# Variants of Significance? The Production and Management of Genetic Risk for Breast and Ovarian Cancer in the Era of Multi-Gene Panel Testing

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ABSTRACT

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This dissertation examines the production and management of genetic risk for breast and ovarian cancer in the United States in the new era of multi-gene panel testing. Drawing on three years of ethnographic fieldwork and in-depth interviews with genetics health professionals and women with mutations, this project is the first social science study to examine how breast and ovarian cancer genetic risk is constructed and managed among women with variants of uncertain significance or moderate-risk mutations. Moving beyond an individual-level focus on women's risk management decisions, this project instead explores how the structures, practices, and organization of genetic medicine constrain and enable those decisions.

There are four key findings from this study. First, the adoption of panel testing has shifted the boundaries of risk, disease, and patienthood and contributed to a spectrum of medicalization of breast and ovarian cancer risk. Women with high-risk breast and ovarian cancer mutations are now typically viewed and treated like full patients with a "disease," while women with moderate-risk mutations occupy a liminal space of qualified patienthood. Second, the structures and organization of genetic medicine in the United States point women with breast and ovarian cancer mutations toward risk-reducing mastectomy and breast reconstruction and encourage choosing those surgical responses over breast surveillance or staying flat. Mastectomy has become the standard "treatment" for the "disease" of genetic risk for breast cancer, regardless of whether women have high- or moderate-risk mutations and despite more conservative recommendations in clinical guidelines.

Third, the structures of genetic medicine and the contemporary gender order in the United States are mutually constituted and co-produced. Breast reconstruction and gynecologic surgery practices both emerge from and reinforce gendered social and cultural norms that prioritize women's appearance and their reproductive capacity over their embodied experiences and daily quality of life. Finally, the discourses and practices of genetic medicine leave many women un- or under-prepared for the duration and severity of the side effects and consequences associated with breast reconstruction and risk-reducing salpingo-oophorectomy. By closely examining the social and structural dimensions of how cancer genetic risk is produced and managed in the United States, this project illuminates how clinical practices that magnify and focus on reducing certain risks simultaneously obscure and generate exposure to others.

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## Dedication

For Renee/Mom/Bubbe
who really took one for the team

## Introduction: "The Wild, Wild West:" The New Era of Multi-Gene Panel Testing

> "So here it is. It's the Wild, Wild West, right?… Many of the panels include genes where if we found a true mutation in one of those genes it would be fair to ask, 'Well, what does that mean for my cancer risk?' And there are genes that we could find mutations in where all I would do is wiggle around uncomfortably in my chair and shrug and go, 'I don't know. Higher than other people?' You know? That's how much we know about some of the genes that are being tested." *(Linda, Genetic Counselor)*

In May 2013, the *New York Times* published "My Medical Choice," an Op-Ed by the famous actress Angelina Jolie about her decision to have risk-reducing mastectomy (RRM)[1] and implant reconstruction after learning she had a mutation on the BRCA1 gene (Jolie, 2013). While there had been coverage of genetic risk for cancer in the media prior to Jolie's Op-Ed, her story launched hereditary risk for breast and ovarian cancer (BOC) into the spotlight and made "BRCA" a household term. Jolie's Op-Ed had such a broad impact that following its publication there were significant increases in internet searches about BRCA mutations and requests for genetic testing and RRM (Bhatti & Redelmeier, 2015; Borzekowski, Guan, Smith, Erby, & Roter, 2014; Desai & Jena, 2016; D. G. Evans et al., 2015; Noar, Althouse, Ayers, Francis, & Ribisl, 2014).

One month after Jolie's Op-Ed made waves through the media, the Supreme Court of the United States issued a unanimous ruling that revoked the patents on the BRCA genes that the laboratory Myriad Genetics had held since their discovery nearly two decades earlier ("Association for Molecular Pathology v. Myriad Genetics," 2013; Azvolinsky, 2013; E. Marshall, 2013).[2] In combination with concurrent increases in the speed and power of genetic

[1] Appendix A provides an alphabetized reference of acronyms used in this study.

[2] Prior to the ruling, other genetics laboratories had been limited to researching and providing tests for mutations on genes besides BRCA1 and BRCA2 that were linked to breast and ovarian cancer.

sequencing methods, that Supreme Court decision transformed the landscape of genetic testing in the United States. Other laboratories quickly entered the BRCA testing market and competed by bundling tests for BRCA mutations with tests for mutations on 20 - 30 other genes associated with low to moderate BOC risk. Compared to the earlier targeted tests of the well-known, high-risk BRCA1/2 genes, these multi-gene panels generated considerably more genetic information for experts to interpret and explain, much of which was not medically actionable. Hence, the rapid shift to panel testing for genetic risk ushered in a new era in genetic medicine rife with scientific and clinical uncertainties just at the moment that public concern about genetic risk rapidly escalated.

As science and technology studies (STS) scholars have argued, processes of scientific classification and medical technologies like panel testing are neither objective nor value neutral. Rather, they take shape in particular social and cultural locations, are influenced by a range of actors, and can be enlisted in achieving particular agendas (Hess, 1997; Latour, 1987, 2005; Montoya, 2011; Rapp, 2000). Now that multi-gene panel tests have become the standard of care, this study explores how certain ideas about BOC genetic risk and approaches to risk management have gained credibility over others and how the discourses and practices of US genetic medicine have shifted in the era of panel testing. Drawing on data collected during three years of ethnographic fieldwork and through in-depth interviews with women with mutations and genetics health professionals, the project moves beyond an individual-level focus on women's psychological and behavioral responses to learning they have cancer genetic mutations. Instead, this study examines how social structures and the organization and practices of BOC genetic medicine in the United States both constrain and enable women's medical decisions.

The central research question of this study is: How is BOC genetic risk produced and

managed in the United States in the era of multi-gene testing? Throughout the analysis, I explore similarities and differences between the experiences of women with high-risk BRCA mutations, moderate-risk mutations (MRMs), and variants of uncertain significance (VUSs), which are genetic variants that scientists have not yet classified as harmful or benign (S. Domchek & Weber, 2008). I also pay specific attention to how structures of gender and genetic medicine intersect and to how the practices of BOC genetic medicine and broader social and cultural contexts in the United States magnify certain risks while obscuring others. By closely examining the social and structural dimensions of the production and management of cancer genetic risk, this project illuminates how the dominant practices of BOC genetic medicine and the contemporary gender order in the United States work to mutually sustain and justify each other.

## Research Context

### *Discovering the BOC Genes*

BRCA1 and BRCA2 (BRCA1/2) are tumor suppressor genes that were discovered in the mid 1990s (Miki et al., 1994; Wooster et al., 1995), and individuals who inherit a mutation[3] on these genes face significantly elevated risks of developing breast and ovarian cancer in their lifetimes. The risk of female breast cancer among women with BRCA mutations is between 3-6 times the normal lifetime risk of 12%, and their risk of ovarian cancer is 5-35 times the normal lifetime risk of 1.5% (Antoniou et al., 2003; Begg et al., 2008; Ford et al., 1998; M. C. King, Marks, & Mandell, 2003; Kuchenbaecker et al., 2017; A. W. Kurian, Sigal, & Plevritis, 2010; National Cancer Institute, 2018d, 2018e; Thorlacius et al., 1997). Mutations on the BRCA genes

[3] The term "variant" refers to a change in the typical code of a gene, but it does not signal the effect of the change on gene function, which may be benign, pathogenic, or uncertain. The term "mutation" refers to a genetic variant that has been interpreted as pathogenic and affects typical gene function.

are also associated with elevated risks of developing melanoma, pancreatic, testicular, male breast, and early-onset prostate cancers, but the cancers they are most commonly associated with are breast and ovarian (PDQ® Cancer Genetics Editorial Board, 2019). Importantly, neither BRCA1 nor BRCA2 has 100% penetrance;[4] not everyone who carries a BRCA mutation will develop cancer. Moreover, while BRCA mutations are considered "high-risk" mutations and have a higher population prevalence than most other cancer-associated mutations (Couch et al., 2017; Kuchenbaecker et al., 2017; PDQ® Cancer Genetics Editorial Board, 2019), genetic mutations, overall, seem to account for only 5% - 15% of all female breast cancers (PDQ® Cancer Genetics Editorial Board, 2019) and approximately 20% of ovarian cancers (National Library of Medicine, 2019; Toss et al., 2015). Hence, while extensive media attention and scientific resources have been devoted to the BRCA genes, they account for a relatively small proportion of all breast and ovarian cancers.[5]

The discovery of the BRCA genes were major breakthroughs in hereditary cancer research. Yet because mutations on BRCA1 and BRCA2 do not account for all of the concentrated familial patterns of breast and ovarian cancers that suggest a hereditary component, scientists have continued searching for and found other genes involved in tumor suppression pathways that also increase BOC risk. Mutations on other genes that have been discovered mostly pose a moderate-risk for breast or ovarian cancer that is higher than the risk among

[4] Penetrance refers to the proportion of individuals carrying a mutation who will manifest the disease.

