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Exploring IRB Chairs’ Views on Genomic Incidental Findings (GIFs) and Informed Consent

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Background: Advances in technology have increased the potential for incidental findings in genetic and genomic research. Current federal policies have yet to address how genomic incidental findings (GIFs) should be managed in studies involving human participants.

Purpose: The purpose of this study was to explore IRB Chairs’ views on informed consent and GIFs.

Method: This exploratory study involved one-to-one phone interviews with 32 IRB Chairs from 30 different GWAS-active institutions. A total of 118 “GWAS-active” institutions were identified by reviewing NIH RePORTER and NHGRI’s GWAS catalog. IRB Chairs were identified by consulting publicly available Biomedical IRB websites linked to the 118 institutions. Letters of invitation were sent to the executive or first-listed IRB Chair at each of these 118 institutions; the response rate was 27%. Each interview was transcribed, validated, and analyzed within and across participants, using qualitative description and descriptive statistics. NVivo was used to assist data management.

Findings: Most Chairs were male (78%), Caucasian (91%), and had PhDs or MD/PhDs (53%). The majority (78%) said their IRBs did not have an explicit policy or plan for handling GIFs in research. Qualitative analysis revealed two categories of thought on GIFs and informed consent. The first category highlighted considerations for determining how proactively consent processes needed to address the prospect of GIFs, including (1) whether GIFs were a possibility given the aims and scope of the genomic study and (2) whether research participants were contactable. The second category included specifics of what should and should not be included in consent processes, assuming that GIFs were possible and participants were contactable. Specifics that IRB Chairs said should be included were (1) a definition of incidental findings, (2) an assessment of their potential risks (e.g., emotional harm, discrimination) and benefits (e.g., opportunity to treat, prevent), (3) a statement that the clinical implications of GIFs may be unclear, (4) a roadmap of how GIFs will be handled in terms of notification and follow-up, (5) a statement on who will/will not cover costs associated with GIFs, and (6) a checkbox for individuals to indicate whether/not they want to be notified if a reportable GIF was discovered. Specifics on what consent processes should not address included (1) projections on the variety of GIFs that potentially may emerge from a given study, (2) probability estimates of GIFs emerging and (3) categorizations of GIFs as a “risk.” The principles of Respect for Persons and Beneficence/Nonmaleficence were repeatedly invoked in explanations of why these specifics should or should not be included.

Conclusion: IRB Chairs in this study outlined several principle-based considerations and specifics with respect to GIFs and informed consent. Their thoughtful reflections are a potentially valuable source of guidance for emerging policy.

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Learning objectives: The learner will be able to:
1) Understand IRB Chair viewpoints on GIFs and informed consent, and,
2) Identify potential policy and best practice implications related to GIFs and informed consent.
Contributions: C. Simon - Directed data analysis and reporting; L. Shinkunas - facilitated data management, analysis, and reporting; J. Williams - co-directed data analysis and reporting.
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The Age of Personalized Medicine: Are We There Yet? Should We Be?

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Objectives:
1. Assess the current and projected state of personal genomics as perceived by those actively involved in its development, with a specific focus on barriers to scaling up genomic sequencing.
2. Determine how the trajectory of personal genomics will inform health policy and clinical guidelines with regard to full-genome sequencing.
3. Identify ethical and social implications for the scale-up of full-genome sequencing.

In 2006, Dr. Francis Collins, then Director of the National Human Genome Research Institute (NHGRI) predicted that in the next two or three years, we would see “an absolute explosion of information about the genetics of common disease,” and that this tidal wave of information would revolutionize clinical care in three ways: preventatively, by predicting disease risk in the healthy; pharmacogenomically, in assessing individuals’ responses to certain drugs; and therapeutically, in developing drugs and treatments based on the study of human genetics.

Four years later, we have made astounding progress in understanding the genetic causes of many diseases, and in developing technologies that allow us to sequence individual genomes at ever increasing speed and decreasing cost. Indeed we are fast approaching the reality of the “$1,000 genome,” when just a few years ago the genome cost millions of dollars to sequence. But have the rapid advances in genomic research and technology development truly ushered in the “age of personalized medicine,” as so many predicted? Many current studies focus on the impact on consumers of receiving the results of personal genomics tests. However, little attention has been paid to the technical and ethical barriers to realizing personal genomics on a wide scale.

