Journal of Genetic Counseling
https://doi.org/10.1007/s10897-018-0243-7

ORIGINAL RESEARCH

Why Patients Decline Genomic Sequencing Studies: Experiences from the CSER Consortium

Laura M. Amendola[1] · Jill O. Robinson[2] · Ragan Hart[1] · Sawona Biswas[3,4] · Kaitlyn Lee[2] · Barbara A. Bernhardt[4] · Kelly East[5] · Marian J. Gilmore[6] · Tia L. Kauffman[7] · Katie L. Lewis[8] · Myra Roche[9] · Sarah Scollon[10] · Julia Wynn[11] · Carrie Blout[12]

Received: 8 August 2017 / Accepted: 18 February 2018

Abstract

Clinical and research settings are increasingly incorporating genomic sequencing (GS) technologies. Previous research has explored reasons for declining genetic testing and participation in genetic studies; however, there is a dearth of literature regarding why potential participants decline participation in GS research, and if any of these reasons are unique to GS. This knowledge is essential to promote informed decision-making and identify potential barriers to research participation and clinical implementation. We aggregated data from seven sites across the National Institutes of Health's Clinical Sequencing Exploratory Research (CSER) consortium on each project's procedures for recruitment, and rates of and reasons for decline. Data were analyzed using descriptive statistics. The decline rate for enrollment at the seven CSER sites ranged from 12 to 64% (median 28%) and varied based on age and disease status. Projects differed in their protocols for approaching potential participants and obtaining informed consent. Reasons for declining GS research were reported for 1088 potential participants. Commonly cited reasons were similar to those reported for clinical single gene testing and non-GS genetic research. The most frequently cited reason for decline was study logistics (35%); thus, addressing logistical barriers to enrollment may positively impact GS study recruitment. Privacy and discrimination concerns were cited by 13% of decliners, highlighting the need for researchers and providers to focus educational efforts in this area. The potential psychological burden of pursuing and receiving results from GS and not wanting to receive secondary findings, a concern specific to GS, have been cited as concerns in the literature. A minority of potential participants cited psychological impact (8%) or not wanting to receive secondary findings (2%) as reasons for decline, suggesting that these concerns were not major barriers to participation in these GS studies. Further research is necessary to explore the impact, if any, of different participant groups or study protocols on rates of decline for GS studies. Future studies exploring GS implementation should consider using standardized collection methods to examine reasons for decline in larger populations and more diverse healthcare settings.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10897-018-0243-7) contains supplementary material, which is available to authorized users.

✉ Laura M. Amendola
Lauraa7@uw.edu

[1] Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, WA, USA

[2] Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, TX 77030, USA

[3] Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA

[4] Division of Translational Medicine and Human Genetics, Department of Medicine, Perelman School of Medicine at The University of Pennsylvania, Philadelphia, PA 19104, USA

[5] HudsonAlpha Institute for Biotechnology, Huntsville, AL 35806, USA

[6] Department of Medical Genetics, Kaiser Permanente Northwest, Portland, OR 97227, USA

[7] Center for Health Research, Kaiser Permanente Northwest, Portland, OR 97227, USA

[8] Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute, Bethesda, MD 20892, USA

[9] Departments of Pediatrics and Genetics, University of North Carolina-Chapel Hill, Chapel Hill, NC 27599, USA

[10] Department of Pediatrics, Baylor College of Medicine, Houston, TX 77030, USA

[11] Department of Pediatrics, Columbia University, New York, NY 10032, USA

[12] Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA

Published online: 01 March 2018

Keywords Exome sequencing · Genome sequencing · Reason for decline · Rate of decline · Clinical Sequencing Exploratory Research (CSER) consortium

Introduction

The incorporation of genomic sequencing (GS) technology into clinical medicine has the potential to revolutionize medical care by providing genetic diagnoses to patients with unsolved phenotypes and identifying individuals at risk to develop health conditions in the future. However, not all who are offered GS testing elect to pursue it. Understanding the reasons individuals decline GS is important to clinicians and scientists alike to be mindful of patients' perspectives and continue to promote autonomous decision-making. GS research may provide insight to answer the questions of how often potential participants decline this testing and why.

