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The Search for an Explanation: Breast Cancer in the Context of Genetic Inheritance

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This case study is an in-depth examination of how Erika (a pseudonym) interpreted and understood her genetic test results for breast cancer susceptibility. Her experience is presented in the form of a biography, which was built from key passages retrieved from the semi structured interview the author conducted at Erika's home. The interview data showed that Erika's interpretation and understanding of her inconclusive test results were embedded in her own and her family's experiences with breast cancer. Her interpretation of her test results was influenced by perception of risk for future breast cancers for herself and her family, as well as from the continued etiological uncertainty of her current breast cancer. Although unfinished, Erika's experience of receiving inconclusive genetic test results for breast cancer susceptibility provides examples of possible universal themes within the experience of others who receive similar test results. *Key Words: Breast Cancer, Genetic Testing, Life Experience, Inconclusive, and Qualitative Research*

Introduction

The findings presented here are part of a doctoral dissertation that looked at how women interpreted and understood their inconclusive genetic test results for breast cancer susceptibility. Many of the participants in the study explained how they looked to genetic testing to explain their breast cancer diagnosis and their family history with the disease. Their journey of learning to live with cancer led many to seek answers from genetic testing. As the participants went through the experience of genetic testing, one of their biggest challenges came when they received what was termed by their testing agency as *inconclusive test results*. Other studies have documented that receiving an inconclusive result from testing for breast cancer susceptibility is common. In fact, the majority (75% or more) of individuals at high risk for breast cancer because of a past diagnosis and significant family history with the disease test inconclusive (Schwartz et al., 2004; Schwartz, Peshkin, Hughes, Main, Isaacs, & Lerman, 2002; van Dijk et al., 2005). Because of these risk factors, an inconclusive result means that the absence of an inherited gene mutation (which may result in cancer) remains unconfirmed (Gritz et al., 2005).

Now that genetic testing for adult-onset hereditary disease has become an important part of clinical genetics practice, there is an increased demand for these tests. It is likely to continue as a result of media coverage of genetic discoveries. To date, very few studies have addressed how inconclusive breast cancer genetic test results are

understood outside the clinic by individuals who receive them. Understanding how inconclusive results can be interpreted by laypeople was one of the aims of this study.

Background

In genetic testing, BRCA1 and BRCA2 are the two most common breast and ovarian cancer genes tested to determine inherited susceptibility to these diseases. *BR* stands for breast and *CA* for cancer, while *1* and *2* represent the order in which the genes were discovered in the mid-1990s (Gritz et al., 2005). Mutations on either the BRCA1 or BRCA2 (BRCA1/2) gene predisposes individuals to breast and ovarian cancers. In some families, there is a cluster of only breast cancers, in other families only ovarian cancers, and, in still others, both. All individuals carry these two genes, which, when not mutated, protect against the development of cancer. They suppress tumours by regulating DNA damage and maintaining genomic[1] stability.

Genetic testing of BRCA1/2 is usually reserved for individuals with a past breast cancer diagnosis who also have a family history of cancer indicative of a possible inherited mutation. A significant family history of breast and ovarian cancer represents having multiple cases of cancer on the same side of the family, with some cancer diagnoses occurring at an earlier age than expected in the general population. When an individual with a past breast cancer diagnosis undergoes genetic testing for BRCA1/2, there are three possible results. First, a mutation can be found in either gene. This is called a positive result. It means that the person's lifetime risk of breast cancer is between 56% to 87%, and their lifetime risk of ovarian cancer 16% to 40% (Di Prospero et al., 2001). Children of individuals carrying an inherited mutation have a 50% chance of inheriting the mutation. The second possible result is that the person is told that she does not carry the inherited mutation previously identified in one of her relatives. This is called a true-negative result. It means that her risk depends on her family's cancer history. The third possibility is an inconclusive result. This means that, although no mutation was found in either BRCA1 or 2, because of the person's personal and family history with breast cancer, it is impossible to confirm that she does not carry an inherited mutation or that her breast cancer may have occurred by chance; hence the term inconclusive. The risk for these people of developing breast and/or ovarian cancer depends on their personal and family cancer history.

