999). In general, the NBAC recommended that the creation of a biorepository should entail transparent consent protocols that enable potential donors to fully understand the decision they are making in terms of permitting the future use of their tissue samples. The scope of such consent can range from enabling participants to refuse all unforeseen future research uses, to "permitting the coded use of their biological materials for any kind of future study" (National Bioethics Advisory Commission, 1999). Although bioethicists generally endorse this approach, permission for such unforeseen research should never be construed as informed consent, as participants do not have adequate information to fully evaluate the risks and benefits of such projects (Greely, 1999). Other ethicists argue that requests for general permission to use biobanked samples for future projects must have additional safeguards, such as consistent IRB review of new projects, clearly stated time limits for the project and sample storage, an absolute right for participants to withdraw tissue samples to foreclose future uses, disclosure of any commercial interests, and information about subsequent re-contacting should results emerge that have health relevance to individual participants (Wolf et al., 2012). Practical implementation of such standards raises significant challenges, because of the difficulties of ensuring absolute withdrawal of data that has been shared, as is common in federally funded research. Most importantly, the NBAC and other ethicists have recommended enhanced IRB scrutiny of projects that may have implications for whole population groups or communities, particularly research that may be viewed as stigmatizing or controversial. This review would also include representatives of potentially affected communities or population groups. Potential participants should be informed that future unforeseen research using their information or bio-specimens could not only have consequences for them as individuals, but also for the groups to which they belong.

Privacy and confidentiality concerns also arise with respect to biological repositories and unforeseen uses of tissues and health information. In genetics research, scientists, ethicists and government regulators in the United States and internationally are divided between the belief that volunteers participate in genetics research to benefit society at large, called 'solidarity' (Cambon-Thomsen, 2004) or 'research altruism' (Brown et al., 2012), versus for personal benefit. This tension has implications in terms of how countries regulate protocols related to privacy protections and data security principles. Some lean more towards solidarity or blanket consent, particularly with respect to the re-use of samples for secondary research or commercial purposes, while others tend more toward individual protections and requiring consent for any additional future research (Cambon-Thomsen, 2004). Moreover, individual participants' perspectives may vary depending on whether future secondary use of their samples is for research conducted by academic scientists or for commercial enterprises. Nevertheless, some views are consistent across nations: where possible, data should be anonymous or de-identified; where identifiable information is necessary to conduct the research, coded information is deemed adequate, and some countries, such as the United States, recommend independent coding by a third party to further protect participants (Godard et al., 2003). In 1996, the Human Genome Organization (HUGO), an international consortium of scientists involved in genetics research, recognized privacy and the need to secure confidentiality as important aspects of genetics research and recommended sample coding, limited access, and protective policies related to the transportation and sharing of samples to uphold these values (Cambon-Thomsen, 2004). However, the unique nature of a DNA "fingerprint" likely precludes the ability to maintain true de-identification of genomic data (Gutmann and Wagner, 2013).

Nevertheless, the proliferation of biobanks with different levels of government oversight related to privacy protections, coupled with increased demands for secondary use of samples and logistical limitations for consultation with participants about future sample use, is drastically changing the ethical terrain around privacy and confidentiality in the post-genomic era. Therefore, sustaining ethical

protocols for the use of biobanked samples in unforeseen biomonitoring and genomics projects requires innovative institutional scaffolding for the long-term governance and oversight of research projects. Winickoff and colleagues propose the establishment of a Biotrust Model, which provides a flexible legal and institutional structure through which the social contract and public benefit of biorepositories could be negotiated, reviewed, and managed (Winickoff and Neumann, 2005; Winickoff and Winickoff, 2003). This form of research governance could also be applied to biomonitoring projects, particularly those that are focused on specific population groups, cohorts, or communities. Details on the structure of a Biotrust are discussed elsewhere (Winickoff and Neumann, 2005), but in summary, biobanks would be administered as a charitable trust governed by a board of trustees that would enable study volunteers to participate in governance and decision-making. The model promotes extensive representation of study participants on the trust's IRB, and on a Donor Advisory Committee, a body that ensures the public benefit of biobanked samples by reviewing research protocols; specifically, the Donor Advisory Committee would evaluate and make decisions about potentially controversial research projects, while also serving as a link between the participant community, the trustees, and the researchers. Communication through periodic forums, email, regular mail, newsletters, and a website can convey information about new projects and enable biobank donors to make informed decisions within a defined time period about whether to participate or withdraw before research begins. CBPR collaboratives could apply this Biotrust framework to promote equitable power-sharing between researchers and communities in the ethical governance and human subjects protection oversight of biobanked samples in long-term biomonitoring projects.

3.4. Public data sharing

As genetic and biomonitoring projects proliferate, researchers have been encouraged to share de-identified health, genetic, and environmental exposure data with the goal of assembling a large-scale, widely-accessible research resource using online repositories. Privacy and confidentiality issues in data repositories have been a critical challenge in genomics research, as each person has a unique DNA "fingerprint" and such information could be used to discriminate (Guttmacher and Collins, 2003; Hudson et al., 2008). In response to these concerns, the Genetic Information Nondiscrimination Act (GINA) was signed into law in 2008 and heralded as a milestone for protecting the public from discrimination on the basis of genetic information. However, the law does not protect people who have actually been diagnosed with a genetic disease (versus those who are known to have a predisposition for disease), and it does not apply to disability insurance, life insurance, or long-term care insurance (Hudson et al., 2008; Rothstein, 2008). Similarly, scientists and regulatory agencies within the United States are encouraging the establishment of chemical biomonitoring data repositories, which can encourage scientific collaboration and advance discoveries about disease causation. For example, the National Center for Computational Toxicology in partnership with US EPA's National Exposure Research Laboratory is creating ExpoCastDB, a publicly accessible repository that integrates data from several observational studies that measure exposures to environmental chemicals.