[5] Most breast and ovarian cancers are a result of environmental exposures, and even genetically-linked cancers have environmental components. Individuals with BRCA mutations typically have one damaged copy of either the BRCA1 or BRCA2 gene. However, people contain two copies of every gene in their bodies—one inherited from their mother and the other from their father. For the tumor suppression function of the BRCA1 or BRCA2 genes to be disrupted, *both* copies of one of the genes must become damaged (Begg et al., 2008; Ford et al., 1998; PDQ® Cancer Genetics Editorial Board, 2019; Thorlacius et al., 1997).

women in the general population but lower than the risk of BRCA mutation carriers (Couch et al., 2017; PDQ® Cancer Genetics Editorial Board, 2019). The most prevalent of these MRMs are on the ATM, CHEK2, and PALB2 genes, which were discovered in 1995, 1998, and 2006, respectively. ATM, CHEK2, and PALB2 mutations are associated with a higher-than-average risk of developing breast cancer (Couch et al., 2017; Matsuoka, Huang, & Elledge, 1998; N. Rahman et al., 2007; Savitsky et al., 1995; Uziel et al., 1996; Xia et al., 2006), and some studies suggest they are also associated with a higher risk of developing ovarian cancer (Minion et al., 2015; Toss et al., 2015). Even though some of the moderate-risk genes were discovered in the 1990s, very few women were tested for MRMs prior to the early 2010s because of legal and regulatory restrictions on testing and limitations in genetic sequencing technologies.

### *The Birth of Panel Testing*

The lawsuit against Myriad, *Association for Molecular Pathology v. Myriad Genetics, Inc.* (*AMP v. Myriad*), had been making its way through the US federal court system since 2009, when lawyers from the American Civil Liberties Union filed a suit on behalf of a group of scientists, genetic counselors, clinicians, and patients. The plaintiffs argued that the patents held on the BRCA1/2 genes by Myriad Genetics since their discovery were hampering scientific and medical research. Previously, Myriad had successfully persuaded the US Patent and Trade Office that the forms of the BRCA1 and BRCA2 genes that they worked with in their labs, which were isolated from their respective locations on chromosomes 17 and 13, did not exist "in nature" and therefore could be patented. But Myriad's interpretations, which had long been challenged by other scientists, were upended in the late 2000s by the discovery that the genomes of fetuses could be recreated from fragments of fetal deoxyribonucleic acid (DNA) found in the blood of pregnant women. Those naturally existing fetal DNA fragments included the BRCA1 and

BRCA2 genes that Myriad had theretofore claimed were “produced” in their labs ("Association for Molecular Pathology v. Myriad Genetics," 2013; Azvolinsky, 2013; E. Marshall, 2013). In *AMP v. Myriad*, the Supreme Court ruled against Myriad, which invalidated their patents and enabled other genetics laboratories to begin testing for BRCA mutations ("Association for Molecular Pathology v. Myriad Genetics," 2013).

The *AMP v. Myriad* decision coincided with technological transformations in the tools and methods used to perform DNA sequencing. Since the 1970s, genetic testing laboratories had used a slow and costly sequencing method (i.e., capillary or Sanger sequencing) that could only sequence one DNA fragment at a time (Shendure & Ji, 2008; van Dijk, Auger, Jaszczyszyn, & Thermes, 2014). As a result, most genetic tests searched for specific, known mutations on one or two genes. In the early 2010s, however, genetic testing laboratories adopted new sequencing technologies developed a few years earlier that could simultaneously sequence millions of DNA fragments (Pareek, Smoczynski, & Tretyn, 2011; Shendure & Ji, 2008; van Dijk et al., 2014). The dramatic increase in sequencing speed and volume made possible by these “next generation sequencing” (NGS) technologies allowed laboratories to shift from conducting targeted gene tests to offering panel tests that could examine dozens of genes for both known and unknown variants at little to no additional cost.

While NGS technologies existed before 2013, until the *AMP v. Myriad* ruling, multi-gene panels were not commonly utilized in BOC genetic testing. Because BRCA mutations are the most prevalent and highest risk BOC mutations, BRCA testing is always recommended among individuals without known mutations in their families. However, since only Myriad could legally test for and conduct research on the BRCA genes prior to the *AMP v. Myriad* decision, other laboratories lacked sizable markets for their panels that only tested for MRMs or low-risk

mutations. Immediately after the *AMP v. Myriad* ruling, however, laboratories and clinics began offering and advertising hereditary cancer panel tests that screened for BRCA1/2 mutations and for variants on moderate- and low-risk genes that had known or possible associations with cancer risk (Figure 1). As Laura, a medical geneticist, explained:

> The impact on the field was almost instantaneous… laboratories were watching this very carefully. And many of them knew that the opportunity was that if the patents got taken down that they would have the opportunity to now start bundling together—number one, be able to offer BRCA1 and 2. But more importantly than that, start bundling together additional genes beyond just BRCA1 and 2. And I think that was for us in hereditary cancer a 90-degree pivot in terms of being able to make a change in direction. *(Laura, Medical Geneticist)*


**Figure 1: Flyer from Ambry Genetics Distributed in the Fall of 2013 (Front Image)[6]**

[6] I obtained this flyer from Ambry's exhibit booth at a national scientific meeting on genetics.

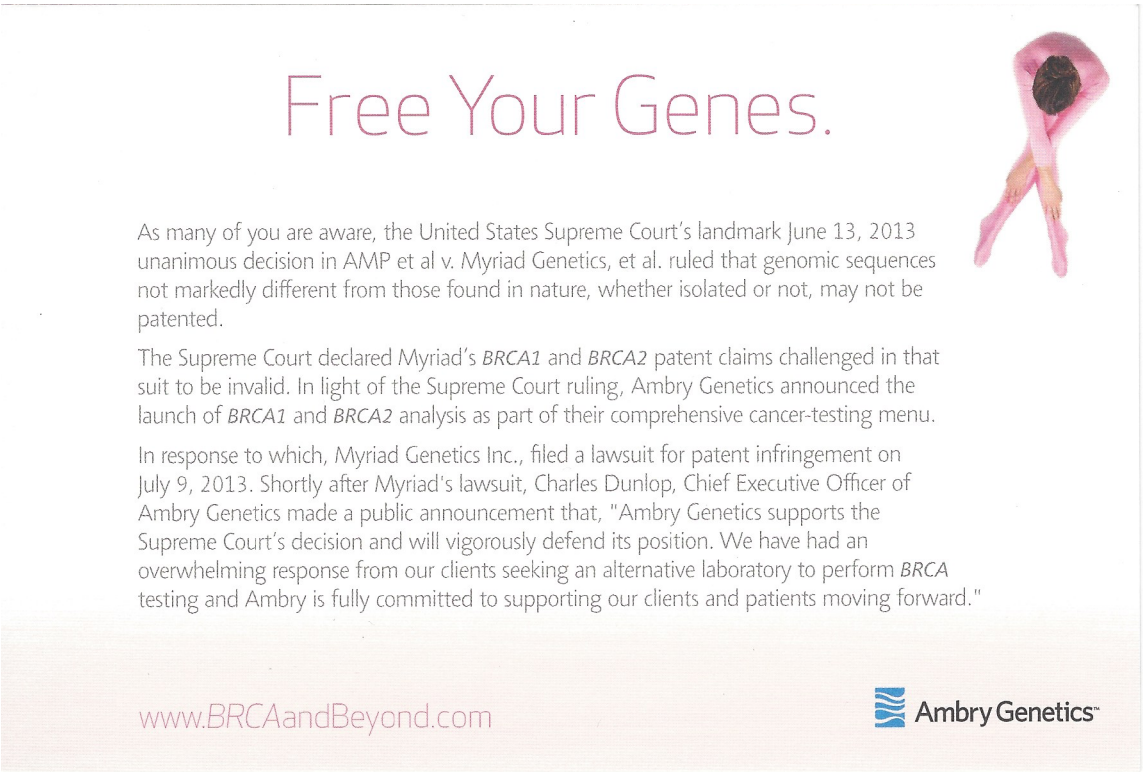


**Figure 2: Flyer from Ambry Genetics Distributed in the Fall of 2013 (Back Image)**

This study examines the consequences of this pivot to panel testing that occurred in the wake of the *AMP v. Myriad* decision and the adoption of NGS technologies. One of the immediate effects of the shift was to increase the accessibility and affordability of cancer genetic testing. When Myriad had a monopoly on the market, it charged approximately $3,000 for a BRCA1/2 test, which made testing inaccessible to most people when it was not covered by insurance. But after the *AMP v. Myriad* decision, market competition between labs, coupled with the ability to bundle services in panel tests, brought prices down dramatically. For example, Color Genomics, a consumer-oriented laboratory that began operating in 2014, offered their hereditary cancer panel for $249. While that price point was still prohibitive for some individuals, at less than 10% of the price Myriad had been charging, testing became more accessible to people forced to pay out of pocket because they lacked or were denied insurance

coverage. Over time, the consumer price for testing has come down even further. Color now charges $199 for their hereditary cancer panel, and another major US laboratory, Invitae, offers a "patient pay" price of $250 (Color Genomics, 2019; Invitae, 2019).