A family history of breast cancer is recognized as one of the most important risk factors for the disease (Yang & Lippman, 1999). Although only a few studies exist on the percentage of those who are likely to receive inconclusive results from their BRCA1/2 genetic tests (Schwartz et al., 2002, Schwartz et al., 2004; van Dijk et al., 2005), Peshkin, DeMarco, Brogan, Lerman, and Isaacs (2001) estimate that 16% to 66% of all families considered at risk of breast cancer do not carry detectable mutations in these two cancer genes. Considering the growing interest in genetic testing for BRCA1/2, especially among individuals with a family history of cancer, we can expect to see a growing pool of individuals who are likely to receive unclear test results, such as inconclusive. Thus, genetic counselors and other health professionals face many challenges, such as how to properly support individuals in making health-related decisions with uncertain information, how to guide these individuals in communicating uncertain test results to

[1] Gene plus chromosome.

family members and, most important, how to live with continued uncertainty about their possible risk of carrying an inherited gene mutation. To answer these questions, there is need to document the interpretation and understanding of individuals who received inconclusive results to an inherited susceptibility of breast cancer.

In this paper I illustrate how one participant, Erika, interpreted and understood her test results for breast cancer susceptibility in the context of her everyday health and illness experiences. Before being eligible for BRCA1/2 testing, Erika had to meet specific criteria; her risk of carrying an inherited mutation had to be above that of the general population. First, Erika was diagnosed with breast cancer at the early age of 35 years old. Second, she had multiple relatives diagnosed with breast cancer. Her maternal grandmother was diagnosed with breast cancer at 50, and her maternal grandaunt was diagnosed at 70. She had a maternal aunt who was diagnosed with two primary breast cancers, one at 40 and the other at 45. All of these relatives died of the disease. Despite this significant personal and family history of breast cancer, after genetic testing Erika was told that no mutation in her BRCA1 and BRCA2 cancer genes had been found. However, because of her personal and significant family history of breast cancer, the clinic could not conclude with certainty that she did not have an inherited mutation.

Along with her inconclusive test results, Erika was given a letter describing four possible interpretations of inconclusive test results: (a) a mutation may exist in the region of the BRCA1 or BRCA2 gene that the lab looked at, but it was not detected by the current testing method; (b) a mutation may be present in the untested portion of the BRCA2 gene (only 72% of the BRCA2 gene was tested examining only areas where most mutations of clinical relevance had appeared thus far); (c) the mutation responsible for their cancer may be in another, as-yet-unidentified, hereditary cancer gene; or, (d) the woman does not have an inherited breast/ovarian cancer gene mutation, which means that her cancer may have occurred by chance. Erika was also told that the inconclusive test results did not mean that an inherited breast cancer gene mutation in their family was completely ruled out. Thus, she remained at increased risk for breast cancer.

Aim of Study

The aim of this case study was to examine in depth one woman's experience of receiving inconclusive test results for breast cancer susceptibility. Her experience is presented in the form of a biographical interpretation (Denzin, 1989). Using a graphic illustration (Figure 1), I present how Erika interpreted and understood her test results. The illustration and therefore the interpretation of Erika's experience was built using key passages retrieved from her interview.

Method

The theoretical foundation of this study was the biographical interpretive method, described by Denzin (1989) within his interpretive interactionism approach. The biographical interpretive method provides understanding of the existential, interactional, and life-history aspects of lived experiences. Analyzing interactional text highlights how the individual's world and the clinical context connect to form an existential experience (Denzin). Biographical interpretation focuses on how the individual experienced and

understood the event, and how it was filtered through the multiple spheres of her life. Thus, this method is well suited to case studies. Further, lived experiences presented in the forms of narratives and artistic displays represent a method of knowing referred as evocative experimental writing and as creative analytical processes (Richardson & St. Pierre, 2006). Richardson and St. Pierre view creative analytical processes as new forms of social representations drawing from literary, artistic, and scientific genres. In this text, Erika's narrative is presented in a creative analytical process with the purpose to evoke a relationship between the text and the case study presented.

Data collection

The key experiences presented in the biographical interpretation were gathered during a semi-structured interview. I conducted the interview in Erika's home, rather than in the genetic testing clinic. I chose the home to elicit everyday discourse and to encourage Erika to explain how she interpreted and understood her inconclusive results, rather than the medical jargon of the clinic. The interview lasted 90 minutes. After the 90 minute period, Erika felt that she had shared as much as she was willing to. She described her interview experience as the beginning of the end of her genetic testing experience. She expressed at this point that I need to move on. Reflective of Leininger's (1994) explanation of saturation, Erika felt that she had provided an exhaustive exploration of her experienced as lived. The interview was transcribed verbatim on the same day. Field notes written immediately following the interview facilitated the recognition of potential beliefs and perceptions in relation to the meanings attached to her making sense process. The interview transcript was transferred into QSR N5™ software for data management and to facilitate the inductive analytic process. Clearance to conduct the study was obtained from the Behavioural Research Ethics Boards of both the hosting institution and of the recruiting agency.

