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'*My funky genetics': BRCA1/2* mutation carriers' understanding of genetic inheritance and reproductive merger in the context of new repro-genetic technologies

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Abstract

INTRODUCTION—Deleterious mutations in the *BRCA1/BRCA2* genes elevate lifetime risk of breast and ovarian cancer. Each child of a mutation-positive parent has a 50% chance of inheriting it. Pre-implantation genetic diagnosis (PGD) permits prospective parents to avoid transmitting a *BRCA1/2* mutation to a child, introducing predictability into a process historically defined by chance. This investigation explored how *BRCA1/2* mutation carriers understand genetic inheritance and consider a child's inheritance of a *BRCA1/2* mutation, given the opportunities that exist to pursue PGD.

METHOD—39 female and male *BRCA1/2* mutation carriers of reproductive age were recruited from urban cancer and reproductive medical centers. Participants completed a standardized educational presentation on PGD and prenatal diagnosis, with pre- and post-test assessments. An interdisciplinary team of qualitative researchers analyzed data using grounded theory techniques.

FINDINGS—Participants expressed the belief that reproduction yields children with unique genetic strengths and challenges, including the *BRCA1/2* mutation, family traits for which predictive tests do not exist, and hypothetical genetic risks. Participants expressed preference for biologically-related children, yet stated their genetically 'well' partner's lineage would be marred

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through reproductive merger, requiring the well partner to assume the burden of the *BRCA1/2* mutation via their children. Participants expressed diverse views of genetically 'well' partners' participation in family planning and risk management decisions.

DISCUSSION—Pressure to use reprogenetic technology may grow as genetic susceptibility testing becomes more widely available. Work with individuals and couples across the disease spectrum must be attuned to they ways beliefs about genetic inheritance play into reproductive decision making.

Keywords

BRCA mutation; pre-implantation genetic diagnosis; human reproduction; couples; genetic inheritance

INTRODUCTION

Inheriting a deleterious mutation in the *BRCA1* or *BRCA2* genes dramatically increases a woman's lifetime risk of developing breast and ovarian cancer. By age 70, an estimated 60-70% of *BRCA1* mutation carriers and 45-55% of *BRCA2* mutation will develop breast cancer, and 40% of *BRCA1* mutation carriers and 20% of *BRCA2* mutation carriers will develop ovarian cancer (Clark & Domchek, 2011). Much of this risk occurs before age 50. Either biological parent can carry a *BRCA1/2* mutation and pass it to a child, and each child of a mutation carrier has a 50/50 chance of inheriting it.

In the last decade, cutting edge screening and preventive options have provided *BRCA1/2* mutation carriers with a number of risk management options. Even more recently, advances in genetically enhanced assisted reproductive technologies, also known as repro-genetic technology, have pushed the possibility of screening and prevention into the realm of reproduction. A number of reproductive options exist that prevent the birth of a child who carries a *BRCA1/2* mutation, including forgoing conventional conception for either adoption or gamete donation. Pre-implantation genetic diagnosis (PGD) is an emerging reproductive option to avoid transmitting a *BRCA1/2* mutation to the next generation (Meister, Finck, Stobel-Richter, *et al.*, 2005; Quinn, Tuya, Murphy, *et al.*, 2012; Sagi, Weinberg, Eilat, et al., 2009; Vadaparampil, Quinn, Knapp, *et al.*, 2009). PGD requires *in vitro* fertilization treatments with an additional genetic testing stage to identify and transfer to the uterus embryos that do not have a deleterious mutation carried by a biologically related parent. Prenatal diagnosis requires that a pregnant woman undergo chorionic villus sampling (CVS) or amniocentesis followed by consideration of selective abortion. Although technically feasible, this is rarely utilized by *BRCA1/2* mutation carriers (Offit, Sagi & Hurley, 2006).

LITERATURE REVIEW

Genetic material from each biological parent is randomly sorted into egg and sperm prior to conception to promote variation. At conception, each child receives a full complement of genes from each parent, including a unique constellation of strengths, vulnerabilities and traits.For would-be parents interested in and able to become biological parents, the mixing of ones' genetic material with that of another in wholly unique ways can be very exciting.

Seeing pieces of oneself in another is a very special part of parenthood, particularly with respect to those traits viewed, either personally or socially, as strengths. However, concern about genetic predisposition to hereditary breast and ovarian cancer and other genetic conditions, and the random nature of genetic inheritance, may complicate these feelings. Prospective parents may "have to do a calculus of how good are the qualities they believe they can pass on in their genes, against how bad are the qualities of the disease they may also pass on" (Katz Rothman, 1998, p. 126).

Increasing availability of PGD to identify gene mutations for adult onset conditions such as hereditary breast and ovarian cancer (Offit, Sagi & Hurley, 2006) and its potential use for non-medical conditions may force would-be parents to examine what they bring to the reproductive table in both concrete ('what I have to pass on'/phenotype) and abstract terms ('what my child could inherit from me'/family history). The National Comprehensive Cancer Network (NCCN, 2011) recommends discussion of family planning wishes and introduction of assisted reproductive technologies, including PGD, during cancer risk counseling. The introduction of PGD during genetic testing may invite those involved in family planning to consider a future child's inheritance of a much broader range of inherited traits and conditions, medical and non-medical, against which the dangers of a *BRCA1/2* gene mutation are measured. The availability of repro-genetic technologies may push would-be parents to consider action (Dommering, van den Heuvel, Moll, et al, 2010) as they anticipate those traits or conditions they hope their children will not inherit, traits they wish to select out.