By conducting semi-structured interviews with leading researchers in the fields of genetics and personal genomics, I have
a) assessed the current and future state of personal genomics, as perceived by those actively involved in its development;
b) identified the obstacles in the way of scaling up genomic sequencing and
c) identified the next steps that need to be taken for the “age of personalized medicine” to be realized, from the perspectives of technology-developers.

In this presentation, I will discuss data from these interviews regarding current and future applications of genome sequencing technologies, perceived hurdles preventing sequencing from being rolled out to the wider population, and the expected benefits and potential harms of applying this technology clinically, pharmacogenomically, or experimentally. Ethical and legal implications will be especially featured, in addition to issues of cost, access, and technical limitations.
Whole genome sequencing in the clinic: new twists on old ELSI questions

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Advances in genome science and technology have provided unparalleled access to the human genome. In particular, the technical barriers to sequencing the entire human genome (Whole Genome Sequencing, WGS) have largely been surmounted, thus enabling considerations of how these tests and resulting information might best be utilized for clinical care. Significant challenges remain, however, specifically in regards to interpreting, understanding and communicating this vast genomic information for diagnostic, therapeutic and/or prognostic purposes. By its very nature, whole-genome sequencing broadens the scope of traditional genetic testing leading to increased applications and complexity. This increased complexity and scope of whole-genome sequencing, necessitate reinvestigation of well studied ELSI issues to probe where currently accepted approaches may require amendment. Such emerging issues include informed consent for unknown-unknowns, testing minors for targeted clinical questions, results disclosure beyond targeted clinical questions, the definition of incidental information and data storage on a vast scale.

Highlighting examples from research and clinical practice, this session will provide an overview of the current practice of clinical genome sequencing framed and challenged by the science and guided by ELSI concepts and research.

The primary goals of this presentation are to:
(1) Review the current science of WGS testing, familiarizing attendees with present clinical applications as well as limitations to its use,
(2) Highlight challenges from scientific, regulatory, clinical, patient and health system perspectives and
(3) Present and briefly discuss unique aspects of ELSI issues for genome sequencing and approaches to them including standards for coverage and error rates, open-ended informed consent, categorization of possible findings for results disclosure, extra data from targeted test questions, testing children and/or families, dynamic nature of sequence interpretation over time, storing results in whole or in part and needs for patient and physician understanding.
Unknown family health history vs. no known family health history

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The family health history has been called the first and the most economical genetic test; it is inexpensive and thought to be available to everyone. The family health history is one of the most accessible tools for genomic and personalized health care, offering insights about genetic inheritance and risk for disease. It is used to stratify risk, to personalize prevention and surveillance strategies based on familial risk, and in some cases to determine the need for genetic testing. However, the family health history is not equally useful for all groups. For people who do not know portions or any of their genetic family health history, the value of this simple genetic test is questionable. Children of single parent families who have no contact with the noncustodial parent and don’t know any of that parent’s genetic family health history are one such group. People who were adopted at an early age and/or from another country are another such group. Clinical practice guidelines and genetic risk stratification tools do not always make a distinction between no family health history of disease versus unknown family health history. For these groups, “no known family health history” of a particular disease involves much more uncertainty than the same statement does for persons who have access to their genetic family health history information. This poster illustrates this problem and presents examples in which misinterpreting unknown family health history as no family health history of disease could result in inadequate prevention and surveillance plans. Deliberate consideration of what constitutes appropriate care for persons with unknown family health history is needed in order to avoid creating health disparities as we attempt to improve health care with personalized genomic medicine.

Learning goals: Recognize the potential for health disparity for persons with unknown family health history; identify the need for research to determine appropriate personalized health care for persons with unknown family health history
Translating the Promise of Personalized Genomic Medicine into the Clinic

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"Personalized Genomic Medicine- (PGM) is one of ill number' of labels that have emerged over the last twenty years to capture the goal of using molecular research and tools to develop individualized, predictive, and preventive health care interventions. The widespread acceptance of the goals as a new paradigm for clinical medicine is reflected in the pioneering academic medical centers in the United States that have already developed “personalized medicine” and “individualized therapy” programs in anticipation of the promises of translational genomic research. While few clinical settings currently offer genome-based clinical interventions to patients those that do are likely to be instrumental in defining PGM through rhetoric. Our rhetorical analysis focuses on academic medical centers’ PGM website, to explore if and how the rhetoric employed by clinical personalized medicine and individualized therapy enacts a “new” approach and/or rebranding of the biomedical enterprise. We are particularly interested in the ethical and social implications of the translation of genomic research into clinical applications, and this rhetorical analysis lays the groundwork for a qualitative exploration of the implications of the uptake of the multi-dimensional concept of “personal” and how it may be realized in clinical practice using new technological developments.