While the *AMP v. Myriad* ruling and adoption of panel testing helped to reduce prices, a provision of the Affordable Care Act (ACA) that went into effect in 2013 expanded insurance-covered access to BOC genetic testing. The ACA requires that all preventative services graded A or B by the U.S. Preventative Services Task Force (USPSTF) be covered without patient cost-sharing (111th Congress, 2010; Johns & Bayer, 2016). BRCA testing has a B grade for women whose personal or familial cancer history suggests the cancers might be hereditary. Therefore, women who meet specific high-risk criteria[7] are entitled to BRCA testing without copays or coinsurance and regardless of any unmet deductibles (US Preventative Services Task Force, 2018). Insurers are not required to cover panel tests and could demand targeted-gene testing for BRCA mutations; however, in practice they rarely do. Hence, by bundling BRCA tests in panels that screen for mutations on other genes linked to hereditary cancer, women considered high-risk gained insurance-covered access to the new panel tests without out-of-pocket costs.

Most cancer panel tests examine 25 - 35 genes for variants, but some screen over 80 genes. However, more information is not necessarily better. Rather, it is an empirical question whether and how the genetic information panels provide is having a positive impact on people's lives and health. With 30 or more genes included in panel tests rather than one or two, panels generate considerably more genetic information for experts to interpret, classify, and explain and for

[7] According to the National Cancer Institute, factors that would suggest a hereditary pattern and indicate BRCA testing include being diagnosed with breast cancer prior to age 50, cancer in both breasts in the same woman, both breast and ovarian cancers in either the same woman or in the same family, multiple breast cancers in the family, cases of male breast cancer in the family, and Ashkenazi Jewish ethnicity (National Cancer Institute, 2018a).

patients to understand and manage. Moreover, since many of the genes included in panel tests are associated with only low or moderate cancer risk, much of the genetic information panels provide is not medically actionable. As women's stories in the following chapters reveal, it can be frustrating and anxiety producing, not empowering, to learn one has an MRM that is associated with an increased risk of breast and other cancers but lacks clear recommendations for additional screenings or services. In addition, the widespread adoption of panel tests has led to an increase in the number of people learning they have VUSs. Scientists classify variants as VUSs when there is not enough data to determine whether they pose any risk. Most VUSs are likely to be harmless; over 90% of VUSs that get reclassified are downgraded to benign (Lincoln et al., 2017; Mersch et al., 2018). Genetics experts agree that until VUSs are reclassified, they should be treated like "negative" findings and should not affect medical management. Yet clinical studies indicate that some women with VUSs are having prophylactic mastectomies (Culver et al., 2013; M. L. Murray, Cerrato, Bennett, & Jarvik, 2011; Ready et al., 2011). Thus, panel tests may be contributing to the mismanagement or overtreatment of mutations or variants with risk-reducing surgical procedures that have their own risks and potential harms.

The adoption of panel testing spawned a new era in genetic medicine. Linda, a cancer genetic counselor who has been practicing since the 1990s, referred to panel testing as the "wild, wild west" because in this era scientific knowledge and best clinical practices are unclear and constantly evolving. This study, which began as the pivot to panel testing occurred and spanned the initial years of clinical adoption of the technology, sheds light on the landscape and consequences of this new frontier in genetic medicine.

## Research Methods

This project involved over three years of qualitative research that included participant observation, in-depth interviews, and document analysis. As is common in qualitative research, I conducted data collection and analysis concurrently, transcribing and coding interviews and field notes soon after they were completed. Preliminary findings from the earlier years of the study informed subsequent data collection, and triangulating data through these three methods enabled me to iteratively test and refine my working hypotheses on how BOC genetic risk is produced and managed in the United States in the era of panel testing. Below is a brief overview of the research methods used in this study. A detailed description of the research methods and approach, including tables of summary characteristics for the 75 women who participated in the study and an account of the challenges I encountered during the research process, are included in Appendix B.

### *Participant Observation and Document Analysis*

Between the fall of 2013 and spring of 2017, I engaged in participant observation at more than 40 professional and patient-centered events. These included national scientific conferences, webinars, and research seminars for genetic scientists, clinicians, and counselors and advocacy conferences, symposia, and webinars on cancer genetic risk for people with BOC mutations and the broader public. The events for scientists and health professionals illuminated how experts communicated with one another about genetic risk, clinical and scientific developments in cancer genetics, and the topics and issues of importance to genetics professionals. The patient-centered and public events were sources of data on the issues of importance to women with mutations, whether and how mutation carriers were forming biosocial identities and communities, and the ways in which experts communicate and translate complex genetic risk information to people

with mutations and lay audiences. During fieldwork, I gathered and systematically analyzed publications, brochures, webpages, and reports produced by the five major US laboratories that perform most BOC genetic testing in the United States: Ambry Genetics, Color Genomics, GeneDx, Invitae, and Myriad Genetics. I also examined materials published by key advocacy groups for BOC mutation carriers, professional societies involved in genetic medicine, and federal institutes or agencies that provide information and data on cancer and genetics.

***Interviews and Recruitment***

Concurrent with fieldwork and document analysis, I conducted a total of 85 in-depth, semi-structured interviews: 75 with women with BOC mutations or variants and 10 with health professionals working in cancer genetics. The conversations with women with mutations and/or variants provided opportunities to elicit detailed narratives about their experiences navigating genetic medicine, their knowledge and beliefs about BOC genetic risk, and their risk management decisions. The interviews with genetic counselors and clinicians provided insights into the processes involved in producing genetic risk and facilitated an analysis of agreements and disjunctures between professionals' and patients' descriptions of the practices of BOC genetic medicine. Interviews lasted, on average, one hour and 15 minutes, and all interviews were conducted via telephone or video-chat and were digitally audio-recorded in order to capture participants' exact responses. I developed semi-structured guides for the interviews that drew on topics and themes I had identified through preliminary fieldwork and existing literature on BOC genetic medicine.

The health professionals were recruited during fieldwork at scientific and professional meetings and through relationships I built at those meetings with key informants. Women with mutations or VUSs were primarily recruited through cancer genetic counselors located

throughout the United States whom I met at national conferences and through the cancer special interest group (SIG) of a professional association for genetic counselors.[8] Genetic counselors shared the study's IRB-approved recruitment flyers with their clients, and then women who were interested in participating contacted me directly. I also recruited women through a modified snowball approach to sampling. At the end of each interview, I asked participants if they would be willing to share information about the study with other women they knew with BOC mutations or VUSs, and if they agreed, I provided them with the same IRB-approved flyers. Finally, I recruited patient participants through national education and advocacy groups that serve people with BOC mutations. All names used in the following chapters are pseudonyms, and quotations or descriptions that contained potential identifying information, such as unique elements of their life stories, have been altered to protect the confidentiality and privacy of participants.

**Theoretical Foundations and Contributions**

One of the major contributions of this study is that it sheds light on the experiences of an emerging and rapidly growing population in BOC genetic medicine that has barely been studied in either the medical or social sciences literatures: women with genetic variants that pose moderate, low, or unknown risk for breast or ovarian cancer. Research on the patienthood experiences of women with MRMs and VUSs has been limited, in part because prior to the shift to panel testing, few women were tested for MRMs and only 5% - 15% of BRCA analyses

[8] This organization has a membership category for professionals who are not genetic counselors but do work related to genetic counseling. In all communications in this group, I was transparent about being a researcher studying the consequences of panel testing and the production and management of BOC genetic risk.

uncover a VUS (Dagan & Goldblatt, 2009; Gibbon, 2007; Hesse-Biber, 2014). In fact, to date, all of the major sociological and anthropological studies conducted on the experiences of women with BOC mutations have included only women with BRCA mutations; there are currently no published social science analyses that focus on women with MRMs or VUSs. Yet, as multi-gene panels have become the standard of care, the proportion of women with BOC variants who have MRMs and VUSs is rapidly increasing, and these women encounter unique issues as they navigate the terrain of genetic medicine.

Another contribution of this project is that it brings sociological, science and technology studies (STS), and gender studies frameworks to the study of BOC genetic risk. Medical researchers have conducted a majority of the studies on BRCA medicine. These analyses tend to assume the objectivity and neutrality of genetic tests and focus on assessing barriers to genetic testing, patients' comprehension of genetic information, and the individual and familial factors that are associated with women's testing and risk management decisions. Instead, this study examines how genetic risk is constructed and made visible and how certain ideas about and responses to genetic risk gain credibility over others. The project also explores how gendered social and cultural norms are both embedded in and reproduced by genetic risk technologies, risk management guidelines, and surgical practices. The study engages with and makes contributions to scholarship on genetic medicine in four overlapping bodies of literature in medical sociology and STS: risk, (bio)medicalization, (pre)patienthood, and gender and embodiment. In the following sections, I broadly describe these literatures and situate this analysis in their respective scholarly conversations.

***Risk***

In contrast to medical studies that present health risks and numeric risk estimates as preexisting "facts" that are uncovered through scientific inquiry, this study explores how risk is actively produced, not discovered. It builds on sociological, anthropological, and STS scholarship that views risk as always constructed because it is an estimated measurement generated by experts who draw on social and cultural assumptions, discourses, and knowledges (d'Agincourt-Canning, 2001; Nina Hallowell, 1999; Klawiter, 2002; Lupton, 1993, 1999; Mozersky & Joseph, 2010; Rapp, 2000; Scott, Prior, Wood, & Gray, 2005; Simpson, 2000). Specifically, this project is in conversation with two broad domains of social sciences scholarship on risk: literature on genetic risk and on breast cancer risk.