Perspectives on PGD in Social and Family Life

Public perception about what PGD permits (eg: designer babies) focuses on what traits could be selected in (eg: eye color, intellectual prowess). Preference for specific genetic profiles or characteristics over others is not exclusive to the age of genetic discovery. Concern that PGD is the first misstep down a 'slippery slope' is shaped by the dark history of sterilization and eugenics as a mechanism of social enhancement and control (Franklin & Roberts, 2006). The characterization of PGD as a tool for made-to-order babies may deter would-be parents interested in reducing a child's risk of pain and suffering. Further, public discourse about PGD is shaped by the more recent concern over the ethically controversial application of repro-genetic technologies to birth 'savior siblings' who can provide stem-cell-rich cord blood to an older child with a known genetic disease, or for sex selection. PGD may also be coupled to anti-abortion sentiment as viable, yet affected embryos created through the techniques of *in vitro* fertilization are discarded after being deemed 'unfit.' Yet, public discourse regarding PGD is shaped by a public with limited exposure to the physical and emotional rigors of *in vitro* fertilization, or the challenges that lead to consideration of PGD (Franklin & Roberts, 2006)

BRCA1/2 mutation carriers' perspectives on the 'slippery slope' (Quinn, Vadarampil, Wilson et al., 2009) may exist in tension with each individual's experience of an illness that 'runs in the family', as well as experiences of care giving and loss (Brouwer-DudokdeWit, Savenije, Zoeteweij, et al., 2002; Chilibeck, Lock & Sehdev, 2011; Hoskins, Roy & Greene, 2012; Sobel & Cowan, 2003). For prospective parents, justification for using PGD may be

couched in attitudes towards and understandings of technology (Rodin & Collins, 1991), in reproductive hopes and challenges, and in family aspirations (Finkler, Skrzynia & Evans, 2011). Like many *BRCA1/2*-related risk management decisions (Hallowell, Foster, Eeles, Ardern-Jones, & Watson, 2004), reproductive decisions are rarely made in social isolation. For couples, the family history of each partner may diverge with respect to experiences and interpretations of illness and loss. *BRCA1/2* mutation-positive individuals may have distinct disease related beliefs and concerns about passing the mutation to a child. These beliefs may or may not dovetail with the experiences of mutation-negative partners, leading to tension in reproductive planning (Werner-Lin & Gardner, 2009). Pressure to use repro-genetic technologies may also emerge from a variety of other individuals invested in the health of the future child and family, including affected and extended family members, in-laws (i.e. future grandparents, aunts and uncles), and health care providers (Rubin, Werner-Lin, Stern, et al. 2011).

PGD introduces the possibility of choice into a situation historically defined by chance (Ehrich & Williams, 2010; Franklin & Roberts, 2006), and suggests a family's genetic line can become unencumbered by a specific inherited disease risk for future generations (Franklin & Roberts, 2006). Yet, PGD is an imperfect technology; it introduces additional uncertainties for *BRCA1/2* gene mutation carriers (Rubin, Werner-Lin, Stern, et al. 2011). PGD involves medically invasive and expensive procedures, does not guarantee a successful pregnancy or a mutation-free baby (Offit, et al., 2006) and presents a host of novel ethical issues about selecting and discarding embryos. This study is situated in the context of a broader investigation of *BRCA1/2* mutation carriers' attitudes about the use of, as well as the ethical and social acceptability of, PGD and prenatal diagnosis to screen embryos and fetuses for a *BRCA1/2* mutation. The broader study sought also to elicit opinions from *BRCA1/2* mutation-positive women and men as to whether and how information about PGD and prenatal diagnosis should be presented during genetic counseling. During discussion of these assisted reproductive technologies, participants revealed the ways they construe genetic inheritance, including how they consider passing on a *BRCA1/2* mutation to a child given the opportunities that exist to pursue PGD. The purpose of this paper is to report on beliefs and values expressed by participants surrounding the process of combining disparate genetic lines to produce children, and the ways participants negotiate the possibility of shaping (through the use of PGD or prenatal diagnosis) the otherwise random process of inheritance.

DESIGN

Sampling and Recruitment

Participants were recruited from the Clinical Genetic Service of a private, comprehensive cancer center in New York City. Inclusion criteria required participants: (1) carried a deleterious *BRCA1/2* mutation documented by Clinical Genetics; (2) were of 'reproductive age' defined as under age 43 for women and under age 50 for men; and (3) that women had not undergone hysterectomy or risk reducing oophorectomy. Ninety-eight eligible Clinical Genetics patients were mailed an invitation letter, followed by a phone call to assess interest and schedule an interview. 45 of 98 prospective participants did not respond to recruitment

efforts, and 19 declined participation upon contact. Among decliners, the majority (10) cited inconvenience, scheduling conflicts, or being too busy. Five decliners felt that topics related to *BRCA1/2* and/or PGD were too emotionally difficult. Data from one participant was excluded due to an active psychiatric episode that rendered her responses unreliable.