The topic of why patients decline clinical genetic tests and genetic research participation is not new. Reasonss cited for declining clinical genetic testing for hereditary breast and ovarian cancer include concerns regarding costs, discrimination, and confidentiality, as well as patient disinterest (Armstrong et al. 2003; Hayden et al. 2017; Peterson et al. 2002). Patients considering genetic testing for hereditary hemochromatosis also cited having concerns about insurance discrimination (Hall et al. 2005). Only 10–20% of individuals at risk for Huntington's disease pursue genetic testing (Meiser and Dunn 2001). The potential psychological burden of this testing and knowledge of results have been proposed as reasons for this low rate of uptake (Asscher and Koops 2010). In a literature review of 14 articles exploring willingness to participate in and opinions about genetic research, Sterling et al. (2006) identified several common themes including concerns about discrimination, confidentiality, or the misuse of information, a lack of interest and no perceived benefit, and the potential for stigmatization of those at risk of genetic conditions. Privacy and confidentiality have also been cited as reasons for declining participation in genome-wide association studies and repository-based research (Trinidad et al. 2010). Participating in GS research presents distinctive considerations including the prospect of identifying unexpected or secondary findings (Mackley et al. 2017), uncovering genetic variants in children that relate to adult onset conditions (Wilfond et al. 2015), and disclosing carrier status findings in individuals not specifically seeking this information for reproductive reasons (Himes et al. 2017). Though a lot is known about reasons for declining clinical genetic testing and genetic research, there is still much to explore regarding reasons patients decline GS.

The National Institutes of Health (NIH)-funded Clinical Sequencing Exploratory Research (CSER) consortium is a group of research programs offering GS for a variety of indications (Green et al. 2016). CSER sites collect data related to their individual project aims, including reasons potential participants choose to decline enrollment, and some sites have reported their project-specific findings in this area (Gilmore et al. 2017; Robinson et al. 2016; Scollon et al. 2014). The CSER consortium provides a unique opportunity to examine GS decline across a diverse set of potential participants that vary in age and indication for testing. Investigating the reasons potential participants decline GS studies, and the rates of decline across varied study contexts, may help identify if there are participation barriers that are specific to, or more commonly cited in, research that involves GS compared to other types of genetic testing. Understanding these barriers could promote informed decision-making as well as advise the development of strategies to increase enrollment and retention rates. The latter will be especially important for future GS studies with larger targeted participant cohorts, which are essential to facilitate the collection of meaningful utilization and outcome data. Findings may also have clinical relevance as the applications of GS expand and testing are implemented across a variety of healthcare settings in different patient populations.

Methods

Each CSER site developed their own protocol and participant recruitment plan independently, and many collected information regarding rates of and reasons for decline. Recruitment for ClinSeq® began in 2007. Enrollment in the other CSER projects took place between December 2011 and May 2016. More details about the CSER consortium and the individual site populations and goals, including information about the types of primary results reported by each CSER site and their reporting of secondary findings, are described elsewhere (Green et al. 2016).

Members of the CSER Genetic Counseling Working Group developed an online survey to capture study-specific information from each participating CSER site across the following domains: recruitment and consent approaches, educational resources provided, and rates of and reasons for decline ascertained by April 2016 (Additional File 1). The survey contained open-ended and multiple-choice items and was administered to a representative from each CSER project. In order to participate, CSER sites had to have collected data on decliners. Participating CSER projects included the following: Baylor College of Medicine's BASIC3 study, Brigham and Women's Hospital and Harvard Medical School's MedSeq project, Children's Hospital of Philadelphia's

PediSeq study, Columbia University's Return of Results project, Kaiser Permanente's NextGen study, NHGRI's ClinSeq® study, and University of Washington's NEXT Medicine study. Each site gathered their data with institutional review board (IRB) approval; no further ethical board review was necessary for this work. The remaining CSER sites did not contribute data as these studies either did not collect information on rate of and/or reason for decline as part of their study designs or collected data in a manner that could not be aggregated for this project.

Definitions for key terms were included in the survey. A decliner was defined as a potential participant who directly told study staff that they were not willing or able to participate after being contacted for recruitment. This included individuals who were mailed a brochure or invitation letter and then contacted by study staff over the phone, individuals who had previously provided consent to be contacted about research opportunities, and individuals who initially expressed interest in the study and declined after agreeing to hear more information. Depending on the project's protocol, decline could take place before, during, or soon after informed consent but before completing any study activities, in person or over the phone, in either a clinical or research setting, and with a healthcare provider (HCP) or other research study personnel. Information on potential participants who did not respond to the initial contact, including a phone call, email, or mailing, was not available for most studies and often incomplete, and was therefore excluded from this study.