In general, these online, integrated repositories are created by de-identifying datasets to protect the privacy of study participants. Information may then be easily shared because analysis on such de-identified datasets is not considered human subjects research under the Common Rule and no longer requires IRB oversight (US Department of Health and Human Services, 2009); nevertheless, such anonymous data repositories can potentially be used to uniquely identify individuals through linkage to other public or commercial datasets (Sweeney, 1997). Although scientists seek to enhance privacy protections through more judicious approaches to de-identification of personal data, some researchers are instead opting for "open consent" where participants acknowledge and agree to the potential risk of re-identification, thereby waiving their right to privacy (Lunshof et al., 2008). For example, the Personal Genome Project (PGP), based at Harvard Medical School, uses an open consent process to enroll participants into a public database with the goal of putting 100,000 genomes online in a format that can be accessed worldwide (Ball et al., 2012). While open consent acknowledges the real challenges of fully de-identifying combined genetic and phentotypic data, even when not combined with other personal data, this alternative form of consent requires that potential participants fully grasp the risks of sharing their data. Moreover, there is also concern that open consent can compromise the validity of genetic studies by contributing to unanticipated forms of selection bias or the creation of study samples that are not representative of target populations. Indeed, enrollment in the PGP is a rigorous process that screens out many potential participants who are required to review study materials and pass a test that assesses their understanding of human subjects research, study protocols, and basic genetics. Of the volunteers meeting minimum eligibility criteria, 44% drop out at the exam step, and 87% of those who successfully complete the test ultimately enroll in the project (Ball et al., 2012). Finally, participants are also encouraged to consult with family members before contributing samples that will be used to sequence their genome.

Despite some of its logistical challenges, open consent disrupts established paradigms of human subjects protection that are familiar to most IRBs. In addition to waiving privacy, PGP participants are given access to their genomic sequences and any variants that are potentially related to specific diseases and medical conditions. Participants can also add to their own profiles with a variety of personal data, including self-collected genetic data, listing enrolled relatives, uploading health records, and providing ancestry information. This data collection and dissemination strategy is analogous to open biomonitoring studies, often conducted by environmental health organizations or advocacy groups, in which study participants openly participate in environmental health research regarding human exposures to environmental chemicals by personally releasing their results in combination with other biographical information through open-access websites (Morello-Frosch et al., 2009). As environmental health researchers are increasingly encouraged to share biomonitoring data with the goal of amassing a publicly accessible, collaborative research resource, open consent could become a viable and novel strategy for direct participant engagement in the scientific enterprise through voluntary and open sharing of data and collaborative interpretation of exposure results.

4. Discussion and conclusions

Ethically engaging participants in biomonitoring studies requires consideration of several issues, including scientific uncertainty of health implications and exposure sources, the ability of participants to practically and financially follow up on potentially problematic results, tensions between individual and community research protections, governance and consent regarding secondary use of samples from biorepositories, and privacy challenges in open access data sharing. Although relatively new for the biomonitoring field, debates about these ethical challenges in genetics and neuroimaging research provide valuable lessons. Indeed, our analytic capacity to detect chemicals, discover genetic variations potentially linked to disease, and enhance neuroimaging techniques, has surpassed our ability to fully interpret data, which raises IRB concerns about whether communicating uncertain results to

study participants may cause more harm than good. However, as previously discussed, while some participants may opt out of learning their results, the majority believe they have a right-to-know (Brody et al., 2007; Morello-Frosch et al., 2009; Nelson et al., 2009b; Sly et al., 2009; Wu et al., 2009). Moreover, in many cases study participants and their communities have effectively collaborated with scientists to develop results communication protocols that successfully balance individual and community research protections. As federal and private funding agencies increasingly support community-based participatory environmental health research, engaging members of differentially affected communities has become critical for increasing trust and broadening stakeholder participation in exposure science as well as human subjects research protection (National Research Council, 2012).

The Belmont Report established principles for the use of human subjects in scientific research and guides IRB oversight of human subjects protection (U.S. Department of Health and Human Services, 1979). Developed partly in response to the Tuskegee syphilis study[1], Belmont identified three basic principles, which are interpreted and applied by IRBs that oversee human subjects research. The first of these principles, "respect for persons," stresses that an individual's decision to become a research participant must be voluntary and calls for special protection for those who lack the capacity to make such decisions themselves (such as children). The second principle, "beneficence," calls on researchers to "do no harm" or barring that, to maximize the benefits of their research while reducing, as much as possible, risks to study participants. Finally, the principle of "justice" requires careful attention to the fair distribution of risks and benefits, calling on researchers to select study participants only "for reasons directly related to the problem being studied" and to vigilantly avoid the selection of subjects for "their easy availability, their compromised position, or their manipulability." Justice also requires that those who bear the risks of research should, whenever possible, be among the first to benefit from its insights (U.S. Department of Health and Human Services, 1979).