Later in the study, a second sample of patients who sought consultation for PGD to screen embryos for a *BRCA1/2* gene mutation were recruited through a Center for Reproductive Medicine in New York City. Eligibility criteria were the same, with the exception that mutation-negative female partners were eligible to participate. The genetic counselor at the Center contacted 11 eligible patients by phone. Seven initially agreed to participate, although one woman actively cycling for *in vitro* fertilization cancelled her scheduled appointment citing it was "a little too much to think about right now." Reasons for declining participation were not recorded for other patients at the Center. Institutional review boards at both medical institutions approved the protocol.

Procedures

Interviews with patients from Clinical Genetics were conducted at the hospital's counseling center. Interviews with patients at the Center for Reproductive Medicine were conducted either at the Center or the patients' home, determined by the patients' preference. The study's Principal Investigator, a licensed doctoral-level clinical psychologist, or a study Co-Investigator, a licensed doctoral-level social worker, completed all interviews. Both had prior clinical and research experience with individuals at hereditary risk for cancer. Participants provided informed consent followed by completion of a demographic questionnaire and assessment of prior experience with and knowledge of prenatal diagnosis and pre-implantation genetic diagnosis.

The study interviewer then presented participants with a standardized educational tutorial, developed in collaboration with a doctoral-level genetic counselor and approved by genetic counselors on the Clinical Genetics Service, reviewing risk and inheritance patterns associated with *BRCA1/2* gene mutations, defining pre-implantation genetic diagnosis and prenatal genetic diagnosis, and describing the procedures and associated features (e.g., ethical considerations, cost) for each. This assured participants shared a basic proficiency in patterns of cancer risk and inheritance associated with *BRCA1/2* gene mutations, and the procedures, features, and risks of both PGD and prenatal diagnosis. Two versions of the tutorial were developed to balance any "order effect" associated with the presentation of PGD or pre-natal diagnosis. We alternated between these two presentations for each consecutive interview. Following the educational presentation, participants completed a brief knowledge assessment to ensure comprehension of the key points of the educational presentation. This demonstrated that participants were able to distinguish PGD from pre-natal diagnosis based on its core biomedical features.

Participants then completed an in-depth, semi-structured interview [see Table 1.] exploring experiences of familial cancer and genetic testing, surveillance and prevention options for *BRCA1/2* mutation carriers, the impact of a *BRCA1/2* mutation on family planning, and attitudes towards the use of PGD and prenatal diagnosis. Religious and family views, and cost were also explored. For the one couple that participated, the educational presentation

was delivered together. Interviews were conducted separately with each partner first, then together afterwards to discuss any additional information. Interviews lasted between 45 and 120 minutes. [Insert Table 1. Excerpted Interview Guide]

Data Management

All interviews were audio-recorded and transcribed verbatim by a professional transcription service. The research team used a grounded theory approach to data management, including: a) constructing analytic codes and categories from data, not from a priori assumptions; b) using the iterative, "constant comparative", method; and c) memo-writing to elaborate and define categories, propose relationships between categories, and identify gaps in understanding (Beeson, 1997; Charmaz, 2000; Strauss & Corbin, 1995).

The interdisciplinary research team included disciplines of medicine, genetic counseling, molecular biology, psychology, social work and anthropology. Two members of the interdisciplinary data analysis team read each transcript line-by-line, and independently created a case summary that included participant demographics, personal and family cancer history, a sum of their responses to key study questions, and key themes that arose during the interview. Members of the team then independently re-read transcripts to generate an initial set of open codes and categories [using Atlas.ti software to manage and organize data]. The team used a set of procedures derived from grounded theory to guide analysis when a project employs multiple coders, to facilitate group discussion towards agreement on a set of codes and categories that best represent the data. These codes and categories formed the initial codebook. The research team met regularly throughout data collection and analysis to revise the coding scheme to accommodate emergent themes. Discrepancies were brought to the full team for discussion, clarification, and resolution.

The primary codebook for this arm of the study focused beliefs about family formation and genetic inheritance, family lineage, and the processes by which prospective parents negotiate family planning. A select group of researchers initiated axial coding procedures, which included grouping codes into conceptually meaningful clusters and hierarchies. During this process, grouped codes are defined and their properties and sub-codes are identified.

Trustworthiness—Collaboration across professional disciplines helped the research team remain reflexive during data management and to ground findings in both the patients' needs and the professional mandates of health care providers. Consultation with qualitative research experts and maintenance of a detailed audit trail [method of tracking decisions and interpretations of data] facilitated rigorous and transparent data collection and management. Outliers were included in analysis and examined for unique contributions to the development of theory and practice recommendations (McPherson & Thorne, 2006).

FINDINGS

Thirty-nine interviews were conducted, with a total of 34 females and 5 males participating. The majority where white (92%), married (76.9%), working full time (59%), and affluent (nearly 70% reported annual incomes greater than $100,000). Just over half of the sample had children (56.4%), and nearly 80% reported they were not finished (or not sure they were

finished) with plans for having children. 64% report being raised Jewish, and 61.5% are currently affiliated in some way with the Jewish faith and traditions. All participants were *BRCA1/2* mutation-positive, except one female participant who was undergoing PGD to identify and screen out a *BRCA1/2* gene mutation carried by her husband. The parameters of the protocol prevented us from interviewing partners of mutation positive women and men because they were not patients at these respective medical institutions. Data from the mutation-negative wife (who was actively cycling at the Center for Reproductive Medicine and was, thus, eligible to participate) and from the couple's joint discussion with the researcher was treated as a unique case and is integrated into the findings anecdotally (and is so noted). Data from one participant was excluded due to an active psychiatric episode that rendered her responses unreliable.