Several social scientists have explored the social implications of using genetic technologies in medicine. Early scholars of genetic diagnostic technologies examined how they could be used to define norms, create social categories, and exert social control (Lippman, 1992; Nelkin, 1992; Nelkin & Tancredi, 1994). Other researchers have focused on the social and political effects of the rapid integration of genetic technologies into standard medical care and reproductive health care (Ettorre, 2002; Rapp, 2000; Rothman, 1986). More recently, scholars have examined the ways in which the social constructs of race, ethnicity, and populations have become entangled with research and practices in the field of genetic medicine (Bridges, 2011; Montoya, 2011; Mozersky & Joseph, 2010; Wailoo & Pemberton, 2006).

Other scholars have examined the constructed nature of the risk estimates and classifications generated by computerized tools used in medicine to assess women's current and lifetime risks for breast cancer. Anthropologist Margaret Lock highlights how the risk estimates for breast cancer produced by these tools are not "facts," but rather are statistical abstractions

from population data that require significant translation and interpretation (Lock, 1998). In Jennifer Fosket's study of the Gail Model, one of those tools, she argues that they are "black boxes" (Latour, 1987) that obscure the constructed nature of the statistical abstractions they generate. Fosket's study reveals that the numeric threshold for "high-risk" of breast cancer that continues to be used to classify women without genetic mutations was arbitrarily established in a clinical trial (Fosket, 2004).

This project integrates and builds on these literatures on genetic risk and breast cancer risk by using STS tools to explore how multiple actors and actants—genetics laboratories, researchers, screening tools, laboratory tests, counselors, clinicians, advocacy groups, and patients—work together to produce BOC genetic risk and make it visible and tangible to patients. In Chapter One, I illustrate that the classification systems for genetic variants are also black boxes, as the processes scientists use to determine whether genetic variants are benign, harmful, or pose uncertain risk are largely obscured. In addition, I highlight inconsistencies in and disagreement about the risk profiles and classifications of certain mutations, including variations in whether and how laboratories report VUSs to patients. Hence, this study contributes to the social science risk literature by illuminating the processes of genetic interpretation, classification, and reporting that actively, but often invisibly, construct BOC genetic risk.

***(Bio)medicalization and (Pre)patienthood***

This study contributes to sociological theory on medicalization and biomedicalization by exploring if and how BOC genetic risk is being defined and treated as an illness and whether patienthood experiences are being transformed through developments in biomedicine. Sociologist Peter Conrad defines medicalization as a social process by which normal human conditions are defined and described in medical language, understood through medical

frameworks, or treated with medical interventions (Conrad, 2007). Building on the concept of medicalization, STS scholar Adele Clarke and her colleagues have argued that technoscientific advances in the 21st century have been transforming the structures of both social life and medicine, producing "increasingly complex, multisited, multidirectional processes of medicalization" that they term "biomedicalization" (Clarke, Shim, Mamo, Fosket, & Fishman, 2003, p. 162).

There is an ongoing conversation among scholars about which concept—medicalization or biomedicalization—has more utility in capturing how science and medicine are operating as forces of social control and change in the 21st century. Rather than enter this debate, I engage with both frameworks in this project, as they raise unique questions about, and illuminate distinct aspects of, how genetic risk is produced and managed in the era of panel testing. For example, the practices of BOC genetic medicine exemplify several of the recent transformations to biomedicine and patienthood identified by Clarke and her colleagues and by sociologist Nikolas Rose, whose theory of vital politics (Rose, 2007) dovetails with the biomedicalization thesis. Scientific and social interest in identifying the genetic mutations linked to cancers illustrate processes of molecularization, and the effort that women devote to identifying and managing BOC genetic risk reflects the processes they term optimization and subjectification (Clarke et al., 2003; Rose, 2007). But in addition, being "at risk" is a normal, human condition—we all face varying types and degrees of risk through unavoidable, everyday aspects of life—and this study reveals that being "at risk" is increasingly defined and regarded as an illness that requires "treatment."

Most STS scholars and medical sociologists who have explored the medicalization of the "at-risk" health status have argued that risk is a liminal state between sickness and health in

which patients' roles and obligations are less clearly defined than in illness (Dagan & Goldblatt, 2009; Gibbon, 2007; Kenen, 1996; Lock, 1998; Rose, 2007; Scott et al., 2005; S. Timmermans & Buchbinder, 2010). Researchers have coined various terms to describe individuals occupying this in-between social location in which they deemed neither healthy nor sick: "pre-patients" (Rose, 2007), "pre-symptomatic ill" (Lock, 1998), "anticipatory patients" (Gibbon, 2007), "beings-at-risk" (Scott et al., 2005), and "patients-in-waiting" (S. Timmermans & Buchbinder, 2010). Some scholars have specifically explored the complexities of pre-patienthood among women with BRCA mutations (Dagan & Goldblatt, 2009; Gibbon, 2007; Hesse-Biber, 2014), but no published social science analyses have focused on women with MRMs or VUSs. By comparing the experiences of women with BRCA mutations with those of the growing numbers of women with VUSs and MRMs, this study illuminates shared and distinct dimensions of (pre)patienthood for women across the spectrum of BOC genetic risk and if and how panel testing has altered the boundaries of health, risk, and illness.

***Gender and Embodiment***

Both professionals within and scholars of genetic medicine have paid little attention to how surgical risk management and breast reconstruction practices affect and are affected by gendered constructs of femininity (A. Finch & Narod, 2011; Nina Hallowell, 2000; Press et al., 2005). While genetic counselors, clinicians, and researchers have emphasized how risk-reducing surgeries affect women's reproductive capacities, their attention to gender and embodiment has been limited to the domains of reproduction and motherhood and tends to overlook other dimensions of women's embodied experiences, such as sexuality. Two scholars of BRCA medicine in the United Kingdom stand out as exceptions. Nina Hallowell's research on mastectomy and reconstruction among women at high risk for breast cancer examines how

women's conceptions of femininity and womanhood shape their surgical decisions (Nina Hallowell, 2000, pp. 166-167). In addition, Sahra Gibbon's analysis of the dimensions of BRCA patienthood explores how the demands of genetic responsibility are gendered (Gibbon, 2007).

Expanding on these analyses of the gendered dimensions of BRCA medicine and patienthood in the United Kingdom, this study explores how structures of gender and BOC genetic medicine in the United States are co-produced, as they simultaneously shape and are shaped by one another. In addition, this study uniquely examines the experiences of women with BOC mutations who refuse or challenge gendered expectations that they actively manage their risk through prophylactic surgeries and maintain feminine bodies through breast reconstruction. In her research on amniocentesis, anthropologist Rayna Rapp describes the women making complex decisions to use or refuse the prenatal testing technology as "moral pioneers":

> In considering whether or not to accept prenatal testing, all were participating in an impromptu and large-scale social experiment: Whether as willing conscripts or draft resisters to biomedicine's technicist promise of more control over pregnancy outcomes, all made conscious a set of values, ethics, and choices which were located in the realm of the private but were shaped and in turn helped to shape a more social terrain. (Rapp, 2000, p. 309)

Women with BOC mutations considering whether or not to have prophylactic surgeries or reconstruct their breasts face similarly complex, private, and yet socially embedded choices that are linked to their values and ethics. They are also responding to "biomedicine's technicist promise[s] of more control," only the promises issued to them are about control over cancer outcomes and feminine appearances. Hence, women with BOC mutations can also can be seen as pioneers, and this project contributes to the literature on genetic medicine by exploring the experiences of women who are "willing conscripts" *and* those who are "draft resisters."

## Conceptual Frameworks

There are three concepts that I use throughout the following chapters that have variable meanings across disciplines: structures, practices, and architecture. In this section, I identify the specific definitions of these terms that I am referencing by briefly describing the theoretical frameworks they are derived from and how I use them in my analysis.

### *Structures and Practices*

Most of the clinical and social science literature on the management of cancer genetic risk explores women's beliefs and feelings about their risk management decisions, the individual or familial factors that shape those decisions, and the outcomes of their surgeries. This study takes a different approach to investigating women's experiences navigating cancer genetic medicine by focusing instead on how social systems and structures constrain and enable what choices are made available to women. For this structural analysis, it is useful to draw on sociologist Raewyn Connell's framework on the mutually constitutive relationship between structures and practices. Connell argues, "Structure is always emergent from practice and is constituted by it. Neither is conceivable without the other… 'structure' specifies the way practice (over time) constrains practice" (Connell, 1987, pp. 94-95). Yet Connell also asserts that structure, which she defines as "the intractability of the social world" (Connell, 1987, p. 92), is not simply a static, restraining force, but rather "is vulnerable to major changes of practice"(Connell, 1987, p. 93). In other words, structures limit social practices, but also are both formed and transformed through practices.

### *Genetic Medicine Fields of Practices: Risk Production and Risk Management*

Utilizing Connell's theoretical framework, the structures of BOC genetic medicine can be divided into two overlapping fields of practices: the field that constructs genetic risk and makes

it visible, and the field that responds to genetic risk and attempts to make it manageable. The "risk production" field of practices that constructs BOC genetic risk encompasses the technologies, methods, materials, people, procedures, policies, and places involved in the collection, sequencing, interpretation, classification, reporting, communication, and translation of people's genetic data. The "risk management" field of practices that *responds* to BOC genetic risk includes the technologies, methods, materials, people, procedures, policies, and places involved in defining, informing, guiding, constraining, and enabling how people in bodies respond to their genetic data. Figure 2 below provides examples of key components in each field of practices, including the primary actors and locations through which the fields overlap.