While suitable for many biomedical applications, IRBs often strictly apply Belmont principles in ways that can become a barrier to some of the protections they are intended to provide (Stark, 2014). Indeed, formalized ethical protocols provide structured guidelines for research, but as the Inuit biomonitoring case demonstrates (Brocking, 2001; Furgal et al., 2005), they do not fully address the ethical challenges faced by researchers as they navigate increasingly dynamic relationships among multiple parties within a research project and the power inequalities between them (e.g. individual study participants, their communities, and the broader public).

We propose the concept of post-Belmont ethics that acknowledges that research integrity and ethics are dynamic, value-laden, and often contested guideposts that must be continuously and self-consciously reflected upon by community and academic partners within the scientific enterprise. This perspective opens novel opportunities for ethical and more democratic forms of human subjects protection oversight in biomonitoring research, such as shared governance of biorepositories, collaborative development of results communication protocols, and the sharing of research resources, including open access databases to which participants can independently contribute information. Mirroring some views in the genetics and medical imaging fields, it encourages a thoughtful and transparent results communication strategy that takes into account study participant expectations and perspectives *a priori* and the evaluation and constant evolution of report-back efforts. While traditional Belmont protections have largely been *restrictive,* a post-Belmont framework, makes results communication and data access for potential participants more *expansive.* That expansiveness encourages broader integration of community-engaged research ethics that democratizes the scientific enterprise, facilitates the co-production of environmental health knowledge between participants, communities, and scientists, and leverages biomonitoring results to advance policy change.

[1] The Tuskegee Syphilis Study was an infamous clinical study conducted between 1932 and 1972 by the U.S. Public Health Service in collaboration with the Tuskegee Institute, to study the progression of untreated syphilis in rural African American men who thought they were receiving free health care from the U.S. government. Researchers enrolled a total of 600 impoverished sharecroppers from Macon County, Alabama; in exchange for participating in the study, the men were given free medical care, meals, and free burial insurance. They were never told they had syphilis, nor were they ever treated for it. According to the Centers for Disease Control, the men were told they were being treated for "bad blood." The 40-year study was controversial because researchers knowingly failed to treat patients appropriately after the 1940s validation of penicillin as an effective cure for the disease they were studying. Revelation of study failures by a whistleblower catalyzed changes in U.S. law and regulation on the protection of participants in clinical studies (Reverby 2009).

Competing financial interest declaration

All authors declare they have no actual or potential competing financial interest.

IRB review

Study protocols were approved by the Institutional Review Boards of the University of California Berkeley (#2010-07-1959) and Northeastern University (#12-08-03).

Acknowledgements

This work was supported by the National Institute of Environmental Health Sciences (R01ES017514) and the California Breast Cancer Research Program (19BB-2900).

References

Adams, C., Brown, P., Morello-Frosch, R., Brody, J.G., Rudel, R., Zota, A., Dunagan, S., Tovar, J., Patton, S., 2011. Disentangling the exposure experience: the roles of community context and report-back of environmental exposure data. J. Health Soc. Behav. 52, 180–196. http://dx.doi.org/10.1177/0022146510395593.

Altman, R.G., Morello-Frosch, R., Brody, J.G., Rudel, R., Brown, P., Averick, M., 2008. Pollution comes home and gets personal: women's experience of household chemical exposure. J. Health Soc. Behav. 49, 417–435.

American Indian Law Center, 1999. Model Tribal Research Code: With materials for Tribal Regulation for Research and Checklist for Indian Health Boards, third ed. American Indian Law Center, Inc., Albuquerque, NM.

Balazs, C.L., Morello-Frosch, R., 2013. The three R's: how community based participatory research strengthens the rigor, relevance and reach of science. Environ. Justice 6, 9–16. http://dx.doi.org/10.1089/env.2012.0017.

Ball, M.P., Thakuria, J.V., Zaranek, A.W., Clegg, T., Rosenbaum, A.M., Wu, X., Angrist, M., Bhak, J., Bobe, J., Callow, M.J., Cano, C., Chou, M.F., Chung, W.K., Douglas, S. M., Estep, P.W., Gore, A., Hulick, P., Labarga, A., Lee, J.-H., Lunshof, J.E., Kim, B.C., Kim, J.-I., Li, Z., Murray, M.F., Nilsen, G.B., Peters, B.A., Raman, A.M., Rienhoff, H. Y., Robasky, K., Wheeler, M.T., Vandewege, W., Vorhaus, D.B., Yang, J.L., Yang, L., Aach, J., Ashley, E.A., Drmanac, R., Kim, S.-J., Li, J.B., Peshkin, L., Seidman, C.E., Seo, J.-S., Zhang, K., Rehm, H.L., Church, G.M., 2012. A public resource facilitating clinical use of genomes. Proc. Natl. Acad. Sci. 109, 11920–11927. http://dx.doi.org/10.1073/pnas.1201904109.

Bloss, C.S., Wineinger, N.E., Darst, B.F., Schork, N.J., Topol, E.J., 2013. Impact of direct-to-consumer genomic testing at long term follow-up. J. Med. Genet. 50, 393–400. http://dx.doi.org/10.1136/jmedgenet-2012-101207.

Bolnick, D.A., Fullwiley, D., Duster, T., Cooper, R.S., Fujimura, J.H., Kahn, J., Kaufman, J.S., Marks, J., Morning, A., Nelson, A., Ossorio, P., Reardon, J., Reverby, S.M., TallBear, K., 2007. The science and business of genetic ancestry testing. Science 318, 399–400. http://dx.doi.org/10.1126/science.1150098.