During discussion of attitudes about PGD, participants revealed perceptions about the *BRCA1/2* gene mutation as one piece of a comprehensive set of genetic traits and conditions they had to offer children via either genetic inheritance or, with adopted children, through nurturing of character. Participants discussed ways in which, through the process of reproduction, genetic lines are combined to produce children with their own set of unique strengths and challenges. The preference for biologically related children was strong, yet participants stated that in creating genetically linked children, the health of their genetically 'well' partner's lineage would be marred. As a result, these well partners would assume the risk and burden of the *BRCA1/2* gene mutation via their children.

"My funky genetics": Merging genetic lines to produce children

Despite the presence of a *BRCA1/2* gene mutation, the desire to bear and invest in ones' genetic progeny was linked, for some participants, to conventional views about the purpose of marriage. A participant stated: *"I felt like marriage is about a lot of things, but one of the things that it's about is creating little people that are both of you and the joy of figuring out what both of you can do"* (PGD034). Yet, during discussion of family planning, participants shared beliefs, opinions, concerns, and hopes about what could and could not be inherited by their children. This included both desirable and undesirable genetic conditions and traits. Consistent with findings from other studies investigating *BRCA1/2* mutation carriers' reproductive concerns (Werner-Lin, 2010), one woman said: *"It's the first thing I thought, you know, my poor kids, that this is what I'm passing on to them"* (PGD026).

Some participants identified the *BRCA1/2* mutation as 'defective' or 'funky.' In contrast, they described a family history without chronic and pervasive disease as indication of 'clean' genetic material. A woman who had recently postponed family planning due to job loss discussed playful teasing by her husband, whose family did not have any indication of inherited disease risk, saying:

> *He comes from a long line of people who live very long and have very few health problems…he's got the great genetics, so he's been teasing me about I brought the defective genes to the family pool. So it's in a teasing kind of vein, that I'm dragging down his perfect genetic record with my funky genetics (pgd028).*

She shares her view that, through reproduction, her 'funky' genetic line is merged with her husband's 'clean' line. As the genetic code of mother and father are intertwined in the child, the well partner assumes the risk, responsibility, and burden of the *BRCA1/2* mutation. Her language indicates the perceptions that she actively participates in this merger by '*dragging down his perfect genetic record.'* While this participant reported the teasing as lighthearted, she went on to say: "*I felt a little bit guilty bringing this issue to their family* "(PGD028). Rather than hoping she would pass on her mutation-negative copy of the *BRCA* gene, resulting in a mutation-negative child, this participant discussed the concern that she would mar her partner's healthy genetic line if she produced a BRCA1/2-positive child. Such an interpretation suggests she understood the *BRCA1/2* gene mutation as overriding, or masking, the contribution of her partner's DNA.

Other participants also expressed guilt about bringing a *BRCA1/2* mutation to a 'clean' genetic line and of their partner's 'inheritance' of those alleles via their children. One mother discussed the importance of her husband attending genetic counseling sessions, saying: "*One of the reasons it was helpful for him to be there is this isn't part of his family's history, but now it is part of his family, right? He needs to have this information to know about this for his own children"* (PGD26). A mutation-positive male, overpowered by the coalition between his carrier mother and his non-carrier wife, lamented that neither woman was interested in considering PGD. He said: "*The kid is just as much hers as mine. She owns the gene as much as I do at this point"* (PGD082).

Some participants created balance in their reproductive merger with partners by identifying the difference between mutations that genetic testing can identify (eg: *BRCA1/2)* and predispositions or family traits potentially carried by themselves or their partners for which genetic tests are not yet available. One participant shared: "*It's just part of the cards I was dealt. His family has depression, I have this*" (PGD057). Another shared: "*Cancer's not a particular problem for him. His family has other problems. [laughs] I guess we all have whatever, but-yeah, there seems to be Alzheimer's in his family*." This participant may frame Alzheimer's as a familial disease (although, like some hereditary cancer syndromes, familial Alzheimer's accounts for only about 5% of cases). This participant articulates the growing lay perception (Emslie, Hunt & Watt, 2003), fed through findings from the Human Genome Project, that every individual carries some genetic defect. This thinking levels the playing field as this participant reconciles her known mutation with the possibility that her partner also brings genetic risks to the reproductive table.

Finally, some participants cited unknown diseases or traits, ones not visible or identified in their own or in their partner's genetic line. These hypothetical genetic risks, such as rare recessive traits, would confer what they believed to be greater risks than a *BRCA1/2* gene mutation.

> *You're not necessarily going to develop cancer just because you carry the gene. So if I screened out an embryo that was a carrier of the BRCA gene maybe that's the embryo that is actually a carrier for something else even more horrible* (PGD070).

The possibility that this prospective parent might actively, yet unknowingly, select an embryo affected by a yet unknown genetic disease left her conflicted about PGD as she considered the possibility of committing a 'sin of commission' (Baron & Ritov, 2004).

"My own kids": Perspectives on the Genetic Link between Parent and Child

Aside from balancing one's genetic material with that of another, participants also struggled to reconcile the mixture of strengths and risks in their own profile.