Data analysis

The interpretive interactionism approach rests on the analysis of stories about turning points in people's lives. Depending on the focus of the interaction, the teller talks about events that are significant to both him/her and his/her audience. The role of the researcher is to locate the teller's self in the story and to write a biography of the individual that incorporates the teller's experience and the context in which the experience takes place. In doing so, the researcher identifies important parts of the story that speaks to the phenomenon studied and interprets them as an informed reader. Throughout this work, the researcher attempts to contrast emerging interpretations with evolving hypotheses from parts of the text already interpreted. When the researcher has finished the analysis, she presents it in the form of a unified narrative.

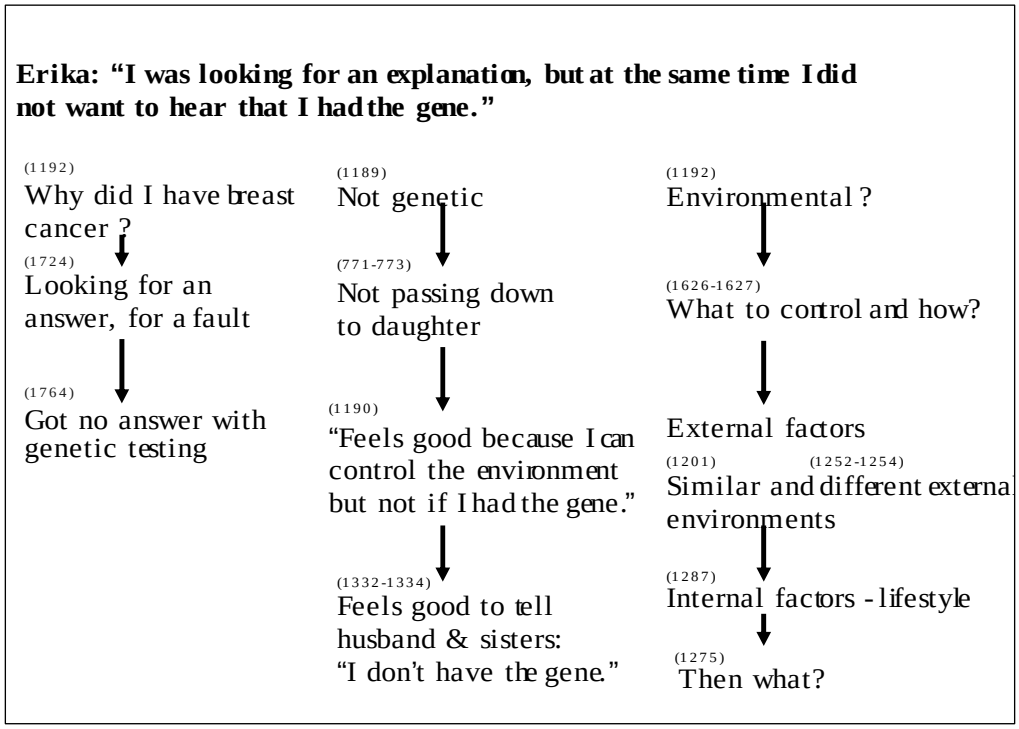
Validity of findings in interpretive studies is defined in their potential to create mental heuristics that confirm hunches of expert clinicians from the field studied where they would see new understandings of their reflective practice observations (Thorne, Reimer Kirkham, & O'Flynn-Magee, 2004; Thorne, Reimer Kirkham, & MacDonald-Emes, 1997). Hence, I sought feedback from expert clinicians within genetics throughout my data analysis in peer-reviewed scientific presentations and nursing rounds at two

different universities. The feedback I received encouraged me to refine my data analysis for clarity and depth of analysis. Field notes and journaling also facilitated the evolution of my reflection during data analysis and led me to question my early assumptions about participants' experiences. One such assumption was presuming that individuals who received a genetic test would automatically want to tell family members. In the course of the interview, it became apparent that such an assumption did not hold true for the Erika. Hence, I shared this assumption with her. She explained that in light of her genetic results, there was no need to worry others at this time. This dialectical approach created space to clarify the meanings Erika brought to her results and allowed in-depth understanding of her experience of receiving inconclusive test results for breast cancer susceptibility. One such understanding was that genetic testing came to play a very small part in her everyday life compared to more stressful events such as her breast cancer experience. Another component critical to interpretive studies is explicit accounting of researcher's biases that may influence his/her study. One such bias is a belief that we, as health professionals, often interpret clinical tests and results differently than our patients do. Consequently, although I interpret the genetic test results that Erika received as inconclusive (meaning that no conclusion can be drawn from her results), in the interviews I referred to her results just as "your genetic test results." I tried not to influence her interpretations of her results by not showing approval or disapproval of her interpretation.