Booth, T.C., Jackson, A., Wardlaw, J.M., Taylor, S.A., Waldman, A.D., 2010. Incidental findings found in "healthy" volunteers during imaging performed for research: current legal and ethical implications. Br. J. Radiol. 83, 456–465. http://dx.doi.org/10.1259/bjr/15877332.
Brocking, S., 2001. Arctic contaminants and country foods. Sci. Indig. Perspect. Environ. Risks Environ. Pract. 3, 103–112.
Brody, J.G., Dunagan, S.C., Morello-Frosch, R., Brown, P., Patton, S., Rudel, R.A., 2014. Reporting individual results for biomonitoring and environmental exposures: lessons learned from environmental communication case studies. Environ. Health 13, 40. http://dx.doi.org/10.1186/1476-069X-13-40.
Brody, J.G., Morello-Frosch, R., Brown, P., Rudel, R.A., 2009a. Reporting individual results for environmental chemicals in breastmilk in a context that supports breastfeeding. Breastfeed. Med. 4, 121. http://dx.doi.org/10.1089/bfm.2009.0006.
Brody, J.G., Morello-Frosch, R., Brown, P., Rudel, R.A., Altman, R.G., Frye, M., Osimo, C.A., Perez, C., Seryak, L.M., 2007. Improving disclosure and consent: "Is It Safe?": new ethics for reporting personal exposures to environmental chemicals. Am. J. Public Health 97, 1547–1554. http://dx.doi.org/10.2105/AJPH.2006.094813.
Brody, J.G., Morello-Frosch, R., Zota, A., Brown, P., Perez, C., Rudel, R.A., 2009b. Linking exposure assessment science with policy objectives for environmental justice and breast cancer advocacy: The Northern California household exposure study. Am. J. Public Health 99, S600–S609. http://dx.doi.org/10.2105/AJPH.2008.149088.
Brown, P., Brody, J.G., Morello-Frosch, R., Tovar, J., Zota, A.R., Rudel, R.A., 2012. Measuring the success of community science: The Northern California household exposure study. Environ. Health Perspect. 120, 326–331. http://dx.doi.org/10.1289/ehp.1103734.
Brown, P., Morello-Frosch, R., Brody, J.G., Altman, R.G., Rudel, R.A., Senier, L., Perez, C., Simpson, R., 2010. Institutional review board challenges related to community-based participatory research on human exposure to environmental toxins: a case study. Environ. Health, 9. http://dx.doi.org/10.1186/1476-069X-9-39.
Brown-Williams, H., 2009. Health Literacy Best Practices in Biomonitoring Results Communication.
Burke, W., Matheny Antommaria, A.H., Bennett, R., Botkin, J., Clayton, E.W., Henderson, G.E., Holm, I.A., Jarvik, G.P., Khoury, M.J., Knoppers, B.M., Press, N. A., Ross, L.F., Rothstein, M.A., Saal, H., Uhlmann, W.R., Wilfond, B., Wolf, S.M., Zimmern, R., 2013. Recommendations for returning genomic incidental findings? We need to talk!. Genet. Med. 15, 854–859. http://dx.doi.org/10.1038/gim.2013.113.
Burke, W., Psaty, B., 2007. Personalized medicine in the era of genomics. JAMA Clinician's Corner 298, 1682–1684. http://dx.doi.org/10.1001/jama.298.14.1682.
California Environmental Contaminant Biomonitoring Program, 2006. ⟨http://www.biomonitoring.ca.gov⟩(accessed 5.8.14).
Cambon-Thomsen, A., 2004. The social and ethical issues of post-genomic human biobanks. Nat. Rev. Genet. 5, 866–873. http://dx.doi.org/10.1038/nrg1473.
Cambon-Thomsen, A., 2007. Trends in ethical and legal frameworks for the use of human biobanks. European 30, 373–382. http://dx.doi.org/10.1183/09031936.00165006.
Consortium Research 2011-12 Annual Report, 2012. Univ. Minn. Consort. Law Values Health Environ. Life Sci. ⟨http://www.ahc.umn.edu/consortlv/AR11/ggresearch.html⟩ (accessed 11.18.12).
Cordner, A., Ciplet, D., Brown, P., Morello-Frosch, R., 2012. Reflexive research ethics for environmental health and justice: academics and movement-building. Soc. Mov. Stud 11, 161–176. http://dx.doi.org/10.1080/14742837.2012.664898.
Delbanco, T., Walker, J., Bell, S.K., Darer, J.D., Elmore, J.G., Farag, N., Feldman, H.J., Mejilla, R., Ngo, L., Ralston, J.D., Ross, S.E., Trivedi, N., Vodicka, E., Leveille, S.G., 2012. Inviting patients to read their doctors' notes: a quasi-experimental study and a look ahead. Ann. Intern. Med. 157, 461–470. http://dx.doi.org/10.7326/0003-4819-157-7-201210020-00002.