Passing on desirable traits

While participants used words like 'defective' and 'dirty' to describe the *BRCA1/2* mutation, many also cited traits they hoped their children would inherit. Consistent with research on families with hereditary non-polyposis colorectal cancer (HNPCC, McAllister, 2003), some participants coupled mental fortitude in the face of illness with inheritance of the *BRCA1/2* mutation. Three participants who described their mothers using terms such as 'storm troopers' (while they actively fought off cancer and maintained family routines during trying cycles of chemotherapy) were particularly adamant about passing on their genetic material, specifically strength of character, to their children. Other positive traits were much more general, such as intellectual prowess, physical traits, talents, and a sense of humor or musicality. Anecdotally, the couple interviewed that was actively undergoing PGD to screen for a *BRCA1/2* gene mutation sat together with the interviewer, and each discussed those traits they hoped their child inherited from the other partner. They reported these were the traits that had attracted them to each other and remained the compliment of strengths that kept them together.

Some participants discussed specific positive and desirable traits they had to offer a child. Mention of these traits was generally couched in discussions of participant preferences for biologically related children. This preference was quite common in our sample, expressed with conviction, and consistent with findings from other recent studies (Leontini, 2010). A participant experiencing infertility discussed her reactions when her reproductive endocrinologist suggested she pursue donor gametes: *"The possibility was that I wouldn't have any children, that I wouldn't pass on any of my genes and to me that was unacceptable. If there was any way at all that I could have my own kids I wanted to do that"* (PGD034). As she spoke, this participant conflated passing on her genes with having 'her own' children. A participant discussing a meeting with her reproductive endocrinologist after her mastectomy used similar language, saying of this conversation: "*my chances were very low of having my own baby, my own genes*" (PGD091). A participant, ambivalent about becoming a parent, said: "*I can't say that I'm really gung-ho about having kids to begin with but then certainly the prospect of having a child with potentially a genetic mutation and have to face the things that I face…"* (PGD056). She went on to say that if she did decide to become a parent, however, she would only be interested in using her own gametes, *"I'm a very intelligent person and my husband's very intelligent —why wouldn't you want to create a child with your own genetic material?"*

Genetic risk of impaired cognitive or emotional health

Individuals with a family history of disorders that impact cognitive and social functioning expressed the attitude that these disorders presented a more pervasive threat than a *BRCA1/2* genetic mutation .In discussing her history of anxiety, one woman shared:

> *There are so many bigger things that I've dealt with in life and I can't say it's because of cancer. I could say it's because I have an anxiety problem…if I was going to start weeding out certain things I would probably take my anxiety disorder away before I would take away the BRCA gene* (PGD67).

This participant integrated the ideas that cancer is increasingly treatable and survivable, that social and psychiatric disorders present a greater and more pervasive threat to quality of life than cancer *risk*, and that children face a range of challenges that may be debilitating as they grow into adulthood. Childbearing, she implies, is fraught with anxieties beyond those specific to a gene mutation that confers susceptibility. She discusses her concerns about using PGD to select a *BRCA* mutation-free embryo in relation to her concerns about other risks:

> *"When they're picking an embryo what if they pick the stupid kid or the ugly kid… You can't predict how much money your child's husband or your child is going to make. Or whether or not it's going to struggle in school or not. And to me those are the bigger things, this is just one little blip"* (PGD067).

Comparing cancer to physical attractiveness and intellectual prowess may seem discordant, yet this participant presents a set of social considerations beyond a parent's control that could threaten a future child's happiness and wellbeing, and shape both the experience of parenting and of the child's social and professional prospects. This participant gives voice to the range of 'genetic', or 'embodied' traits that may shape the ebb and flow of daily life (Geelen, Van Hoyweghen & Hortsman, 2011), This life includes provisions not only for a future child's physical health, but for their social and emotional health as well. As prospective parents consider the full range of risks a child might face, the *BRCA1/2* gene mutation may not be only one of many considerations.

"He's a mini me": *Nature/Nurture Revisited*

A small number of participants were actively seeking or had pursued adoption after attempts at a conventional pregnancy had failed. Each of these participants prized parenting above continued attempts at a genetic link to a child. Consideration of adoptions pushed them to wonder about the extent to which traits are nurtured or inherited, and the meaning of having, or not having, a genetic link with one's child. A male participant whose wife conceived while they were in the process of adopting shared of his son:

> *Yeah, he's a complete wise ass just like I was. He's a mini me. Would my son if he was an adopted Korean baby look like me? No. But would he have acted like me, would he have picked up on my traits, would he have had the same sense of humor? I don't know about the whole nature versus nurture thing but you know I'd like to think I would have felt as close to an adopted baby as I did a biological baby* (PGD090).

This participant spent time emotionally invested in the possibilities of parenting both a biological and an adopted child. In his biologically related son he sees aspects of his own character and identifies with him powerfully around those traits (‘*he’s a mini me*’). Yet, he distinguishes a desire for children to inherit certain qualities from the love and care a parent feels for a child regardless of their genetic kinship. Although parents may fantasize about a child looking, sounding, or thinking like them, this participant alludes to the notion that the parent/child relationship is not defined by shared genetics but rather by experience and emotion.