Study population information, including age of participants and disease status, was aggregated from progress reports provided to the National Institutes of Health (NIH) by each study site. Sites were queried regarding who initially approached potential participants and if this approach was made directly, either by phone or in person, or indirectly, via mail. Details of informed consent procedures at each site were also collected including whether decline took place before, during, or after the informed consent conversation, and who conducted the informed consent sessions. Finally, each site was asked to provide information about any educational materials given to potential participants and whether their institution's IRB had designated their project to be minimal risk or more than minimal risk (Supplementary Document 1). Follow-up questions were sent via email when clarification or further information was needed to supplement survey responses.

The sites also provided their rate of decline and reasons provided for decline. Sites captured reasons for decline from individual potential participants in varying ways including open-ended responses and/or collecting responses to multiple-choice questions (Supplementary Document 2). All reasons for decline across sites were aggregated and categorized, and overlapping categories were consolidated. Categories were not mutually exclusive, as more than one reason could be cited by the same potential participant. The percent of total decliners in each reason category was calculated by dividing the number of decliners who cited that reason by the total number of potential participants across all sites who provided any reason for decline.

For each site, descriptive statistics were used to describe the study population, the rate of decline, and the recruitment approaches and informed consent protocols. ClinSeq® was excluded from the calculation of decline rate across sites by disease status because their data included the overall combined decline rate for both seemingly healthy potential participants and those with a disease phenotype.

Results

Variation in Study Populations, Site Recruitment, Consent, and Design

The characteristics of each study's population and relevant information regarding their study protocol and informed consent procedures are presented in Table 1. Two projects recruited children and five recruited adults. Two studies recruited individuals because of a personal and/or family history of cancer, while the remaining five studies enrolled individuals based on a variety of personal phenotypes including intellectual disability, cardiomyopathy, hearing loss, or seemingly healthy status.

Protocols for recruitment and consent were developed independently by each site per their study design. Across sites, potential participants were initially approached by a variety of professionals including non-genetics and genetics physicians, genetic counselors, nurse practitioners, and research assistants; this approach was made over the phone, by mail, and/or in person. Only one site always provided genetic counseling prior to recruitment, while other sites sometimes or never provided genetic counseling prior to study recruitment. Per each site's study protocol, a diverse set of providers with different training backgrounds performed the informed consent. Individuals declined participation before, during, and after the informed consent discussions. Almost all projects provided some form of educational resource to potential participants, the most common being a study brochure. Three of the seven projects were deemed by the IRB to be more than minimal risk.

Rates of Decline

Data on the rate of study decline varied across the seven sites from 12 to 64%, with a median of 28%. Rates of decline across sites are presented in Table 1. The average rate of decline was 36% for the five CSER projects recruiting adults and 21% for the two CSER projects recruiting children. The average decline rate in healthy individuals across three sites was

Table 1 Site study population, design characteristics, and rate of decline

Study	Population		Protocol		Timing of decline	IRB designation more than minimal risk	Rate of decline[b] (%)
	Adult vs. pediatric	Disease status (phenotype)	Primary provider of initial contact[a]	Primary provider of informed consent (IC)			
PediSeq	Pediatric	Known disease (various)	Healthcare provider	Healthcare provider	Before, during, and after IC[c]	No	12
BASIC3	Pediatric	Known disease (cancer)	Study personnel	Study personnel	After IC	Yes	30
ClinSeq®	Adult	Seemingly healthy and known disease (coronary artery disease)	Healthcare provider or study personnel	Healthcare provider	Before and during IC	No	16
Next Medicine	Adult	Known disease (cancer)	Healthcare provider	Healthcare provider or study personnel	Before and during IC	Yes	28 (healthcare provider) 23 (study personnel)
Columbia	Adult	Seemingly healthy	Study personnel	Study personnel	During IC	No	28
MedSeq	Adult	Seemingly healthy and known disease (cardiomyopathy)	Healthcare provider	Study personnel	Before, during, and after IC	Yes	38 (seemingly healthy) 27 (known disease)
NextGen	Adult	Seemingly healthy (preconception screening)	Study personnel	Healthcare provider	Before, during, and after IC	Yes	64

[a] Healthcare providers include MD physicians, nurse practitioners, and genetic counselors. Project personnel include study research assistants, research coordinators, and project managers