Learning Objectives:
1. To describe the characteristics of clinics offering personalized genomic medical services to patients
2. To analyze the rhetoric used by personalized genomic medicine clinics
3. To assess the ethical and social implications of the varied uptake of personalized genomic medicine label by academic medical centers
Decision Making Following a Prenatal Diagnosis of Down Syndrome: A Systematic Review

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Decision Making Following a Prenatal Diagnosis of Down Syndrome: A Systematic Review

Prenatal screening for Down syndrome (DS) has become a routine part of prenatal care in many countries. Because of this, there is growing interest in the choices women make following a prenatal diagnosis of DS. Therefore, the purpose of this presentation is to describe what is known about actual and hypothetical decision making following a prenatal diagnosis of DS. A search was conducted of empirical studies published in English during the period 1999 to September, 2010. Potentially relevant studies were identified through electronic databases, major journals, and reference lists with the key words of Down syndrome, attitude, abortion, termination, prenatal diagnosis, diagnostic test, and decision making. A total of 11 studies met the inclusion criteria and all of these were cross-sectional, quantitative studies. The studies were conducted in 6 countries: 3 in US, 2 in UK, 2 in Canada, 1 in Netherlands, 1 in Uruguay, 1 in Israel, and 1 in Hong Kong China. Sample size ranged from 69 to 1467.

The decision to terminate a pregnancy varied depending on whether participants were prospective parents of reproductive age recruited from the general population (23-33%), pregnant women at increased risk for having a child with DS (46-86%), or women who had received a positive diagnosis of DS during the prenatal period (89-97%). Factors that appear to influence decision making following a prenatal diagnosis of DS include demographic factors (e.g., religion, maternal age, gestational age, number of existing children, and history of termination), perceived quality of life (e.g., parenting burden/reward and quality of life for child with DS), attitudes toward and comfort with people with disabilities, and support from others (partner, health care provider, community, and society as a whole).

The findings from this review suggest that more research is needed on decision making following a prenatal diagnosis of DS. There is growing sentiment in some countries that women who choose to continue a pregnancy following a prenatal diagnosis of DS are making the wrong choice. Moreover, because it was "their choice" to have the child with DS, they should not be eligible for support from their government. Attitudes such as these are likely to interfere with a woman's right to make an informed decision following the prenatal diagnosis of a child with DS. Health care professionals who believe that the "right choice" following a prenatal diagnosis of DS is to terminate the pregnancy are unlikely to provide pregnant women with balanced, up-to-date information concerning their range of options (prepare for the baby's birth, give the baby up for adoption, or terminate pregnancy). Moreover, they are unlikely to include other family members in the decision making process.

Learning objectives:

1. To describe what is known about actual and hypothetical decision making following a prenatal diagnosis of Down syndrome (DS).
2. Discuss ethical and social implications of current approaches to and attitudes about prenatal testing for DS.
3. Discuss ethical, legal, and social implications of whole genome analysis.
The Missing Link: Genetic Researcher Perspectives on Psychiatric Genetic Testing

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The objectives of this presentation are:
1. To present a sample of genetic researchers perspectives regarding the development and implementation of genetic tests for psychiatric disorders.
2. To discuss differences and similarities in concerns and expectations of psychiatric genetic tests between genetic researchers and other stakeholders.
3. To discuss ways to integrate different stakeholder perspectives into an ethical framework for psychiatric genetic testing utilization.

Genome-wide association studies and examination of genomic structural variation have led to renewed interest in developing genetic tests for psychiatric disorders. Although currently genetic testing for mental illness is too premature to be clinically valid, this could rapidly change as more data are collected. The possibility of using genetic testing for mental illness brings up a list of concerns including a reminder of the not-so-distant legacy of eugenics and the potential use of tests outside the clinical sphere. Surveyed stakeholders of psychiatric genetic testing have identified various potential benefits and harms for these tests, as well as suggestions for adoption and implementation of these tests for clinical use.