A single female participant recovering from breast cancer and multiple breast surgeries consulted with one of her fertility specialists and learned that her chance of conceiving a viable embryo, even with donor gametes, was low. She decided to pursue adoption only to learn that her cancer diagnosis would likely prevent her from adopting internationally. She addressed the core nature/nurture debate as she discussed her curiosity about her soon-to-be privately and domestically adopted son:

> *You might get your overall constitution from your genes, which then has you strong or weak. I have a very strong constitution…very grounded, logical. So it will be interesting because I’m going to give that to my child. It will be interesting if he will have that, too…I talked to this young lady I’m adopting from and she does not have that. She has quite the opposite. But it’s hard to tell if it’s from her environment or if it’s from her genes* (PGD091).

Although this participant says she believes one’s core self grows from one’s genetic material, she also alludes to her perception that the environment within which an individual is raised has an impact on the development of character. She discusses ‘giving’ her adopted son a stronger constitution than the one offered by his birth mother, yet she is unsure about whether the birth mother’s life circumstances or her genetic blueprints shaped her character.

“It’s half their child”: Negotiating Family Planning with Partners

Interwoven with participant beliefs about the nature of a *BRCA1/2* mutation and the importance of maintaining genetic lineage were beliefs about how (and whether) non-carrier partners should be involved in reproductive planning. Findings were mixed, and differences in opinion about partner participation may have been tied to variations in understanding cancer risk and perceptions of severity.

A prime theme addressed the dual responsibility for *BRCA1/2* mutation-positive women to manage physical and emotional aspects of both pregnancy and cancer risk. A participant planning a conventional pregnancy with her husband stated: *“It’s your child together but yet it′s your body…plus I′m the one with the gene. If anyone has strong feelings about this it’s me”* (PGD02). Other married women, like this one, did not feel the full weight of reproductive decision-making, describing egalitarian discussion with her partner about the use of PGD. She shared:

> *Being partners we’d want to come to some kind of compromise as to how we want to go along with having our kids and what have you, and what we want to transfer or not transfer…for me everything is a discussion with my husband* (PGD074).

Family planning negotiations were ongoing (or anticipated) in the context of an established union.

Yet, even when coupled participants saw a shared process, for some the ultimate responsibility for reproductive decision making lay with the woman, whether or not they were mutation-positive. One participant discussed the interplay between her interest in an egalitarian process and her ownership of the physical burdens of both pregnancy and cancer risk.

> *I mean we've talked about it and I think we're kind of on the same page. Technically it's ultimately my decision because it's my body, but at the same time it's our family… I think it's good to have somebody who's supportive of what we have to do* (PGD085).

The following participant articulated this differently. She stated:

> *Even though it's half their child I think they get much too much say in these things. Until they can actually be more than a sperm donor in something like IVF he certainly can have input. But if I say no what I say has to hold. I should listen to him and hear him out, but ultimately I think I should have like 51% vote* (PGD52).

Women who were not in committed relationships discussed attitudes about a hypothetical partner's participation in reproductive decision-making. A single participant shared her beliefs about marriage and negotiating uptake of assisted reproductive technologies: "*In my ideal marriage it would be an equal process…my belief is most of the time the people we marry are people who share similar views to your own. So, ideally we would be on the same page"* (PGD08). Another young, single participant stated simply: "*Having a baby is 50% him, 50% me, so I think definitely he should be fully involved"* (PGD06).

The small subset of mutation-positive male participants warranted their own analysis. Male carriers concurred that, even though they carried the *BRCA1/2* mutation, they had '49%' of the power over reproductive decisions compared to their non-carrier wives. Several unrelated male and female participants indicated that men have 49% of the vote, while women have 51%. Participants were not asked to quantify power differentials during interviews; they offered these numbers spontaneously. The fact that this split centers around 50% alludes to equity. Yet, as one female participant said when asked to qualify these numbers, "*You only need 51%."*

For these men, family planning decisions involved considerable participation by non-carrier wives, as was evident in the couple interviewed together. A married, mutation-positive male whose wife, mother, and sister were diagnosed with breast cancer within a few years of each other discussed his views on balancing ownership of the mutation with reproduction:

> *I forget that it's me and not her. It's just like 'we,' you know? I almost feel like it's more of a 'her' thing, because as much as the mutation is mine, the pregnancy is hers, and one we have some control over, the other we don't. So the one that we have control over, the pregnancy, the nature of it and how it's started, is hers"* (PGD092).

A married male participant whose wife suffered several miscarriages that he described as "worse than cancer," when asked how much sway he had over reproductive decisions, answered simply: *"Forty nine per cent"* (PGD090). Another husband struggled with the need for his non-carrier wife to endure invasive procedures to achieve a pregnancy with a *BRCA* mutation-free baby as a result of his *BRCA* carrier status. He shared:

> *I guess the whole pregnancy thing, I just look at it as you know it's the wife not the husband…I mean it's her body. Again, I mean it's our child and our pregnancy together, but I do feel like she has 51% of the vote. But, again, when I tell her that I know I feel a little bit guilty saying, "Oh, you figure it out." … The fact that it's me who's positive, not my wife, doesn't even a little bit give me any sort of pride of place in the decision making process* (PGD098).

A third young husband recognized his interest in conceiving a *BRCA* mutation-negative baby was secondary to his wife's lack of interest in (or desire to avoid) PGD. He says:

> *It's a lot easier for me to say, "Hey, I think it's a good idea." When it really isn't affecting me nearly…I mentioned it to [wife and mother], and neither were too hot on it. So I was like, I guess I'm wrong. I really haven't brought it up again* (PGD082).