[b] Decline defined as a potential participant who directly told study staff that they were not willing or able to participate after being contacted for recruitment

[c] Decline that took place after informed consent does not include participants who withdrew from the study after completing study-related activities

Table 2 Reasons for declining participation in GS studies across participating sites

Category	Number of decliners citing reason	Percent of decliners citing reason[a] ($n = 1088$)	Number of sites with potential participants who cited reason ($N = 6$)
Time commitment/study logistics[b]	377	35	5
No reason/unknown	174	16	3
Privacy/discrimination	137	13	6
Not interested (research activities/in general)	127	12	4
Overwhelmed with current situation	92	8	2
Psychological impact	85	8	3
Does not want research results[c]	53	5	1
Does not want secondary findings	21	2	1
Current healthcare sufficient	21	2	1
Family/social implications	1	0.1	2

[a] Percent of decliners providing reason equals more than total number of decliners ($n = 1088$) as individuals could cite more than one reason for decline

[b] Time commitment/study logistics includes potential participants who cited the following reasons for decline: time commitment or study logistics ($n = 325$), blood draw ($n = 12$), overcommitted already ($n = 27$), study-specific factors ($n = 5$), and not enough incentive ($n = 8$)

[c] May include participants who declined based on not wanting secondary finding results. This data was not captured by the reporting site

43% (range 28 to 64%). The average decline rate in individuals with a disease phenotype across four sites was 25% (range 12 to 30%).

Reason for Decline

Six of the seven participating sites provided data on reason for decline. Sixteen percent of individuals who declined participation did not provide a reason. Thirty-five percent of potential participants declined because of time commitment/study logistics (this category also included potential participants who cited the blood draw, being overcommitted already, study-specific factors, and/or not enough incentive as their reason for decline). The next most frequently cited reasons for decline were privacy or discrimination concerns (13%) and lack of research interest (12%). The least commonly cited reasons for declining participation were not wanting to learn secondary (or unanticipated) findings (2%), that current healthcare is already sufficient (2%), and family/social implications of participation (0.1%) (Table 2). The top three most frequent reasons for decline in each study are presented in Table 3.

Discussion

The CSER consortium is a highly heterogeneous group of projects, which enables the exploration of rates of and reasons for decline in patient populations of different ages and disease status being approached for GS research. Across the seven participating CSER projects, rates of decline ranged from 12 to 64%, with a median of 28%. This variation is consistent with a large range of decline rates cited in the literature for non-GS genetic research (Sterling et al. 2006) and genetic testing (Asscher and Koops 2010; Hayden et al. 2017). The average rate of decline varied for CSER projects recruiting adult (36%, $N = 5$ projects) vs. pediatric participants (21%, $N = 2$ projects), and healthy individuals (43%, $N = 3$ projects) vs. those with a disease phenotype (25%, $N = 4$ projects). It is

Table 3 Most frequently cited reasons for decline across participating sites

Site	Top 3 most frequent reasons for decline (% of decliners who cited reason)[a,b]
BASIC3	Overwhelmed with current situation (47) Psychological impact (18) Privacy/discrimination (17)
ClinSeq®	Not interested in research activities/in general (55) Time commitment/study logistics (27) Psychological impact (9)
MedSeq	Time commitment/study logistics (55) Privacy/discrimination (26) Psychological impact (12)
NextGen	Time commitment/study logistics (36) Not interested (research activities/in general) (27) Does not want research results (22)
Next Medicine	Time commitment/study logistics (41) Not interested (research activities/in general) (20) Does not want research results (12)
PediSeq	Privacy/discrimination (57) Not interested (research activities/in general) (36) Time commitment/study logistics (7)

[a] Does not include no reason/unknown responses

[b] These categories were not mutually exclusive, i.e., more than one reason could be cited by the same patient

likely that factors other than just age and disease status of potential participants contributed to this variation. Larger study populations are needed to understand if these and other study design-specific factors, such as who is approaching potential participants and conducting informed consent conversations, significantly impact the rate of decline for GS studies.

The CSER project with the highest rate of decline was the NextGen site at Kaiser Permanente, which was the only site performing GS for carrier status in healthy adults. Genetic professionals express high interest in offering expanded carrier screening (Lazarin et al. 2016); however, uncertainty and concern about negative consequences have been cited by patients (Ekstrand Ragnar et al. 2016; Schneider et al. 2016). Thus, it is possible that offering GS in the context of reproductive planning could warrant unique considerations.