A group of stakeholders in psychiatric genetic testing that has been surprisingly underrepresented in the research literature so far are genetic researchers. However, their views are significant because the goals and perceived benefits of genetic researchers may not be in alignment with those of downstream users of psychiatric genetic tests. This presentation summarizes perspectives of a sample of genetic researchers investigating genetic markers for bipolar disorder, depression, and schizophrenia. As arguably the most knowledgeable group regarding the current state and future development of psychiatric genetic tests, genetic researchers will provide a unique viewpoint regarding if, how and when psychiatric genetic tests should be marketed, for what conditions, their strengths and limitations, and what training mental health providers might need to interpret genetic tests effectively for their patients.
The passage of the Genetic Information Nondiscrimination Act (GINA) together with Healthcare reform HR 3590 (Patient Protection and Affordable Care Act): The Perceived Uptake of Predictive Genetic Testing for Common Disease

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The fear of genetic discrimination has been in existence as long as medicine has been able to understand heritability patterns in families. The idea that an individual’s genetic make-up could affect their ability to be employed and to have access to health insurance was a social concern that the genetics community had little ammunition to refute. This has changed in recent years with the 2008 passage of the Genetic Information Non-discrimination Act (GINA) and the 2010 passage of healthcare reform (H.R. 3590 the Patient Protection and Affordable Care Act). With the completion of the Human Genome Project and the extensive use of genome wide association studies (GWAS), genetic testing is no longer limited to rare conditions affecting a relatively small proportion of the population. The development of genetic tests for predisposition to common diseases is becoming a reality. The question is no longer “if”, but rather “when”, these sorts of tests will become commonplace with direct to consumer companies leading the way. A random sampling of 1560 individuals 18 years of age and older was recruited from local public venues in Winston Salem, North Carolina and randomly given one of two survey packets to assess their intent to have predictive genetic testing. The sole difference between the packets was that the informed packet contained additional information regarding genetic discrimination, the Genetic Information Nondiscrimination Act (GINA) and healthcare reform (H.R. 3590, Patient Protection and Affordable Care Act). The overall objective was to understand how the knowledge regarding the passage of GINA and the Healthcare Reform Act affected the uptake of predictive genetic testing for common diseases. The goals of the study were to 1) compare the intent to have predictive genetic testing for common diseases between the informed and uninformed groups, 2) identify specific populations that would be more or less likely to have predictive genetic testing, and 3) hypothesize barriers in populations that would be less likely to have testing in order to promote education within these populations. The breakdown of the two groups showed an equal proportion, 50.1% uninformed; 49.8% informed, of participants. There was no statistically significant difference (p= > 0.05) between the uninformed and informed groups regarding demographic variables. Ten common diseases were studied and all but one, prostate cancer, showed the informed population had a higher interest in predictive genetic testing than the uninformed population. The difference among the two groups was highly statistically significant for three diseases: ovarian cancer (OR=1.53, 95% CI: 1.10-2.13, p=0.01); heart disease (OR=1.39, 95% CI: 1.06-1.83, p=0.01); and asthma (OR=1.40, 95% CI: 1.11-1.77, p=0.005). Logistic regression analysis was performed for each independent demographic variable which identified populations that were significantly more and less interested in testing. While a more culturally and geographically diverse study would be needed to confirm the results, these findings have important implications to not only the genetics community but to primary care physicians. That is, a little bit of imparted knowledge can go a long way to help relieve the fear that can accompany genetic testing.
New technology, new challenges: Barriers to informed decision-making for 1st trimester aneuploidy screening

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Introduction: First trimester aneuploidy screening is a new test developed to identify fetal risk for aneuploidy several weeks earlier than conventional modalities. While expanding pregnant patients’ options, this new screen introduces challenges for informed decision-making. One of the leading concerns is that barriers to informed consent already existed for conventional forms aneuploidy testing (e.g. the Quadruple Screen) that were unaddressed before the advent of this new 1st trimester screen. Thus, the translation of 1st trimester aneuploidy screening brings to light the magnitude of these unmet informed decision-making challenges and the potential of new prenatal genetic testing technologies to amplify them.

The clinical introduction of 1st trimester aneuploidy screening raises salient questions about if patients will be able to provide their informed consent for this novel test and how clinicians will able to facilitate patients’ informed decision-making. Given the importance of informed consent for prenatal genetic testing and the limited number of genetic counseling resources available to patients, we developed this study to investigate key aspects of the decision-making process for 1st trimester aneuploidy screening. Using this information, we intend to identify barriers to informed decision-making and develop targeted interventions to improve informed consent for this new form of prenatal genetic testing.