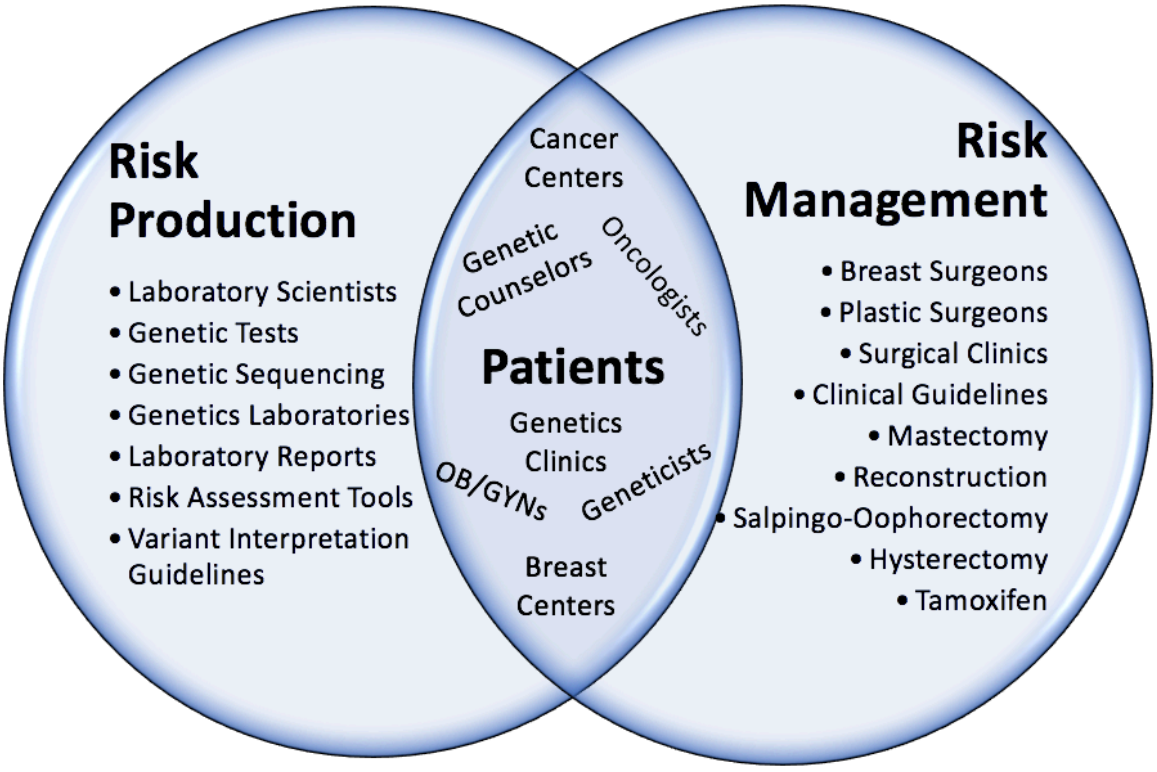


**Figure 3: Fields of Practices in BOC Genetic Medicine in the United States**

As Figure 2 highlights, the Risk Production and Risk Management fields of practices intersect and are mutually constitutive. For example, scientists' interpretations and classifications

of genetic data form evidence that clinical experts use to develop guidelines on the management of genetic risk for cancer. These clinical guidelines, in turn, affect what procedures are and are not offered to patients and whether those procedures are covered by insurance. Conversely, as it has become evident that some women are undergoing prophylactic surgeries for VUSs, laboratories and genetic counselors have modified how they report and translate VUS data to clients in ways that minimize their visibility and salience.

***Architecture***

The various components that operate within the risk production and risk management fields of practices, and the ways in which those components are assembled and organized, are diverse and in-flux. In her cross-national comparison of the development of BRCA testing systems in the United States and United Kingdom (UK), science studies scholar Shobita Parthasarathy coined the term *architecture* to refer to the distinctive organization of components and linkages within each country's system (Parthasarathy, 2007). Throughout this analysis, I borrow Parthasarathy's concept to distinguish between the *structures* of genetic medicine in the United States—the fields of practices involved in producing and managing genetic risk—and the *architecture* of US genetic medicine, which refers to how the components within these fields are configured and connected.

Parthasarathy's research reveals notable differences between the structures and architectures of BRCA medicine within the US's market-based health system and the UK's nationalized system. Her findings underscore how social science research on genetic medicine in countries with nationalized health care systems are not fully generalizable to the US context. Yet the vast majority of social science scholarship on BOC genetic medicine has been conducted

outside of the United States,[9] in countries such as the United Kingdom (Gibbon, 2007; Nina Hallowell, 1999; Nina Hallowell, Foster, Eeles, Ardern-Jones, & Watson, 2004; Mozersky, 2013); Israel (Dagan & Goldblatt, 2009); and Canada (d'Agincourt-Canning, 2006). In fact, there was no published sociological or anthropological literature on US women with BRCA mutations prior to the 2014 publication of Sharlene Hesse-Biber's research on the testing and decision-making experiences of women with BRCA mutations (Hesse-Biber, 2014). Hence, through its focus on women and health professionals in the United States, this project contributes to the literature on genetic medicine by shedding light on the distinct features of BOC genetic patienthood and the transition to panel testing in a market-based system.

***Notes on Writing***

This is a study of BOC genetic medicine in the United States. While I will periodically draw attention to that specific context, to avoid repeatedly using the acronyms "BOC" and "US," I will typically use the unmodified phrases "genetic medicine" and "genetic risk." If at any point I intend to signal the inclusion of other national contexts, sub-fields of genetic medicine, or types of genetic risk, I will make that explicit. Similarly, I will generally use the term "mastectomy" to refer to "risk-reducing mastectomy (RRM)" in the following chapters in order to avoid the repeated use of another acronym. When I discuss mastectomy in the context of cancer treatment, I will specify that in the analysis. However, even with these adaptations, this is an acronym-heavy text. As such, I have provided an alphabetized glossary of acronyms in Appendix A, and I will reintroduce acronyms the first time they appear in each chapter. In addition, the term "mutation" in this text always refers to a genetic variant that has been interpreted as harmful and

[9] There is a considerable body of *clinical* research on women with BRCA mutations in the United States, but qualitative social science research on their experiences has been limited.

affects typical gene or protein function. However, "variant" is an umbrella term that refers to any identified change in the typical code of a gene, and therefore could be a variation that is benign, pathogenic, or uncertain.

**Chapter and Themes Roadmap: Revisiting the Jolie Op-Ed**

To provide a roadmap for the issues that I explore in the chapters that follow, it is helpful to return to Angelina Jolie's Op-Ed, as it reflects and condenses many of the key points and themes of this project. Published just one month before the *AMP v. Myriad* ruling, the Op-Ed expanded awareness about BRCA mutations, genetic testing, prophylactic mastectomy, and breast reconstruction just as NGS technologies, the Supreme Court decision, and the ACA combined to generate the shift to panel testing and increase access to testing services. In the month after the Op-Ed ran in the New York Times, Jolie's story was discussed on the morning shows of all the major US television networks and featured in over 100 articles in US, UK, and Canadian newspapers (Kamenova, Reshef, & Caulfield, 2014). The Op-Ed also spread like wildfire on social media platforms like Facebook and Twitter, and it continues to circulate; as of 2018, it had been shared over 600,000 times. In fact, it caused such a stir that several researchers have examined what they have termed the "Angelina Jolie effect"—whether and to what degree her Op-Ed was related to a subsequent rise in BOC genetic testing and/or mastectomy (Bhatti & Redelmeier, 2015; Borzekowski et al., 2014; Desai & Jena, 2016; D. G. Evans et al., 2015).

Since the wide circulation of her story, Jolie has become a symbol for being BRCA-positive and a starting point for understanding the issues surrounding cancer genetic testing and risk. During my research, when I would describe the study to people, they responded with comments such as, "Oh, you're studying people like Angelina Jolie!" Similarly, several of the women with BOC mutations who participated in this study said they used Jolie's Op-Ed as a way

to explain their "at-risk" status to their friends. Hence, Jolie's Op-Ed is important because it has functioned as a social anchor for conversations about genetic risk, influenced the social context in which panel testing emerged, and increased demand for testing. But in addition, the Op-Ed strikingly contextualizes broad themes and specific arguments in the following chapters.