The potential of GS to identify results that are unrelated to the indication for testing but may inform the risk of developing future disease is a unique feature of this technology. Only one CSER site, the Next Medicine study at the University of Washington, reported that potential participants cited not wanting secondary findings as a reason for decline, and this reason was given by 15% of the decliners at this site (N = 136). This finding may have been influenced by protocol differences across studies. If, how, and what types of secondary findings were disclosed greatly varied by study (Green et al. 2016), for example, the Pediseq project allowed participants to opt out of secondary findings that were determined to be not immediately medically actionable (Berg et al. 2013). Regardless, recent research indicates that the majority of individuals who pursue GS express interest in secondary findings (Shahmirzadi et al. 2014).

Apprehension regarding the psychological burden of pursuing and receiving results from GS has been cited as a concern in the literature (Janssens 2015; Weiner 2014; Wolf et al. 2013). Eight percent of the total number of potential participants across six CSER projects cited psychological impact as a reason for decline. This suggests that the prospect of learning GS information did not raise significant emotional concerns in most that declined participation. Consistent with best practices for non-GS genetic testing, the potential psychological impacts of receiving GS results should be discussed during informed consent and during posttest genetic counseling.

Eight percent of decliners across the six CSER sites that contributed data on reason for decline cited being overwhelmed by their current situation as a reason for decline of GS. Though this reason was not cited by a large number of potential participants overall, it was the most frequently cited reason for decline (47% of decliners) in the BASIC3 study at Baylor College of Medicine which recruited pediatric participants with cancer diagnoses. The project approached potential participants for enrollment within 60 days of their diagnosis in an attempt to give families time to adjust to a new diagnosis (Scollon et al. 2014). This finding highlights how context may impact future GS study design considerations, such as when potential participants and families may be more receptive to learning about and/or pursuing such opportunities. Additionally, the affected status of the proband, and whether the proband is a child or adult, is also likely to impact cited reasons for decline.

Fear of insurance discrimination has been discussed as a reason for potential participants declining predictive genetic testing (Bombard et al. 2008) and translational research studies (Green et al. 2015). Similarly, concern regarding privacy and discrimination was cited by 13% of the total potential participants in this study and was the only reason for decline cited by potential participants at each of the six CSER sites that provided data on reasons for decline. Privacy and discrimination may have been discussed during consent conversations for these CSER projects, and related language was likely included in informed consent documents (cser1.cser-consortium.org/resources). This finding highlights the importance of having a balanced discussion about discrimination during the informed consent process. Many potential participants and many non-genetic providers may have limited or no knowledge regarding the Genetic Information Non-Discrimination Act (GINA) (Green et al. 2015; Laedtke et al. 2012) or the evidence of genetic discrimination in medicine (Joly et al. 2013). Further research should explore if, and how, the mere mention of insurance discrimination, especially in the context of currently changing healthcare policy, might influence decline rates.

The most commonly cited reason for declining GS study participation across the six sites was related to study logistics (35% of potential participants). This finding is not unique to these GS study populations (Foster et al. 2004; Newington and Metcalfe 2014), but highlights the importance of developing GS study protocols that take into account participant burden and required commitment. Performing genetic testing on saliva instead of a blood sample, providing incentives for participation, and/or offering online or phone options for recruitment and/or consent have all been cited as ways to increase genetic research enrollment (Close et al. 2013; Ewing et al. 2015; Huynh et al. 2014). These practices may also improve enrollment rates in GS projects, an important consideration for future large scale GS research studies. Interestingly, study logistics was one of the top two most frequently cited reasons for decline for the three studies enrolling healthy adults. It is possible that healthy adults may be less motivated to complete the logistical requirements of study involvement due to the perception that they have less to gain than those seeking a genetic diagnosis.

Study Limitations

This work offers a unique cross consortium look into rates of and reasons for decline across a variety of different GS

projects; however, we recognize there are limitations. These seven CSER projects were all conducted at large, urban institutions with active clinical genetics programs. Thus, these results may not be generalizable to individuals considering GS in community and more rural healthcare settings. Similarly, these results may not be generalizable to the clinical genetics setting since factors that impact the pursuit of clinical genetic testing, such as costs and insurance coverage for testing, did not apply here. This work was also restricted by the small sample size of the seven participating sites which limited our ability to analyze the data beyond providing descriptive summaries. Our analyses were further limited by the absence of individual-level data on decliners from all sites, so other factors that could potentially affect GS study decline rate and rational, such as patient race, ethnicity, or gender, could not be evaluated.