Methods: Pregnant patients (N=137) were recruited from outpatient OB/GYN clinics in Northeastern Ohio. Participants completed a self-administered, multiple-choice questionnaire assessing knowledge and decision-making factors for 1st trimester aneuploidy screening, demographics, gestational age, and reproductive history. Data analysis was performed using R 2.9.1.

Results: Participants demonstrated an overall low understanding of the key concepts associated with 1st trimester screening. Specific knowledge gaps pertained to Down syndrome with 42.1% of participants unfamiliar with intellectual disabilities and 64.0% unfamiliar with health issues associated with Down syndrome. Participants were unfamiliar with the indications for 1st trimester screening, with 42.0% unable to correctly identify current recommendations for universal screening of all pregnant women and 62.3% unfamiliar or uncertain about testing procedures. Only 29.1% were able to identify personal risk from the screening test result in contrast to 70.9% who were incorrect or uncertain about interpretation of an abnormal test result. Participants demonstrated knowledge gaps about follow-up options for an abnormal screen result, with only 35.1% aware of the role of second trimester sequential protocols. In terms of immediate diagnostic testing, 67.8% were familiar with CVS but only 26.8% demonstrated understanding of procedure-related risks.

Conclusions: While 1st trimester aneuploidy screening provides fetal genetic information at an earlier time in the pregnancy, it also introduces novel challenges for informed decision-making. Our data demonstrate significant challenges for the process of patient education and informed consent can spin off a number of significant ethical and social implications for patients. These findings have important relevance for the delivery of prenatal care and the health and well-being of pregnant patients.
Objectives:
1. To understand the unique set of challenges raised by 1st trimester aneuploidy screening.
2. To recognize the extent to which these barriers generate ethical and social challenges and their effects on the health and well-being of pregnant patients.
The Incongruous Paths of Prenatal Genetic Testing and Maternal Choices

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Genetic testing has an increasingly robust presence in prenatal care. Because opportunities for fetal testing have become so prolific, an increasing number of pregnant women now must come face to face with the ethical, legal, and social implications of prenatal genetic investigations and the limited choices available to them in the aftermath.

Part of this growing presence is due to health policies and practice patterns surrounding prenatal care. In 2007, the American College of Obstetricians and Gynecologists modified their practice recommendations regarding prenatal genetic testing, changing how every pregnant woman in the United States interfaces with fetal genetic testing technology. The result was the recommendation for universal fetal aneuploidy testing for all patients, independent of baseline risk.

Recent advances in genetic technology are another factor. Translational research has vastly increased our knowledge of health and disease. Initially used in adult testing indications, these technologies are now finding a home in obstetrics where pregnant women and their partners have access to a vast array of fetal testing options. With the growing recognition of the role of fetal health in adult onset disease, it should be anticipated that increasing emphasis will be placed on strategies to optimize fetal in utero health through the use of genetic technologies, shaping the landscape of prenatal genetic testing in the years to come.

While genetic and genomic research has opened up new possibilities to assess fetal health, management options after diagnosis continue to be limited. Despite the fact that modern science allows us to detect multiple genetic abnormalities, we have yet to develop a way to alter a DNA-level mutation in a therapeutic fashion. The fields of maternal-fetal medicine and neonatology stretch what is possible to alleviate the downstream effects of a genetic condition. However, most interventions are considered experimental and limited in their efficacy. For some patients, pregnancy termination is the only acceptable next step because of an expected unacceptable level of suffering for the future child or the inability to assemble adequate resources for his or her special needs. Yet, access to abortion services (even for fetal genetic anomalies) is a growing concern as the number of healthcare providers who are able or willing to perform these procedures is dwindling and healthcare and legal barriers are increasing. Peculiarly, many of these restrictions have developed in tandem with the expansion of genetic technology.

Like pushing on the gas while the break is on, the tires of prenatal genetic science are spinning but the field cannot move forward. If prenatal genetic testing is to serve the purpose of empowering patients' decisions about the course of the pregnancy, then we must acknowledge and address the challenges that come to pregnant women and their partners as they engage with this technology in the hope of having a healthy child.

Objectives:
1. To identify how new developments stemming from advances in prenatal genetic technology present challenges for pregnant patients.
2. To discuss how these challenges are a barrier to the advancement of prenatal care.