Delbanco, T., Walker, J., Darer, J.D., Elmore, J.G., Feldman, H.J., Leveille, S.G., Ralston, J.D., Ross, S.E., Vodicka, E., Weber, V.D., 2010. Open notes: doctors and patients signing on. Ann. Intern. Med. 153, 121–125. http://dx.doi.org/10.7326/0003-4819-153-2-201007200-00008.
Dewailly, E., Ryan, J.J., Laliberte, C., Bruneau, S., Weber, J.P., Gingras, S., Carrier, G., 1994. Exposure of remote maritime populations to coplanar PCBs. Environ. Health Perspect. 102, 205–209.
Dunagan, S., Brody, J., Morello-Frosch, R., Brown, P., Goho, S., Tovar, J., Patton, S., Danford, R., 2013. When Pollution is Personal: Handbook for Reporting Results to Participants in Biomonitoring and Personal Exposure Studies. Silent Spring Institute, Newton, MA.
Emmett, E.A., Zhang, H., Shofer, F.S., Rodway, N., Desai, C., Freeman, D., Hufford, M., 2009. Development and successful application of a "community-first" communication model for community-based environmental health research. J. Occup 51, 146–156. http://dx.doi.org/10.1097/JOM.0b013e3181965d9b.
Environmental Protection Agency, 2010. HPV Chemical Hazard Data Availability Study. ⟨http://www.epa.gov/HPV/pubs/general/hazchem.htm⟩ (accessed 10.15.11).
Environmental Protection Agency, 2011. TSCA Chemical Substance Inventory|US EPA. ⟨http://www.epa.gov/oppt/existingchemicals/pubs/tscainventory/index.html⟩ (accessed 12.17.12).
Evans, J.P., 2013. Finding common ground. Genet. Med. 15, 852–853. http://dx.doi.org/10.1038/gim.2013.150.
Fernandez, C.V., Weijer, C., 2006. Obligations in offering to disclose genetic research results. Am. J. Bioeth. 6, 44–46. http://dx.doi.org/10.1080/15265160600938575.
Freeman, W.L., 2004. The Protection of Potential Individual Volunteers and Tribal Communities in Research Involving the Indian Health Service (IHS) (IRB Appendix). Northwest Portland Area Indian Health Service Institutional Review Board, Portland, OR.
Frickel, S., 2004. Chemical Consequences: Environmental Mutagens, Scientist Activism, and the Rise of Genetic Toxicology. Rutgers University Press, New Brunswick, NJ.
Fujimura, J.H., Duster, T., Rajagopalan, R., 2008. Introduction: race, genetics, and disease questions of evidence, matters of consequence. Soc. Stud. Sci. 38, 643–656. http://dx.doi.org/10.1177/0306312708091926.
Furgal, C., Powell, S., Myers, H., 2005. Digesting the message about contaminants and country foods in the canadian north: a review and recommendations for future research and action. ARCTIC 58, 103–114. http://dx.doi.org/10.14430/arctic404.
Godard, B., Schmidtke, J., Cassiman, J.J., Ayme, S., 2003. Data storage and DNA banking for biomedical research: informed consent, confidentiality, quality issues, ownership, return of benefits. A professional perspective. Eur. J. Hum. Genet. 11, 88–122. http://dx.doi.org/10.1038/sj.ejhg.5201114.
Goetz, T., 2007. 23AndMe Will Decode Your DNA for $1,000. Welcome to the Age of Genomics. WIRED.
Greely, H.T., 1999. Breaking the stalemate: a prospective regulatory framework for unforseen research uses of human tissue samples and health information. Wake For. Law Rev 34, 737–766.
Green, R.C., Berg, J.S., Grody, W.W., Kalia, S.S., Korf, B.R., Martin, C.L., McGuire, A.L., Nussbaum, R.L., O'Daniel, J.M., Ormond, K.E., Rehm, H.L., Watson, M.S., Williams, M.S., Biesecker, L.G., 2013. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet. Med. 15, 565–574. http://dx.doi.org/10.1038/gim.2013.73.
Green, R.C., Roberts, J.S., Cupples, L.A., Relkin, N.R., Whitehouse, P.J., Brown, T., Eckert, S.L., Butson, M., Sadovnick, A.D., Quaid, K.A., Chen, C., Cook-Deegan, R., Farrer, L.A., 2009. Disclosure of APOE genotype for risk of Alzheimer's disease. N. Engl. J. Med. 361, 245–254. http://dx.doi.org/10.1056/NEJMoa0809578.
Gutmann, A., Wagner, J.W., 2013. Found your DNA on the web: reconciling privacy and progress. Hastings Cent. Rep. 43, 15–18. http://dx.doi.org/10.1002/hast.162.