Results

Figure 1 presents the basic units of Erika's story about how she interpreted and understood her genetic test results. As Denzin (1989) instructs, the life of the storyteller must always be in the forefront of the interpretation. The research process and structure must blend with the storyteller's experiences in order to not lose sight of the individual studied.

Figure 1. *Erika's interpretive framework of her experience with receiving inconclusive genetic results for breast cancer susceptibility.*



The title for Figure 1 was taken from a passage in Erika's interview: "I was looking for an explanation for my breast cancer, but at the same time I didn't want to hear that I had the gene." This statement reflected Erika's need to find the etiology of her breast cancer diagnosis. In her interview, she referred to having a mutation as "having the gene." Next are interview excerpts that expand on key passages presented in Erika's interpretive framework found in Figure 1. The numbers in brackets represent positions in the interview where the key passages were retrieved. The interview excerpts are rewritten statements of Erika's experience. They represent a thick description and interpretation of her lived experience. Thick description, as opposed to thin description that simply states facts, provides the context of the phenomenon explored, uncovers meanings that organise experiences, and traces the phenomenon's evolution. Thick description presents meanings and feelings as a text that can be interpreted (Denzin, 1989).

"Why did I have breast cancer?" (1192)

> You know, that is the big question. Why did I get it? Why did I get breast cancer in the first place? Was it environmental or diet? And if there is a family history and I do not have the gene, then how is it passed on? So at the time I thought, Okay, did I do something, like my karma, you know? You are reaching for anything, anything that will give you an answer. So, in that respect, a positive genetic-test result would have been like, Okay, no, it was not my fault (1724). It was just there, and it just happened. But no, my genetic testing did not give me that answer, or no answer (1764).

"I am not passing the gene to my daughter." (1189)

> But now I am glad that my breast cancer is not genetic or inherited (1189). I wanted ways to sort of, hopefully, do the best I could possibly to help prevent breast cancer from happening to my daughter (1190). At least by not having the gene, there is a possibility that I might have some control over breast cancer from happening to me again, or to my family. But if you have the gene, it is like you lose all preventive control (771-773). But now, with my inconclusive results, it feels there are no answers yet if it is completely environmental or genetic. But then, if I do not have those genes, why did I get breast cancer? In some ways, it would have almost have been better to say, Okay, you have got the gene, that is why you got breast cancer. But, at the same time, it feels good to be able to say, Oh, I do not have that gene. It feels good to be able to tell my husband, Oh, you know, I got the results, and I do not have the gene. And it feels great to be able to tell my sisters that, too (1332-1334). You know, I can't control whether I have this gene or not, but perhaps, through diet and exercise, I can better control my environment. And that maybe my daughter can, you know, perhaps control how the environment can affect her risk of breast cancer and, or maybe, maybe, how the gene might mutate or not with the environment. So I was just trying to find out. So it is mostly for my daughter. And I also wanted the information in terms of my sisters.

"If not genetic, then why did I get breast cancer?" (1192)

> Then why did I get it? Why did I get cancer in the first place? Was it environmental? Sometimes, is it environmental? If I cannot figure out if it is environmental or not, then how am I suppose to know what to control (1626-1627)? Because from where I grew up, there was this huge pulp mill, and they were producing this chemical and blowing out these fumes. And, an interesting thing happened when I was receiving my treatment at the clinic. I was there one day, and my sister was with me, and this woman came out of the washroom as I was about to go in. And I looked at her, and I thought I recognized her. And I said, 'Vivian!' And it was a girl that I was really good friends with in high school. And we had sort of lost touch over the years as we went on to university and what not. And now, she had breast cancer in the same breast, in almost the same location and the same size of tumour as me. She was just about 3 months behind me in terms of her treatments. I think she was just starting her treatments. And I was actually doing my radiation, and she was just starting her chemo. You know, we both grew up in the same city. And I just thought, I do not know, am I reaching for straws or something? But it is just a thought. Is there some sort of connection there that we both happened to get it at the same time, same age? You know, it is the same kind of circumstances.

External factors (1201, 1252-1254)

> I do not know if there is an explanation there, because my sisters, they are both past 35. And they have not, to their knowledge, developed anything, and they grew up in the same environment as me. Ya, 35 years old was sort of the number, you know, that is when I was diagnosed with my breast cancer.