Summary

Participants discussed the experience of reconciling a *BRCA1/2* mutation with the desirable and undesirable traits they had to offer a child, whether through genetic inheritance or through parenting. In thinking about PGD to screen embryos for a *BRCA1/2* mutation, participants thought explicitly about those desirable and undesirable traits their partner contributed to a future child, including both identifiable and hypothetical risks. As participants framed the *BRCA1/2* mutation as one piece of a comprehensive set of genetic and social strengths and risks, they attempted to reconcile the random nature of reproduction with the imperfect, expensive and medically invasive, yet seemingly more certain technology of PGD. Yet, PGD introduces additional risks into reproduction including the possibility that a would-be parent might commit a sin of commission by selecting in something 'worse' than increased risk of breast and ovarian cancer while selecting out a *BRCA1/2* mutation. The decision to engage with assisted reproductive technology required consideration (and for some, rejection) of partner preferences with respect to family planning and a child's potential for inherited cancer risk.

Limitations

Participants experienced genetic counseling between 2000-2009, representing a broad time frame within which recommendations for prevention and opportunities for PGD changed substantially. As a result, participants had uneven exposure to PGD-related information during their genetic counseling experiences. To correct for this, we designed the educational presentation to provide biomedical, psychosocial, and financial information about PGD and prenatal diagnosis. The tutorial mentions (1) that more individuals diagnosed with cancer are now surviving, and (2) the possibility for scientific discoveries that might improve early detection, prevention, and treatment of *BRCA*-related cancers. While these statements are

supported by widely available national data sets (Ries, Melbert, Krapcho, et al., 2007), this information may have skewed participants towards optimistic biases or towards a biomedical view of reproduction and risk reduction. Alternatively, since PGD is an invasive and costly option, its introduction may have suggested greater severity of *BRCA1/2* cancer risk than participants were comfortable with and participants may have minimized their own cancer risk in reaction to perceptions of PGD as a drastic option. Further, one reason for declining participation in this study was expressed emotional difficulty with the topic, and many did not cite a specific reason for declining. As a result, it is unclear what other sampling biases might have been introduced.

Recruitment was limited to two unique medical environments located in a dynamic, urban, progressive community serving an affluent and educated demographic. Recruitment did not approach saturation for non-white groups, and few participants were of lower socioeconomic status. The under-representation of minority groups in current at-risk clinical populations, due, in part, to lower uptake of genetic counseling and testing (Thompson et al., 2002, Halbert et al., 2006) and to the higher incidence of receiving a variant result (Nanda et al, 2005) poses a limitation to this project. We were unable to reach saturation in interviews with ethnic minority women and men, whose views might diverge significantly from those of whites due to differences in spiritual beliefs and cultural and social experiences. Due to restrictions on chart review instituted by the human subjects review board, we have limited information about decliners, despite cursory responses about their expressed reason for declining participation. Finally, our sample was composed of predominantly heterosexual couples; issues of genetic inheritance may be quite different for same-sex couples already considering gamete donation and the use of assisted reproductive technology (Mamo, 2007).

DISCUSSION

Findings from the Human Genome Project suggest, and participants echoed, that we might all be genetically vulnerable in some way. The *BRCA1/2* gene mutation is separate from many other inherited susceptibilities merely in that we can identify it through genetic testing. The purpose of pursuing genetic testing is ostensibly to become proactive in managing inherited cancer risk to prevent disease and to reduce mortality. A primary concern for patients of reproductive age is the 50% chance of each child inheriting the deleterious mutation. As repro-genetic technologies become more widely available for adult onset disorders, and as awareness of their availability grows, pressure to use them may increase for would-be parents. Partners, extended family, and physicians, as well as notions about what makes a ‘good patient’ and a ‘good parent’ may exert pressure on *BRCA1/2* mutation carriers who experience a sense of obligation not only to protect a future child from a mutated genetic line (and painful family history), but also to preserve a partner’s ‘clean’ bloodline.

Essentialist Genetics and the Nature/Nurture Debate

Genetic discovery in the last decade has linked specific gene mutations (or combinations of mutations) to the expression of specific conditions and traits. These links favor a ‘nature’ based view of birth and illness outcomes, privileging the genetic contributions to disease,

while diminishing the 'nurture' components of our social and physical environments and the complex interplay between genes and these environments (Shakespeare, 1995). As the nature/nurture debate is revisited from an essentialist perspective, preference for a biologically related child who is 'of' the couple is pitted against social pressure for able-bodied children (Ettorre, 2000), and remains in tension with cultural imperative to birth healthy children by all means possible (Rapp, 1999, Finker, 2000). Participants balanced feelings about the *BRCA1/2* mutation as evidence of a "damaged" genetic line (Werner-Lin, 2007) with the understanding that this mutation constitutes only one piece of what a child inherits from each genetically linked parent. The rapidly evolving nature of genetic research and the likelihood that susceptibility testing will be available in the future for other common disorders lead participants to view the *BRCA1/2* mutation as one risk among potentially many.