Guttmacher, A.E., Collins, F.S., 2003. Welcome to the genomic era. N. Engl. J. Med. 349, 996–998. http://dx.doi.org/10.1056/NEJMe038132.
Harris, S., Kaplan, J.T., Curiel, A., Bookheimer, S.Y., Iacoboni, M., Cohen, M.S., 2009. The neural correlates of religious and nonreligious belief. PLoS One 4, e7272. http://dx.doi.org/10.1371/journal.pone.0007272.
Hartwigsen, G., Siebner, H.R., Deuschl, G., Jansen, O., Ulmer, S., 2010. Incidental findings are frequent in young healthy individuals undergoing magnetic resonance imaging in brain research imaging studies: a prospective single-center study. J. Comput. Assist. Tomogr. 34, 596–600.
Health Research for Action, 2011. Biomonitoring: chemicals within us. Perspectives 6, 1.
Hernick, A.D., Brown, M.K., Pinney, S.M., Biro, F.M., Ball, K.M., Bornschein, R.L., 2010. Sharing unexpected biomarker results with study participants. Environ. Health Perspect. 119, 1–5. http://dx.doi.org/10.1289/ehp.1001988.
Hoggard, N., Darwent, G., Capener, D., Wilkinson, I.D., Griffiths, P.D., 2009. The high incidence and bioethics of findings on magnetic resonance brain imaging of normal volunteers for neuroscience research. J. Med. Ethics 35, 194–199. http://dx.doi.org/10.1136/jme.2008.025502.
Holmes, S., 2013. Fresh Fruit, Broken Bodies. University of, Berkeley, CA.
Hoover, E., Cook, K., Plain, R., Sanchez, K., Waghiyi, V., Miller, P., Dufault, R., Sislin, C., Carpenter, D.O., 2012. Indigenous peoples of North America: environmental exposures and reproductive justice. Environ. Health Perspect , http://dx.doi.org/10.1289/ehp.1205422.
Hudson, K.L., Holohan, M.K., Collins, F.S., 2008. Keeping pace with the times—The Genetic Information Nondiscrimination Act of 2008. N. Engl. J. Med. 358, 2661–2663. http://dx.doi.org/10.1056/NEJMp0803964.
Illes, J., Desmond, J.E., Huang, L.F., Raffin, T.A., Atlas, S.W., 2002. Ethical and practical considerations in managing incidental findings in functional magnetic resonance imaging. Brain Cogn. 50, 358–365.
Illes, J., Kirschen, M., Edwards, E., Bandettini, P., Cho, M., Kulynych, J., Macklin, R., Michael, D., Wolf, S., Grabowski, T., Seto, B., 2008. Practical approaches to incidental findings in brain imagine research. Neurology 70, 384–390.
Illes, J., Kirschen, M.P., Edwards, E., Stanford, L.R., Bandettini, P., Cho, M.K., Ford, P.J., Glover, G.H., Kulynych, J., Macklin, R., Michael, D.B., Wolf, S.M., 2006a. Incidental findings in brain imaging research. Science 311, 783–784. http://dx.doi.org/10.1126/science.1124665.
Illes, J., Kirschen, M.P., Gabrieli, J.D.E., 2003. From neuroimaging to neuroethics. Nat. Neurosci. 6, http://dx.doi.org/10.1038/nn0303-205 (205–205).
Illes, J., Kirschen, M.P., Karetsky, K., Kelly, M., Saha, A., Desmond, J.E., Raffin, T.A., Glover, G.H., Atlas, S.W., 2004. Discovery and disclosure of incidental findings in neuroimaging research. J. Magn. Reson. Imaging 20, 743–747. http://dx.doi.org/10.1002/jmri.20180.
Illes, J., Racine, E., Kirschen, M.P., 2006b. A picture is worth 1000 words, but which 1000. In: Illes, J. (Ed.), Neuroethics: Defining the Issues in Theory, Practice, and Policy. Oxford University Press, New York, pp. 149–168.
Indigenous Peoples Council on Biocolonialism, 2000. Indigenous Research Protection Act.
Janssens, A.C.J.W., Gwinn, M., Valdez, R., Narayan, K.M.V., Khoury, M.J., 2006. Predictive genetic testing for type 2 diabetes. BMJ 333, 509–510. http://dx.doi.org/10.1136/bmj.38953.598947.80.
Katzman, G.L., Dagher, A.P., Patronas, N.J., 1999. Incidental findings on brain magnetic resonance imaging from 1000 Asymptomatic volunteers. JAMA J. Am. Med. Assoc 282, 36–39. http://dx.doi.org/10.1001/jama.282.1.36.
Kaufman, D., Murphy, J., Scott, J., Hudson, K., 2008. Subjects matter: a survey of public opinions about a large genetic cohort study. Genet. Med. 10, 831–839.
Kim, B.S., Illes, J., Kaplan, R.T., Reiss, A., Atlas, S.W., 2002. Incidental findings on pediatric MR images of the brain. Am. J. Neuroradiol 23, 1674–1677.