Chapter One examines how panel testing has contributed to the geneticization and medicalization of risk and shifted the boundaries of patienthood. I explore how genetic risk is actively produced and made visible and challenge common discourses that frame cancer genetic risk as a firm, quantifiable fact that is discovered through testing. The language and numeric estimates that Jolie uses to describe her risk both mirror and reproduce those discourses. She opens the Op-Ed by sharing that her mother died from cancer at age 56, after a decade of living with the disease, and she describes explaining this to her children:

> We often speak of "Mommy's mommy," and I find myself trying to explain the illness that took her away from us. They have asked if the same could happen to me. I have always told them not to worry, but the truth is I carry a "faulty" gene, BRCA1, which sharply increases my risk of developing breast cancer and ovarian cancer. My doctors estimated that I had an 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer, although the risk is different in the case of each woman. Only a fraction of breast cancers result from an inherited gene mutation. Those with a defect in BRCA1 have a 65 percent risk of getting it, on average. Once I knew that this was my reality, I decided to be proactive and to minimize the risk as much as I could. (Jolie, 2013)

Jolie describes the risk associated with her mutation using precise values, a practice that was also common among women in this study because risk was typically presented to them, both in conversations with their providers and in their genetic test reports, as a static fact that was uncovered through testing. While Jolie notes that "the risk is different in the case of each woman," she uses specific percentages to describe her own risk, implying that firm estimates can be generated for other women. Yet, Chapter One reveals how genetic risk is actively interpreted and produced, not discovered. Both whether particular genetic variants are classified as "risky"

and the specific numeric estimates of the ranges of risk associated with those variants vary widely across studies and over time.

Chapter Two examines how mastectomy has become the "treatment" for the "disease" of BOC genetic risk in the United States. The experiences of women in this study reveal that mastectomy is regularly offered even to women with MRMs, for whom it is not recommended, and despite it not being significantly more effective than screening at reducing mortality. One of the key arguments I make linking Chapters One and Two is that cancer genetic testing and mastectomy are practices that co-constitute and generate demand for one another, and Jolie's Op-Ed exemplifies that mutually constitutive relationship. Jolie describes learning about her mutation and her cancer risk as if they happened simultaneously. She states that once she tested positive for a BRCA1 mutation, she then "knew" that her high risk for breast cancer was a "reality," and those test results were what motivated her to "be proactive" and surgically minimize her risk. Yet Jolie's family history alone would have placed her in a higher-than-average risk category for both breast and ovarian cancer, and thus real knowledge of her risk existed prior to testing. In Chapter One, I illustrate how in making cancer risk a tangible, quantifiable "fact," genetic testing makes risk feel more "real," which in turn motivates women to take action and reduce that risk through surgery. Then, in Chapter Two, I reveal how genetic tests are frequently used, in practice, to determine whether or not women are candidates for prophylactic surgeries, and therefore the availability of mastectomy as a "treatment" for cancer genetic risk is often what motivates people to seek out genetic testing in the first place.

In Chapter Two, I also examine two discursive slippages I observed during fieldwork and in interviews that were exhibited in Jolie's Op-Ed: a conflation between the risk of developing breast cancer and the risk of dying from it, and a parallel conflation between mastectomy's

success at reducing cancer incidence and its success at reducing cancer mortality. While Jolie acknowledges that the decision to have breast surgeries was "not easy," she explains that she is glad she made that choice, stating, "My chances of developing breast cancer have dropped from 87 percent to under 5 percent. I can tell my children that they don't need to fear they will lose me to breast cancer" (Jolie, 2013). Here Jolie jumps from a statement about her risk of developing breast cancer to one about her possibility of dying from the disease. Yet, as I illustrate in Chapter Two, most women who develop breast cancer will not die from it, and while mastectomy significantly reduces women's lifetime risk of *developing* the disease, it does not significantly reduce women's risk of *dying* from breast cancer if they follow the guidelines for high-risk screening (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010; Li et al., 2016).

One theme I explore across Chapters Two and Three is how the discourses and practices of genetic medicine position mastectomy and reconstruction as the "empowered" and "right" choices, thereby encouraging women to undergo the procedures. Jolie's Op-Ed is both infused by and perpetuates these rhetorics of "choice" and "empowerment." She explicitly states that she wants to encourage women who "might be living under the shadow of cancer" to not be scared by their risk, but instead to "make [their] own informed choices," "know that they have strong options," and "take on and take control" of their lives. Yet like any piece of writing rooted in personal experiences, Jolie's Op-Ed does not, nor could it, comprehensively reflect the range of options available to women. Rather, as a personal story, the piece reflects her individual concerns, the options that were available to her, and the decisions she made among those options. In fairness to Jolie, no woman should ever be put in the untenable—and impossible—position of being asked to speak for or to all women. But the power of Jolie's celebrity magnified and elevated the specific decisions she made in the unique context of her life—to undergo

mastectomy and reconstruction—while it minimized other options available to women with BOC mutations, such as ongoing surveillance or staying flat. Companies pay celebrities large sums of money to promote their products and services precisely because it makes those products and services seem more desirable. Hence, while Jolie's stated intentions in writing the Op-Ed were to help inform women, her fame functioned as a de-facto "endorsement" of her specific decisions, framing them as the "strong" and best ones.

Another issue I explore in Chapter Three is how the architecture and practices of BOC genetic medicine in the United States funnel women toward reconstruction by pairing the procedure with mastectomy. The title of Jolie's Op-Ed, "My Medical Choice," implies that she made a single decision. However, *reconstruction is a separate choice* with its own risks. In fact, the majority of the risks of breast surgeries are associated with reconstruction, not mastectomy. Yet, Jolie does not convey grappling with or actively "choosing" reconstruction, nor does she discuss the physical complications and risks posed by reconstructive surgeries. In Chapter Three, I reveal how breast reconstruction is typically presented to patients in genetic medicine just as it is in Jolie's Op-Ed—as an assumed, inherent part of the process of a prophylactic mastectomy.

Jolie's Op-Ed also mirrors two additional key themes in Chapter Three: how women are often left un- or under-prepared for the side effects and complications of reconstructive surgeries and how practices in BOC genetic medicine reflect and reinforce the dominant gender order in the United States. Jolie describes reconstruction as a relatively quick process, saying that "nine weeks" after mastectomy, the "final surgery of the breasts is completed with the reconstruction of the breasts with an implant" (Jolie, 2013). Yet, as the stories from women in this study illustrate, reconstructive surgeries often require multiple revisions and have enduring side effects. In addition, even if the initial reconstructive surgery has no complications, all breast implants have

to be replaced approximately every 15 years (Cordiero, 2008; Eisemann & Spiegel, 2018). Therefore, a woman Jolie's age would require, on average, at least three additional surgeries over the course of her lifespan; her "final" surgery would not be just nine weeks after mastectomy. Jolie then emphasizes how her reconstructed breasts look rather than describing her internal experience of having them, a practice that this study shows is common in US genetic medicine. She states, "I do not feel any less of a woman. I feel empowered that I made a strong choice that in no way diminishes my femininity," and she reassures readers that reconstruction "results can be beautiful," noting that her children "see nothing that makes them uncomfortable… small scars and that's it." (Jolie, 2013). Yet nowhere in the piece does Jolie describe her embodied experiences with reconstruction.

Chapter Four explores women's under-preparation and under-treatment for risk-reducing salpingo-oophorectomy (RRSO) and how it is linked to tension between the clinical emphasis on ovarian cancer risk and prevention and the predominant social and cultural focus on breast cancer risk and prevention. There are currently no evidence-based screening tools for ovarian cancer, and it often presents with vague symptoms that are mistaken for other common health conditions. As a result, ovarian cancer is typically diagnosed at later stages and has a poorer prognosis than breast cancer. Ovarian cancer has a five-year survival rate of only 47%, while the five-year survival rate for breast cancer is nearly double that, at 90% (National Cancer Institute, 2018d, 2018e). In addition, unlike mastectomy, RRSO has been robustly associated with an increase in survival among women with BRCA mutations and is firmly recommended in clinical guidelines (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010; Li et al., 2016; National Comprehensive Cancer Network, 2018b). Yet, despite these data and the fact that Jolie's mother died from ovarian cancer, not breast cancer, her initial concern and the focus of her blockbuster

Op-Ed was, like most media coverage, on breast cancer risk and prevention. In fact, when the New York Times published a second Op-Ed by Ms. Jolie two years later in which she discussed her experiences with RRSO, that piece was ignored by the media; I only heard that Op-Ed discussed within hereditary breast and ovarian cancer communities. In Chapter Four, I argue that the social focus on breast cancer risk and prevention over ovarian cancer risk and prevention that was reflected in both the content and media coverage of Jolie's Op-Eds contributes to women's under-preparation and under-treatment for the side effects of medically induced menopause.

In the final chapter, I present policy and practice recommendations that address the key findings of the study. Interestingly, just as Jolie's Op-Ed marked the beginning of this research project, another celebrity essay about BOC genetic risk and mastectomy marked its conclusion. In February 2019, Nina Garcia, the editor-in-chief of Elle magazine and a long-time judge on the television show Project Runway, published a piece in Elle about her decision to schedule a prophylactic mastectomy after years of following the high-risk screening protocol and experiencing numerous false positive results (N. Garcia, 2019). Titled "A Personal Choice," Garcia's essay deploys the rhetorics of choice and empowerment that are embedded in Jolie's Op-Ed and circulate throughout genetic medicine. But importantly, Garcia's essay marks the new era of panel testing. Her mutation is on the BARD1 gene, a low-to-moderate-risk gene that is included in most BOC panels. Compared to mutations on CHEK2, ATM, and PALB2, which are the three moderate-risk genes that I highlight in this study, BARD1 mutations are less prevalent and are supported by less robust data on risk (Couch et al., 2017). Garcia acknowledges the clinical uncertainty of BARD1 mutations, stating, "Doctors think it increases cancer risk, but there isn't enough data to know by how much" (N. Garcia, 2019). Garcia's essay underscores the importance of several of the recommendations I issue in the conclusion, such as creating a clear

system for classifying the risk and risk management recommendations of all genes included in panel tests in order to help patients navigate the uncertain risk information the tests often generate. Nearly six years into the era of panel testing, it is critical to understand the implications of this shift in genetic medicine and to structurally address the challenges it has produced. This project aims to makes progress on both fronts.