Conclusions

The rates of decline in these CSER GS studies varied across the seven participating sites, and differences were seen based on potential participant age and disease status. Several of the reasons cited for declining GS study participation were similar to those cited in the literature in patients being approached for clinical genetic testing and genetic research (Armstrong et al. 2003; Asscher and Koops 2010; Hall et al. 2005; Hayden et al. 2017; Peterson et al. 2002; Sterling et al. 2006). This includes study logistics which, if addressed, may positively impact GS study enrollment. Concerns across the six sites regarding privacy and insurance discrimination highlight the sensitivity of these issues. It is important to provide balanced education about the potential for discrimination to both providers, especially those who may be less familiar with this topic, and potential participants. Most potential participants did not cite disinterest in secondary findings, a GS specific concern, as a primary reason for decline and the majority did not express that psychological concerns were a factor in their decision not to participate in GS research, which has been previously noted as a concern with GS (Janssens 2015; Weiner 2014; Wolf et al. 2013). Thus, in these CSER GS studies, the most commonly cited reasons cited for decline were not unique to, or intensified by, GS technology. Moving forward, it will be important to further explore the commonly cited reasons for declining GS in this project, especially in healthy populations, to better understand if these factors may impact broader GS implementation. Further research using standardized collection instruments is also necessary to validate these findings in larger sample sizes and to explore this topic in patients in more diverse healthcare settings.

Acknowledgements We thank Gail Jarvik and Kurt Christensen for their review and comments on drafts of this paper.

Funding Information CSER Coordinating Center U01HG007307; Hudson Alpha UM1HG007301; NCGenes U01HG006487; Next Medicine U01HG006507; BASIC3 U01HG006485; MedSeq U01HG006500; NextGen UM1HG007292; PediSeq U01HG006546; Columbia Return of Results study and Genomic Consent study R21 HG006596, R01 HG006600, P50 HG007257; and ClinSeq® are supported by the Intramural Research Program of the National Human Genome Research Institute, National Institutes of Health.

Compliance with Ethical Standards

Conflict of Interest Laura M. Amendola, Jill O. Robinson, Ragan Hart, Sawona Biswas, Kaitlyn Lee, Barbara A. Bernhardt, Kelly East, Marian J. Gilmore, Tia L. Kauffman, Katie L. Lewis, Myra Roche, Sarah Scollon, Julia Wynn, and Carrie Blout declare that they have no conflict of interest.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). For this type of study, formal consent is not required.

References

Armstrong, K., Weber, B., FitzGerald, G., Hershey, J. C., Pauly, M. V., Lemaire, J., Subramanian, K., & Asch, D. A. (2003). Life insurance and breast cancer risk assessment: adverse selection, genetic testing decisions, and discrimination. *American Journal of Medical Genetics. Part A, 120a*(3), 359–364. https://doi.org/10.1002/ajmg.a.20025.

Asscher, E., & Koops, B. J. (2010). The right not to know and preimplantation genetic diagnosis for Huntington's disease. *Journal of Medical Ethics, 36*(1), 30–33. https://doi.org/10.1136/jme.2009.031047.

Berg, J. S., Amendola, L. M., Eng, C., Van Allen, E., Gray, S. W., Wagle, N., et al. (2013). Processes and preliminary outputs for identification of actionable genes as incidental findings in genomic sequence data in the Clinical Sequencing Exploratory Research Consortium. *Genetics in Medicine, 15*(11), 860–867. https://doi.org/10.1038/gim.2013.133.

Bombard, Y., Penziner, E., Suchowersky, O., Guttman, M., Paulsen, J. S., Bottorff, J. L., & Hayden, M. R. (2008). Engagement with genetic discrimination: concerns and experiences in the context of Huntington disease. *European Journal of Human Genetics, 16*(3), 279–289. https://doi.org/10.1038/sj.ejhg.5201937.

Close, S., Smaldone, A., Fennoy, I., Reame, N., & Grey, M. (2013). Using information technology and social networking for recruitment of research participants: experience from an exploratory study of pediatric Klinefelter syndrome. *Journal of Medical Internet Research, 15*(3), e48. https://doi.org/10.2196/jmir.2286.