Kirschen, M.P., Jaworska, A., Illes, J., 2006. Subjects′ expectations in neuroimaging research. J. Magn. Reson. Imaging 23, 205–209. http://dx.doi.org/10.1002/jmri.20499.
Knoppers, B.M., Chadwick, R., 2005. Human genetic research: emerging trends in ethics. Nat. Rev. Genet. 6, 75–79. http://dx.doi.org/10.1038/nrg1505.
Koelsch, S., Skouras, S., Jentschke, S., 2013. Neural correlates of emotional personality: a structural and functional magnetic resonance imaging study. PLoS One 8, e77196. http://dx.doi.org/10.1371/journal.pone.0077196.
Kohane, I.S., Mandl, K.D., Taylor, P.L., Holm, I.A., Nigrin, D.J., Kunkel, L.M., 2007. Reestablishing the researcher–patient compact. Science 316, 836–837. http://dx.doi.org/10.1126/science.1135489.
Lasso, R.A., 2010. The ethics of research biobanking. JAMA Book Media Rev. 304, 908–910. http://dx.doi.org/10.1001/jama.2010.1212.
Levy, S., Sutton, G., Ng, P.C., Feuk, L., Halpern, A.L., Walenz, B.P., Axelrod, N., Huang, J., Kirkness, E.F., Denisov, G., Lin, Y., MacDonald, J.R., Pang, A.W.C., Shago, M., Stockwell, T.B., Tsiamouri, A., Bafna, V., Bansal, V., Kravitz, S.A., Busam, D.A., Beeson, K.Y., McIntosh, T.C., Remington, K.A., Abril, J.F., Gill, J., Borman, J., Rogers, Y.-H., Frazier, M.E., Scherer, S.W., Strausberg, R.L., Venter, J.C., 2007. The diploid genome sequence of an individual human. PLoS Biol. 5, e254. http://dx.doi.org/10.1371/journal.pbio.0050254.
Logothetis, N.K., 2008. What we can do and what we cannot do with fMRI. Nature 453, 869–878. http://dx.doi.org/10.1038/nature06976.
Lougheed, T., 2010. The changing landscape of arctic traditional food. Environ. Health Perspect. 118, a386–a393. http://dx.doi.org/10.1289/ehp.118-a386.
Lunshof, J.E., Chadwick, R., Vorhaus, D.B., Church, G.M., 2008. From genetic privacy to open consent. Nat. Rev. Genet. 9, 406–411. http://dx.doi.org/10.1038/nrg2360.
Magnus, D., Cho, M.K., Cook-Deegan, R., 2009. Direct-to-consumer genetic tests: beyond medical regulation? Genome Med, 1. http://dx.doi.org/10.1186/gm17.
Miller, F.G., Mello, M.M., Joffe, S., 2008. Incidental findings in human subjects research: what do investigators owe research participants? J. Law Med. Ethics 36, 271–279. http://dx.doi.org/10.1111/j.1748-720X.2008.00269.x.
Morello-Frosch, R., Brody, J., Brown, P., Altman, R., Rudel, R., Perez, C., 2009. Toxic ignorance and right-to-know in biomonitoring results communication: a survey of scientists and study participants. Environ. Health 8, 6.
Morello-Frosch, R., Pastor, M., Sadd, J.L., Prichard, M., Matsuoka, M., 2012. Citizens, science and data judo: leveraging secondary data analysis to build a community-academic collaborative for environmental justice in Southern California. In: Israel, B.A., Eng, E., Schultz, A.J., Parker, E.A., Josey, B.R. (Eds.), Methods for Community-Based Participatory Research for Health. Wiley and Sons Publishers, New York, NY, pp. 547–580.
Morello-Frosch, R., Zavestovski, S., Brown, P., McCormick, S., Mayer, B., Gasior, R., 2006. Social movements in health: responses to and shapers of a changed medical world. In: Frickel, S., Moore, S.K. (Eds.), The New Political Sociology of Science: Institutions, Networks, and Power. University of Wisconsin Press, Madison, WI.
Morris, Z., Whiteley, W.N., Longstreth, W.T., Weber, F., Lee, Y.-C., Tsushima, Y., Alphs, H., Ladd, S.C., Warlow, C., Wardlaw, J.M., Al-Shahi Salman, R., 2009. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ 339, b3016. http://dx.doi.org/10.1136/bmj.b3016.
National Bioethics Advisory Commission, 1999. Research Involving Human Biological Materials: Issues and Policy Guidance (No. Volume 1), Report and Recommendations of the National Bioeethics Advisory Commission. Rockville, MD.
National Research Council, 2012. Exposure Science in the 21st Century: A Vision and a Strategy. The National Academies Press, Washington, D.C.
Nelson, J.W., Scammell, M.K., Altman, R.G., Webster, T.F., Ozonoff, D.M., 2009a. A new Spin on research translation: The Boston Consensus Conference on Human Biomonitoring. Environ. Health Perspect. 117, 495–499. http://dx.doi.org/10.1289/ehp.0800037.
Nelson, J.W., Scammell, M.K., Altman, R.G., Webster, T.F., Ozonoff, D.M., 2009b. A new Spin on research translation: The Boston Consensus Conference on Human Biomonitoring. Environ. Health Perspect. 117, 495–499. http://dx.doi.org/10.1289/ehp.0800037.
Park, A., 2009. 10 Ideas Changing the World Right Now. Time.
Quandt, S.A., Doran, A.M., Rao, P., Hoppin, J.A., Snively, B.M., Arcury, T.A., 2004. Reporting pesticide assessment results to farmworker families: development, implementation, and evaluation of a risk communication strategy. Environ. Health Perspect. 112, 636–642.
Rappaport, S.M., Smith, M.T., 2010. Environment and disease risks. Science 330, 460–461.
Ravitsky, V., Wilfond, B.S., 2006. Disclosing individual genetic results to research participants. Am. J. Bioeth. 6, 8–17. http://dx.doi.org/10.1080/15265160600934772.
Reardon, J., 2001. The human genome diversity project a case study in coproduction. Soc. Stud. Sci. 31, 357–388. http://dx.doi.org/10.1177/030631201031003002.
Reverby, S., 2009. Examining Tuskegee: The Infamous Syphilis Study and its Legacy. University of North Carolina Press, Chapel Hill.