Social scientists have critiqued scientific and public discourse for essentializing genetics in the expression of conditions or traits and minimizing context and environments (Finkler, 2005;) and medicalizing kinship and family formation (Finkler, Skrzynia & Evans, 2003) rather than develop more holistic, comprehensive ecological models (Sluzki, 2007). This discourse implicitly elevates the genetic link from parent to child above legal or emotional ties (Strathern, 1995). The Western idealized family form (heterosexual, married couple with genetically linked children) continues to be prized above other increasingly common family forms, for example: lesbian couples parenting children related biologically to neither parent, to one parent, or, in more complicated ways, to both parents, such as when one partner becomes pregnant with an embryo using the other partner's egg. The tension between genetic essentialism and the integration of nature *and* nurture was evident in participant interviews. Participants who discussed family formation expressed a preference for a genetic link to their children. Although participants did not want their children to inherit the *BRCA1/2* mutation, they expressed hopes for their children's inheritance of other prized traits and discussed their beliefs about the extent to which these traits are socialized in the context of family life or are purely inherited (Hortsman & Finkler, 2011; Richards, 1996).

Couple Dynamics, Sex, and Gender

Individuals with disparate exposure to family illness and loss may bring divergent opinions about genetic inheritance and reproduction to family planning endeavors. This may create tension for couples with significantly different medical family histories and may have implications for therapeutic work and future research with couples and families (McDaniel, 2005) considering genetic counseling (Hoskins, Roy, Peters, Loud & Greene, 2008) or the use of genetically enhanced assisted-reproductive technologies. Participants in this investigation struggled to varying degrees with when and how to involve non-*BRCA* carrying partners in decisions about the use of PGD, especially when perspectives about inheritance, adoption, and illness diverged. Some participants coupled reproductive and cancer risk management decisions, proceeding on their own terms with minimal input and influence from their partners. Others approached these issues separately, addressing family planning as a joint decision about the family's future and addressing cancer risk management individually as unique to the woman's health. Individuals and couples

negotiating these issues might be counseled to approach reproductive decisions in a thoughtful and deliberate manner, and to identify whether and how to include a real or future partner's illness histories, preferences, and beliefs into decision processes.

Male mutation carriers discussed their unique role vis-à-vis their mutation-negative wives. The confluence of lower risk estimates and their inability to be '*more than a sperm donor'* (PGD052) in reproduction shaped a perspective expressed by the few men we interviewed: the *BRCA1/2* mutation was a shared vulnerability in their marriage. Yet pervasive in the sample, among both women and men, was the belief that, despite whatever negotiations or conflicts arise between partners, women have the ultimate control over when and how they care for their bodies and pursue family planning. This perspective may be specific to our sample: educated, Westernized, affluent, liberal individuals seeking care at a highly respected medical institution.

Implications for Future Research

Research is needed to investigate the experiences of *BRCA1/2* mutation-positive men. Existing cross sectional survey data together (Menon, Harper, Sharma, et al., 2007; Quinn, et al., 2010), and the few in-depth interviews presented here identify key issues faced by men from families affected by hereditary breast and ovarian cancer, yet these data remain insufficient. Due to the widely disparate *BRCA*-related risk estimates, lower uptake of genetic testing, and the lack of screening protocols or preventive measures, male carriers are sorely underrepresented in the literature (Moynihan, 2011). As one male participant told us, the genetic counselor framed his carrier status as an issue for his (as-of-yet nonexistent) daughters, not for him. This perspective may marginalize men in both family and medical settings and deny them needed support (Maughan, Heyman & Matthews, 2002) as their mutation status disables men from traditional notions of familial paternalism, limiting their ability to protect children from dangers.

BRCA genetic counseling frequently pushes reproductive decisions earlier in the life cycle. As a result, research should address the critical experiences of women considering family planning and the use of repro-genetic technology before they otherwise would and, potentially, outside the context of an established partnership. Finally, this particular arm of the study interviewed only one couple. Future research should attempt prospective designs by recruiting individuals and couples actively engaged in family planning. Exploratory research should approach couples as the primary unit of study (Kayser, Watson & Andrade, 2007; Lammens, Bleiker, Aaronson, et al., 2009) to identify points of congruence and difference and how differences are actively negotiated.

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Table 1

Excerpted Interview Guide

	Interview Guide
1	Tell me about your experience of cancer in your family.
2	How do you feel about the screening and prevention options for *BRCA* mutation carriers?
Personal Plans for Childbearing	
3	Did thinking about your cancer risk affect your plans for children *before genetic testing*?
4	Did thinking about your family's history with cancer impact your thoughts or plans to have children? If so, how?
5	How, if at all, did your thoughts or plans change *after genetic testing?*
6	What challenges have you faced carrying a BRCA and (thinking about) planning a family? Have you spoken with your family/partner about these challenges? Have you spoken with your genetic counselor or physician about these challenges?
7	How do you feel about your child's risk for inheriting a *BRCA* mutation?
8	How have you managed your feelings about the possibility of your child inheriting a *BRCA* mutation? Have you discussed these feelings with your partner? With your family?
9	Have you or are you considering using PGD to prevent transmission of the *BRCA* gene mutation to your child? Tell me about any other reproductive options you considered.
Pre-implantation Genetic Diagnosis (PGD)	
As a reminder, PGD is the identification of a condition in an embryo before it is transferred to the uterus. PGD requires that couples have *in vitro* fertilization treatment with an additional genetic testing phase.	
10	Tell me about any experience you have had with Assisted Reproductive Technologies, such as IVF.
11	What are your feelings and attitudes about the possibility of using PGD to prevent transmission of a BRCA mutation?
Genetic Counseling about PGD and PND	
12	How, if at all, do you think genetic counselors should talk with patients about the option of PGD? About the option of prenatal diagnosis?