Ekstrand Ragnar, M., Tyden, T., Kihlbom, U., & Larsson, M. (2016). Swedish parents' interest in preconception genetic carrier screening. *Upsala Journal of Medical Sciences, 20*, 1–6. https://doi.org/10.1080/03009734.2016.1218575.

Ewing, A., Thompson, N., & Ricks-Santi, L. (2015). Strategies for enrollment of African Americans into cancer genetic studies. *Journal of Cancer Education, 30*(1), 108–115. https://doi.org/10.1007/s13187-014-0669-z.

Foster, C., Evans, D. G., Eeles, R., Eccles, D., Ashley, S., Brooks, L., et al. (2004). Non-uptake of predictive genetic testing for BRCA1/2 among relatives of known carriers: attributes, cancer worry, and

barriers to testing in a multicenter clinical cohort. *Genetic Testing, 8*(1), 23–29. https://doi.org/10.1089/109065704323016003.

Gilmore, M. J., Schneider, J., Davis, J. V., Kauffman, T. L., Leo, M. C., Bergen, K., Reiss, J. A., Himes, P., Morris, E., Young, C., McMullen, C., Wilfond, B. S., & Goddard, K. A. (2017). Reasons for declining preconception expanded carrier screening using genome sequencing. *Journal of Genetic Counseling, 26*, 971–979. https://doi.org/10.1007/s10897-017-0074-y.

Green, R. C., Lautenbach, D., & McGuire, A. L. (2015). GINA, genetic discrimination, and genomic medicine. *The New England Journal of Medicine, 372*(5), 397–399. https://doi.org/10.1056/NEJMp1404776.

Green, R. C., Goddard, K. A., Jarvik, G. P., Amendola, L. M., Appelbaum, P. S., Berg, J. S., et al. (2016). Clinical sequencing exploratory research consortium: accelerating evidence-based practice of genomic medicine. *American Journal of Human Genetics, 98*(6), 1051–1066. https://doi.org/10.1016/j.ajhg.2016.04.011.

Hall, M. A., McEwen, J. E., Barton, J. C., Walker, A. P., Howe, E. G., Reiss, J. A., Power, T. E., Ellis, S. D., Tucker, D. C., Harrison, B. W., McLaren, G. D., Ruggiero, A., & Thomson, E. J. (2005). Concerns in a primary care population about genetic discrimination by insurers. *Genetics in Medicine, 7*(5), 311–316.

Hayden, S., Mange, S., Duquette, D., Petrucelli, N., & Raymond, V. M. (2017). Large, prospective analysis of the reasons patients do not pursue BRCA genetic testing following genetic counseling. *Journal of Genetic Counseling, 26*, 859–865. https://doi.org/10.1007/s10897-016-0064-5.

Himes, P., Kauffman, T. L., Muessig, K. R., Amendola, L. M., Berg, J. S., Dorschner, M. O., Gilmore, M., Nickerson, D. A., Reiss, J. A., Richards, C. S., Rope, A. F., Simpson, D. K., Wilfond, B. S., Jarvik, G. P., & Goddard, K. A. (2017). Genome sequencing and carrier testing: decisions on categorization and whether to disclose results of carrier testing. *Genetics in Medicine, 19*, 803–808. https://doi.org/10.1038/gim.2016.198.

Huynh, L., Johns, B., Liu, S. H., Vedula, S. S., Li, T., & Puhan, M. A. (2014). Cost-effectiveness of health research study participant recruitment strategies: a systematic review. *Clinical Trials, 11*(5), 576–583. https://doi.org/10.1177/1740774514540371.

Janssens, A. C. (2015). The hidden harm behind the return of results from personal genome services: a need for rigorous and responsible evaluation. *Genetics in Medicine, 17*(8), 621–622. https://doi.org/10.1038/gim.2014.169.

Joly, Y., Ngueng Feze, I., & Simard, J. (2013). Genetic discrimination and life insurance: a systematic review of the evidence. *BMC Medicine, 11*, 25. https://doi.org/10.1186/1741-7015-11-25.

Laedtke, A. L., O'Neill, S. M., Rubinstein, W. S., & Vogel, K. J. (2012). Family physicians' awareness and knowledge of the Genetic Information Non-Discrimination Act (GINA). *Journal of Genetic Counseling, 21*(2), 345–352. https://doi.org/10.1007/s10897-011-9405-6.