Lifestyle (1287)

> It is just that you want to be able to feel like you can do something. I do not know what I can do. Maybe it is as simple as lifestyle. I am always thinking that maybe I should not be eating that. Can I do this? Am I being diligent enough? Am I just inviting this cancer back by not doing this or that? And there are so many conflicting reports. I mean, I want the information, I want to know. But, at the same time, I went through a whole period there where I did not want to eat anything. And I went through a phase where it was, like, click, I turned off. I did not want to read or hear of anything anymore of breast cancer. I had had enough. And, besides, I could not even process the information anymore. It was almost as if it was too much. I do not know what to do with the information, because there are so many studies being done. And one study says, uh, oh caffeine is bad for you if you have cysts and breast cancer. And it was even in Susan Love's book on breast cancer that she said you can have that extra cup of

> coffee and the link to that, between caffeine and fibrocystic breast disease, is nonexistent. And then 2 years ago, I was going to my family practitioner, and she felt some lumps. She said, 'I really do not think you should have caffeine anymore.' So I gave up caffeine. But you know what I mean, it is like, Okay, what did I do? And I think about the lifestyle, too, and the quality of life, too. I cannot cut off everything. So then, if I do not know in the first place what caused my breast cancer, how can I know that I am not continuously exposing myself to risk factors that may yet produce another cancer?

Then What? (1275)

> Researcher (R) speaking to Erika (E):
> R: So, although you have had these results, do you still feel that maybe there is a mutation in your family?
> E: Well, I wonder. I mean, there is breast cancer in the last three family generations.
> R: So, then, do you make any more sense of your results other than you do not have the gene, and therefore you are not passing down the mutation to your daughter?
> E: No, Not really, I guess I am still waiting to see, to see what the next set of tests will bring. I am waiting to see. For now, it is somewhat of a relief to know that no gene for my breast cancer was found.

Discussion

Erika shared that she did feel relief after receiving her genetic test results: she perceived that her breast cancer did not result from an inherited genetic mutation and that, therefore, her daughter is probably not at risk of such a mutation. But Erika did not, however, get relief from her worry about her breast cancer's etiology. She still wondered whether her cancer came from her family history with the disease or was caused by exposure to an environmental toxin. She decided that, until further gene discoveries are available, she would not interpret her results beyond concluding that she was not found to carry the "gene" (in her words).

Erika stated twice that she was looking for an explanation to her breast cancer diagnosis but was hoping not to hear that it was the result of a genetic mutation. In this statement, there is a notion of continuous uncertainty that individuals must learn to live with when they receive inconclusive results of breast cancer susceptibility testing. According to a theory of uncertainty by Mishel (1988, 1990, 1997), living with uncertainty can lead to distress. For this reason, educational materials and clinical support would be helpful to individuals who receive inconclusive test results. Psycho-social support in the form of written material and in providing open communication with a health professional helps in reducing uncertainty (Mishel, 1988; Stiegelis et al., 2004). It does so by providing assurance of the stability of the environment that individuals participated in, in this case having preceded to genetic testing services. An example in providing an open communication could be a onetime follow-up telephone call.

This case study highlights the conflictual, contradictory nature of lived experiences and how they can influence individuals' understanding of medical events. The case study also shows that no single interpretation can ever fully capture a problematic event and that the interpretation of problematic events is never complete. Just as Denzin (1989) explains, interpretations from biographical analysis, although unfinished, provide examples of universal themes that can structure the moment in history being studied. This means that health professionals and genetic counselors need to be aware that multiple interpretations may exist of the experience of receiving inconclusive genetic test results for breast cancer susceptibility. They must also remember that these interpretations evolve as recipients' lives do.

From this perspective, recommendation for clinical practice would be to continually assess individuals' experience of genetic testing. The evolving context and possibilities of genetics is likely to prompt change in how individuals will make sense of their inconclusive results. Further recommendation is for the use of biographical interpretation to capture individual and aggregate experiences of genetic testing. It is my belief that, by studying and interpreting people's experiences with genetic test results, better understanding of their personal struggles will be possible. Ongoing study of many individuals' experiences will reveal commonalities and differences. The resulting aggregate knowledge will illuminate variations within the process of making sense of inconclusive results. Knowledge of the aggregate experience and its variations will then help us to better counsel each individual and family we meet. By comparing and contrasting individuals' specific experience to aggregate experience provides opportunity to normalize the experience. This approach of providing social comparison information has been successful in past studies in reducing uncertainty (Stiegelis et al., 2004).

In conclusion, this case study highlights the inner struggles individuals with personal and family histories of breast cancer must face after they receive inconclusive genetic test results. The study points to a need: to evaluate, with our clients, their lived experience of having personal and family cancer histories and its impact on the understanding of genetics and genetic inheritance.

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