## Chapter 1: "Half a Diagnosis with Half a Recommendation": The Geneticization and Medicalization of Breast and Ovarian Cancer Risk

> "I think the big issue in the battlefield, if you will, that is going on right now is around moderate penetrance genes. Are they going to be slotted into the same mental construct as BRCA? Or are we going to somehow carve out a different space for them in terms of risk? And I know that we see a reasonable number of people who come for second opinion counseling for moderate-penetrance mutations who have been told to be managed exactly like a BRCA mutation, you know? Prophylactic mastectomy, prophylactic oophorectomy, and—even without necessarily the strong family history." *(Steve, Oncologist)*

> It seems like they do not quite know how to handle you. There is nobody to coordinate the information because CHEK2 is such an emerging area. The information is not all the same; it depends on which source you are getting it from. It has been very overwhelming. *(Josephine, Age 41, CHEK2)*

### Introduction

The meanings and implications of the "at-risk" health status have been explored at length in sociological, anthropological, and science studies literatures. Previous studies have argued that people at genetic risk for illnesses occupy a liminal state of "prepatienthood" between sickness and health in which patient identity and the course of action is often unclear. (Dagan & Goldblatt, 2009; Gibbon, 2007; Kenen, 1996; Lock, 1998; Rose, 2007; Scott et al., 2005; S. Timmermans & Buchbinder, 2010). As multi-gene panels have become the testing standard for assessing genetic risk for cancer, both the number of people identified as "at-risk" for developing breast and/or ovarian cancer (BOC) has increased and the range of affected genes, and therefore the extent of people's risks, has widened. However, social scientists have not examined variability in how individuals *within* this expanding "at-risk" population are viewed, positioned, and treated in the US health care system.

This chapter examines recent shifts in and current practices of BOC genetic medicine in the United States, with special attention to the experiences of women with moderate-risk

mutations (MRMs) and variants of uncertain significance (VUSs). Drawing on ethnographic data from scientific and lay conferences, reports and documents from genetic testing laboratories, and interviews with providers and women with genetic variants, I explore how familial cancer risk has been geneticized through panel testing and how genetic cancer risk has, in turn, been medicalized. I analyze the technologies, documents, and practices that are used to construct BOC genetic risk and render it tangible, "factual," and manageable in order to reveal how panel testing has transformed the boundaries of risk, disease, and patienthood.

I begin by illustrating how panel testing accelerated the geneticization of BOC risk and generated a shift from subjective to (dis)embodied sources of risk knowledge. I argue that obscuring the scientific interpretation and production of genetic risk contributes to the feeling among women with positive test results that breast cancer is inevitable without the use of preventative surgical interventions. I then explore how BOC genetic risk has been medicalized, arguing that multi-gene panels have contributed to a spectrum of medicalization in which women with BRCA1/2 mutations are treated as patients and have fully medicalized experiences, while women with MRMs are regarded as "qualified patients" and have only partially medicalized experiences. In contrast, I show how VUSs are a contested instance of medicalization in which genetics experts typically challenge the attribution of patienthood status while women with VUSs may seek patienthood status. In the final section, I examine why and how patients and providers attempt to transform the uncertainty of VUSs and MRMs into certainty and seek or provide risk management services that are not recommended. By closely examining the tools and practices used to assemble genetic risk and render it factual and manageable among women with high-risk mutations, MRMs, and VUSs, this chapter sheds light on how the changing landscape of US genetic medicine has generated concomitant shifts in the boundaries of patienthood.

### *Geneticization of Cancer Risk*

In her book *Building Genetic Medicine,* Shobita Parthasarathy argues that with its patent on the BRCA genes, Myriad Genetics constructed a new category of risk: *hereditary* risk for cancer. Myriad distinguished hereditary risk, which was diagnosable through the company's tests for BRCA mutations, from *familial* risk, which was rooted in a family history of the disease (Parthasarathy, 2007). Parthasarathy asserts that Myriad used this rhetorical maneuver to help generate a market for their test. But in addition, by creating a sub-type of risk that could be defined and identified only through genetic screening, Myriad initiated a process of geneticizing BOC risk that this study reveals was hastened and cemented with the shift to panel testing.

First coined by social epidemiologist Abby Lippman in the early 1990s, geneticization is a broad concept that is both an "ideology and a practice" (Lippman, 1998, p. 64). The term refers to how people are, or might be, classified and differentiated according to their genetics, or "reduced to their DNA codes," and to the ways in which "most disorders, behaviors and psychological variations [are] defined, at least in part, as genetic in origin" (Lippman, 1991, p. 19). But in addition, geneticization refers to the increasing tendency for scientists and clinicians to use genetic technologies to "diagnose, treat, and categorize conditions previously identified in other ways" (Lippman, 1998, p. 64). Using this latter definition, the shift away from using the knowledge generated by family histories of cancer and toward using genetic test results to define cancer risk and determine appropriate interventions is an example of "geneticization."

Lippman was critical of geneticization because she was concerned about the possibility of genetic determinism and its social consequences. She envisioned a potential future in which the social, environmental, and structural roots of inequity and disease were ignored, and instead people were reduced to their genes (Lippman, 1991, 1992, 1998). Since the completion of the

Human Genome Project (HGP), multiple scholars have critically examined the utility of the concept of geneticization, noting that the worst of Lippman's fears about the process never became reality (Arribas-Ayllon, 2016; Susan E. Bell & Figert, 2015; Shostak & Moinester, 2015). Sociologists Susan Bell and Anne Figert highlight how the proliferation of genomics research in the 21st century has disrupted rather than reinforced deterministic thinking about genetics by revealing multiple factors involved in gene expression and activation and a non-linear relationship between genes and behavioral or physical outcomes (Susan E. Bell & Figert, 2015). Similarly, science studies scholars Sara Shostak and Margot Moinester argue that the deterministic discourse of geneticization is limited because it is rooted in a nonexistent binary between genes and the environment that overlooks complex gene-environment interactions (Shostak & Moinester, 2015).

I concur with these and other scholars that the social consequences of geneticization have not been as bleak as Lippmann imagined and that the original "zero-sum relationship" (Shostak & Moinester, 2015) she posited between genes and the environment was flawed. However, with the current emphasis on personalized medicine that is reflected in large research initiatives such as "All of Us" and the "Cancer Moonshot" (National Cancer Institute, 2018b; National Institutes of Health, 2018), an increasing number of "disorders, behaviors and psychological variations" are, as Lippmann posited, being studied and defined, "at least in part, as genetic in origin" (Lippman, 1991, p. 19). Moreover, clinical practices in genetic medicine lag far behind scientific and theoretical understandings of genetics; while scientists know there are epigenetic factors and gene-environment and gene-gene interactions that affect gene expression, their mechanisms are poorly understood and therefore that knowledge rarely informs clinical applications of genetics. In fact, the findings of this study reveal that in the era of panel testing, genetic tests have become

essential to the "diagnosis, treatment, and categorization" of being high-risk for breast and ovarian cancer, and thus the concept of geneticization is still useful in describing contemporary configurations of genetic medicine.

In fact, BOC risk has become narrowly defined as genetic risk since the adoption of panel testing as the industry standard. Before the discovery of the BRCA genes in the mid-1990s, a family history of breast cancer was the primary way in which women were identified as at high-risk of the disease. Between the discovery of the BRCA genes and the widespread use of multi-gene panel tests, clinicians often triangulated familial and hereditary sources of information to determine women's lifetime BOC risk, such as detailed family histories of cancer (i.e., cancer "pedigrees"), estimates produced by computerized risk-assessment tools that assess lifestyle and biological factors,[10] and the results of one or more carefully selected single-gene tests. However, familial patterns of breast and ovarian cancer are now largely used to determine women's eligibility for genetic testing, and those tests are then used to confirm and validate BOC risk and women's eligibility for additional risk management services. Thus, panel testing accelerated and completed the geneticization of cancer risk that Myriad set in motion.

***Moving from Subjective to (Dis)embodied Knowledge***

The older and broader concept of familial risk for breast cancer that was established through women's family histories of the disease is a form of subjective knowledge, as it is gathered through people's lived experiences and the stories that circulate in families. Here I am distinguishing technical knowledge about a specific incidence of cancer in a family member and

[10] Computerized risk-estimation tools, such as the Gail Model and Tyrer-Cuzick tool, account for a multitude of factors that have been robustly associated with an increased lifetime risk of developing breast cancer, including cancer in first degree relatives, age at menarche and menopause, parity, breastfeeding, lifestyle factors (i.e., exercise, alcohol consumption, tobacco use), and environmental exposures. Some of these tools have been developed or modified to incorporate genetic testing results in their models (Centers for Disease Control and Prevention, 2018; Millstine, David, & Pruthi, 2014).

what that person's cancer suggests *for other family members* about their *risk* of cancer. While specific biological information about a person's cancer, such as lymph node involvement or tumor grade, would initially be gathered through imaging or testing, that technical, biomedical information is not required, and in fact is rarely used, to constitute other family members' knowledge of their familial risk. Rather, a family history of cancer is an observable pattern of disease across multiple family members. The general knowledge that certain people within a particular family had cancer can circulate without mediation or translation by technoscientific tools, yet that knowledge still serves to make risk visible. To contextualize this point, it is helpful to draw on an example from my own life. My mother learned she had a BRCA1 mutation in 1997. However, growing up in the 1980s, I did not need a clinician or scientist to run tests on me, nor did I need the technoscientific details of her tumor tests, to know that I was considered at "high risk" of developing breast and ovarian cancer. With a grandmother who died from ovarian cancer at age 57 and a mother who was diagnosed with breast cancer at age 39 and then ovarian cancer six years later, the lived experiences of my relatives attuned me to my risk and made it visible long before the BRCA genes were even discovered.