Lazarin, G. A., Detweiler, S., Nazareth, S. B., & Ashkinadze, E. (2016). Genetic counselors' perspectives and practices regarding expanded carrier screening after initial clinical availability. *Journal of Genetic Counseling, 25*(2), 395–404. https://doi.org/10.1007/s10897-015-9881-1.

Mackley, M. P., Fletcher, B., Parker, M., Watkins, H., & Ormondroyd, E. (2017). Stakeholder views on secondary findings in whole-genome and whole-exome sequencing: a systematic review of quantitative and qualitative studies. *Genetics in Medicine, 19*(3), 283–293. https://doi.org/10.1038/gim.2016.109.

Meiser, B., & Dunn, S. (2001). Psychological effect of genetic testing for Huntington's disease: an update of the literature. *The Western Journal of Medicine, 174*(5), 336–340.

Newington, L., & Metcalfe, A. (2014). Factors influencing recruitment to research: qualitative study of the experiences and perceptions of research teams. *BMC Medical Research Methodology, 14*, 10. https://doi.org/10.1186/1471-2288-14-10.

Peterson, E. A., Milliron, K. J., Lewis, K. E., Goold, S. D., & Merajver, S. D. (2002). Health insurance and discrimination concerns and BRCA1/2 testing in a clinic population. *Cancer Epidemiology, Biomarkers & Prevention, 11*(1), 79–87.

Robinson, J. O., Carroll, T. M., Feuerman, L. Z., Perry, D. L., Hoffman-Andrews, L., Walsh, R. C., et al. (2016). Participants and study decliners' perspectives about the risks of participating in a clinical trial of whole genome sequencing. *Journal of Empirical Research on Human Research Ethics, 11*(1), 21–30. https://doi.org/10.1177/1556264615624078.

Schneider, J. L., Goddard, K. A., Davis, J., Wilfond, B., Kauffman, T. L., Reiss, J. A., et al. (2016). "Is It Worth Knowing?" focus group participants' perceived utility of genomic preconception carrier screening. *Journal of Genetic Counseling, 25*(1), 135–145. https://doi.org/10.1007/s10897-015-9851-7.

Scollon, S., Bergstrom, K., Kerstein, R. A., Wang, T., Hilsenbeck, S. G., Ramamurthy, U., Gibbs, R. A., Eng, C. M., Chintagumpala, M. M., Berg, S. L., McCullough, L. B., McGuire, A. L., Plon, S. E., & Parsons, D. W. (2014). Obtaining informed consent for clinical tumor and germline exome sequencing of newly diagnosed childhood cancer patients. *Genome Medicine, 6*(9), 69. https://doi.org/10.1186/s13073-014-0069-3.

Shahmirzadi, L., Chao, E. C., Palmaer, E., Parra, M. C., Tang, S., & Gonzalez, K. D. (2014). Patient decisions for disclosure of secondary findings among the first 200 individuals undergoing clinical diagnostic exome sequencing. *Genetics in Medicine, 16*(5), 395–399. https://doi.org/10.1038/gim.2013.153.

Sterling, R., Henderson, G. E., & Corbie-Smith, G. (2006). Public willingness to participate in and public opinions about genetic variation research: a review of the literature. *American Journal of Public Health, 96*(11), 1971–1978. https://doi.org/10.2105/ajph.2005.069286.

Trinidad, S. B., Fullerton, S. M., Bares, J. M., Jarvik, G. P., Larson, E. B., & Burke, W. (2010). Genomic research and wide data sharing: views of prospective participants. *Genetics in Medicine, 12*(8), 486–495. https://doi.org/10.1097/GIM.0b013e3181e38f9e.

Weiner, C. (2014). Anticipate and communicate: Ethical management of incidental and secondary findings in the clinical, research, and direct-to-consumer contexts (December 2013 report of the Presidential Commission for the Study of Bioethical Issues). *American Journal of Epidemiology, 180*(6), 562–564. https://doi.org/10.1093/aje/kwu217.

Wilfond, B. S., Fernandez, C. V., & Green, R. C. (2015). Disclosing secondary findings from pediatric sequencing to families: considering the "Benefit to Families". *The Journal of Law, Medicine & Ethics, 43*(3), 552–558. https://doi.org/10.1111/jlme.12298.

Wolf, S. M., Annas, G. J., & Elias, S. (2013). Point-counterpoint. Patient autonomy and incidental findings in clinical genomics. *Science, 340*(6136), 1049–1050. https://doi.org/10.1126/science.1239119.