Rosen, B.R., Savoy, R.L., 2012. fMRI at 20: has it changed the world? NeuroImage 62, 1316–1324. http://dx.doi.org/10.1016/j.neuroimage.2012.03.004 (20 Years of fMRI).
Rosen, J., 2007. The Brain on the Stand. N. Y. Times.
Rothstein, M.A., 2006. Tiered disclosure options promote the autonomy and well-being of research subjects. Am. J. Bioeth. 6, 20–21. http://dx.doi.org/10.1080/15265160600934871.
Rothstein, M.A., 2008. Putting the genetic information nondiscrimination act in context. Genet. Med. 10, 655–656.
Rudel, R.A., Seryak, L.M., Brody, J.G., 2008. PCB-containing wood floor finish is a likely source of elevated PCBs in residents' blood, household air and dust: a case study of exposure. Environ. Health 7, 2. http://dx.doi.org/10.1186/1476-069X-7-2.
Seki, A., Uchiyama, H., Fukushi, T., Sakura, O., Tatsuya, K., 2010. Japan Children′s Study Group, 2010. Incidental findings of brain magnetic resonance imaging study in a pediatric cohort in Japan and recommendation for a model management protocol. J. Epidemiol. 20, S498–S504. http://dx.doi.org/10.2188/jea.JE20090196.
Senier, L., Mayer, B., Brown, P., Morello-Frosch, R., 2007. School custodians and green cleaners new approaches to labor—environment coalitions. Organ. Environ. 20, 304–324. http://dx.doi.org/10.1177/1086026607305740.
Shalowitz, D.I., Miller, F.G., 2005. Disclosing individual results of clinical research. JAMA J. Am. Med. Assoc 294, 737–740. http://dx.doi.org/10.1001/jama.294.6.737.
Sharp, R.R., Foster, M.W., 2002. Community involvement in the ethical review of genetic research: lessons from American Indian and Alaska Native populations. Environ. Health Perspect. 110, 145–148.
Shostak, S., 2013. Exposed Science: Genes, the Environment, and the Politics of Population Health. University of California Press, Berkeley, CA.
Sly, P.D., Eskenazi, B., Pronczuk, J., Šrám, R., Diaz-Barriga, F., Machin, D.G., Carpenter, D.O., Surdu, S., Meslin, E.M., 2009. Ethical issues in measuring biomarkers in children′s environmental health. Env. Health Perspect., 117.
Smith, K., 2012. Brain imaging: fMRI 2.0. Nature 484, 24–26. http://dx.doi.org/10.1038/484024a.
Special Issue on the ethical, legal and social implications of genetics and genomics, 2012. Genet. Med. 14.
Special “Themed issue” on incidental findings, 2013. Genet. Med. 15.
Stark, L., 2014. Declarative bodies: bureaucracy, ethics and science-in-the-making. In: Kleinman, D., Moore, K. (Eds.), Handbook of Science, Technology and Society. Routledge, New York.
Sweeney, L., 1997. Weaving technology and policy together to maintain confidentiality. J. Law. Med. Ethics 25, 98–110. http://dx.doi.org/10.1111/j.1748-720X.1997.tb01885.x.
Topol, E.J., Murray, S.S., Frazer, K.A., 2007. The genomics gold rush. JAMA J. Am. Med. Assoc. 298, 218–221. http://dx.doi.org/10.1001/jama.298.2.218.
U.S. Department of Health and Human Services, 1979. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Bethesda, MD.
US Department of Health and Human Services, 2009. Code of Federal Regulations, 45 CFR 46.
Vayena, E., Tasioulas, J., 2013. Genetic incidental findings: autonomy regained? Genet. Med. 15, 868–870. http://dx.doi.org/10.1038/gim.2013.104.
Vernooij, M.W., Ikram, M.A., Tanghe, H.L., Vincent, A.J.P.E., Hofman, A., Krestin, G.P., Niessen, W.J., Breteler, M.M.B., van der Lugt, A., 2007. Incidental findings on brain MRI in the general population. N. Engl. J. Med. 357, 1821–1828. http://dx.doi.org/10.1056/NEJMoa070972.
Wild, C.P., 2005. Complementing the genome with an “Exposome”: the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol. Biomark. Prev. 14, 1847–1850. http://dx.doi.org/10.1158/1055-9965.EPI-05-0456.
Winickoff, D.E., Neumann, L.B., 2005. Towards a social contract for genomics: property and the public in the “Biotrust” Model. Life Sci. Soc. Policy 1, 8. http://dx.doi.org/10.1186/1746-5354-1-3-8.
Winickoff, D.E., Winickoff, R.N., 2003. The charitable trust as a model for genomic biobanks. N. Engl. J. Med. 349, 1180–1184. http://dx.doi.org/10.1056/NEJMsb030036.
Wolf, S.M., Crock, B.N., Van Ness, B., Lawrenz, F., Kahn, J.P., Beskow, L.M., Cho, M.K., Christman, M.F., Green, R.C., Hall, R., Illes, J., Keane, M., Knoppers, B.M., Koenig, B.A., Kohane, I.S., LeRoy, B., Maschke, K.J., McGeveran, W., Ossorio, P., Parker, L. S., Petersen, G.M., Richardson, H.S., Scott, J.A., Terry, S.F., Wilfond, B.S., Wolf, W. A., 2012. Managing incidental findings and research results in genomic research involving biobanks and archived data sets. Genet. Med. 14, 361–384.
Wolf, S.M., Lawrenz, F.P., Nelson, C.A., Kahn, J.P., Cho, M.K., Clayton, E.W., Fletcher, J. G., Georgieff, M.K., Hammerschmidt, D., Hudson, K., Illes, J., Kapur, V., Keane, M. A., Koenig, B.A., LeRoy, B.S., McFarland, E.G., Paradise, J., Parker, L.S., Terry, S.F., Van Ness, B., Wilfond, B.S., 2008. Managing incidental findings in human subjects research: analysis and recommendations. J. Law. Med. Ethics 36, 219–248. http://dx.doi.org/10.1111/j.1748-720X.2008.00266.x.
Wu, N., McClean, M.D., Brown, P., Aschengrau, A., Webster, T.F., 2009. Participant experiences in a breastmilk biomonitoring study: a qualitative assessment. Environ. Health 8, 4. http://dx.doi.org/10.1186/1476-069X-8-4.