Some social scientists have theorized and analyzed hereditary genetic risk, not familial risk, as a specific form of subjective knowledge: embodied knowledge (Brown et al., 2011; Nina Hallowell, 2000; Kavanagh & Broom, 1998; Lorentzen, 2008). This may make sense, as genetic risk for cancer obviously involves and implicates bodies. Deoxyribonucleic acid (DNA) encodes the protein building blocks that quite literally make up our bodies, and therefore a harmful mutation in a portion of our DNA can have significant embodied consequences. In addition, patients are the experts on what it means to *live with* genetic risk, and the potential outcomes of and responses to that risk—cancer and surgeries—are unquestionably embodied.

However, while genetic risk is *of the body*, it is not embodied. People cannot internally feel whether they have genetic risk, nor can they independently determine whether or to what degree their risk exists. Unlike, for example, activists in environmental breast cancer movements (Fosket, 2000; Klawiter, 2008; Ley, 2009) or DES daughters (Susan E. Bell, 2009), who have drawn on embodied knowledge, women at genetic risk for breast and ovarian cancer are not yet sick, so they do not share a phenotype or experience similar physical symptoms. In addition, because most forms of embodied knowledge originate from patients' inner experiences or their phenotypic characteristics, they are the primary experts on and translators of that knowledge. However, in sharp contrast, information about whether or not someone is at genetic risk is knowable and verifiable only through clinical testing, genetic sequencing, and numeric or statistical abstractions. As a result, knowledge about genetic risk originates with scientists, clinicians, and genetic counselors and is always translated by those experts to patients. Hence, while genetic risk resides inside patients' bodies and has serious embodied implications, the power to identify and define genetic risk lies outside of those bodies, and as such, it is not embodied in the ways that term is most commonly understood.

Instead, I argue that BOC genetic risk is *(dis)embodied,* a concept I use to signal the two important dimensions of genetic risk that I have highlighted in this section: first, how it is simultaneously located inside and outside of the body, and second, that it is constructed through technoscience and can only be abstractly known, not physically felt or seen. Like other forms of scientifically produced expert knowledge, the molecularized, (dis)embodied knowledge about cancer risk constructed through the various processes of panel testing is deemed more precise, objective, and therefore valid than the subjective knowledge of family history. Yet as I will illustrate in the following sections, knowledge about genetic risk is not factual information that is

discovered through biomedical testing. Rather, cancer genetic risk is a moving target that is coproduced through both technoscientific and social processes.

**Making Risk Factual: The Black Boxes of Genetic Testing**

DNA molecules are often colloquially referred to as "blueprints" because, similar to architectural plans, they contain instructions for assembling the building blocks of life. The structure of DNA molecules, called a "double helix," looks like a twisted ladder and is comprised of two connected, winding strands made up of four chemical bases that pair specifically with one another: adenine (A) with thymine (T), and cytosine (C) with guanine (G). Sequential groupings of the base pairs of A, C, T, and G tell the body how to produce and assemble amino acids to form proteins, which are vital to cellular structures and functions throughout the body. The National Human Genome Research Institute (NHGRI) uses a language analogy to explain how DNA encodes for protein production: "The order of the As, Ts, Cs and Gs determines the meaning of the information encoded in that part of the DNA molecule just as the order of letters determines the meaning of a word" (National Human Genome Research Institute, 2015a).

When a person undergoes genetic testing, a sample of either their tissue or blood is sent to a genetics laboratory for DNA sequencing, which involves determining the order of base pairs on the genes included in their test. The sequence of base pairs on their genes is then compared to the sequence of base pairs in what are referred to as "wild types"[11] of the genes—the most common

[11] In *Biocapital,* Rajan argues that genetic "wild types" are constructed analytical tools, not examples of what is typically found in nature. He states: "A wild-type organism is, however, very much an artificial construct. Nature is extremely unlikely to have wild types (indeed, the very concept of a genotype that is not mutated is an anachronism, since genotypes themselves have arisen as a consequence of both natural selection and mutation), only a range of uncontrolled and uncharacterized mutants, some with a greater selective advantage than others" (Rajan, 2006, p. 160).

sequences of that gene that correctly encode for protein production (National Human Genome Research Institute, 2015b). There are rarely discrepancies between the major US genetics laboratories that conduct cancer genetic testing in their DNA sequencing results.[12]

***Discordant Variant Classifications***

When testing is done with reputable laboratories, there is usually agreement as to *whether* and *where* a variant exists in a person's genetic code;[13] however, disagreement between labs on the *significance* of variants is not uncommon because variant interpretation and classification practices are neither objective nor standardized (Balmaña et al., 2016; Lincoln et al., 2017; Phimister, 2015; Thomas P. Slavin, Blazer, & Weitzel, 2016). Linda, a cancer genetic counselor who has been practicing in the field since its inception in the 1990s, explained how machines perform DNA sequencing and then scientists have to interpret the meaning of those results:

> So, when you do a genetic test you send in the blood, and if all of our genes are like a big library, whatever genes you tell them to test, they go in and find both of your copies of that gene and then they proofread them, right? They read through the sequence of whatever genes you tell them to. And the first thing they do is they find all the spots where yours doesn't match the one on file. And no matter whose blood we send in we all have lots of variability in the way our genes are spelled out. So, there's a lot of normal variation. And what the labs have to do is kind of tell the signal from the noise. So, the machines now find all of the variations. And then people have to look at each one of those and figure out, okay, is that just another normal human variation or does that interfere with the function of this gene? *(Linda, Genetic Counselor)*

As scientists "try to tell the signal from the noise," they typically use a five-item classification

[12] The five US laboratories most commonly used for BOC genetic testing are Myriad, Ambry, Invitae, GeneDx, and Color. However, there are other major reputable labs in the United States.

[13] A recent study found significant variation among labs worldwide that conduct BRCA testing along specific technical dimensions, such as their minimum read depth, whether they sequenced non-coding regions of the genome, and the techniques they used for large rearrangement detection. However, there was less variation among US labs, and the differences that did exist would not be likely to contribute to discrepancies in determining *whether* an individual had a specific variant on a BOC gene (Toland et al., 2018).

scale for genetic variants: pathogenic, likely pathogenic, uncertain significance, likely benign, and benign (Richards et al., 2015).

As Linda noted, genetic variation is normal. Everyone has variants in their DNA, and variants are sometimes advantageous—species evolve through a combination of genetic variation and natural selection. But the vast majority of genetic variants are harmless "noise," so when those variants are identified through testing, scientists classify them as likely benign or benign. Just as the small differences between British and American spellings of certain English words (e.g., "colour" and "color") do not make those words indecipherable or alter their meaning, a slight variation in a person's genetic sequence will often have no effect on gene or protein function, and, therefore, on their bodies or health. When existing data suggest that variants are likely to affect protein production or genetic function,[14] scientists classify them as pathogenic or likely pathogenic and refer to them as "mutations." Using Linda's framework, mutations are the "signals" that the scientists are attempting to weed out and identify. Variants get classified as VUSs when their impact on protein production is unclear and/or there is not yet enough data on them to determine whether there are statistically valid associations between that genotype and the phenotype of interest.

Classifying variants requires drawing on scientific expertise and judgement, which varies across laboratories and scientists. While an increasing number of genetics laboratories are sharing their interpretations of variants through online databases like ClinVar (ClinGen, 2018;

[14] Scientists consider numerous sources of data to make variant classifications and interpretations. For example, they draw on information in population, disease, and sequence databases; existing literature on genetic conservation and variation in human and animal studies; predictive algorithms; and data from functional studies. In addition, certain types of variants (e.g., nonsense and frameshift) and/or specific coding regions within a gene can indicate whether those variants are likely to affect protein production or function (Rebbeck et al., 2015; Richards et al., 2015).

Landrum et al., 2018) and aligning their variant interpretation practices with industry guidelines jointly issued by the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) (ClinGen, 2018; Richards et al., 2015), some labs are not participating in these efforts. For example, Myriad, which has the most extensive data on BRCA variants due to its patent on the genes for over 15 years, has actively resisted calls for transparency and data-sharing (Guerrini, McGuire, & Majumder, 2017; McGowan, 2018). Instead, Myriad maintains its own trademarked classification system and database of results and promotes those as scientific strengths that distinguish the company in the BOC genetic testing market. Laura, a clinical geneticist, discussed this "unfortunate" corporate decision:

> There are notable exceptions to laboratories that don't participate and don't contribute their data to ClinVar. Myriad in this case being the biggest one of those. And so that does—I mean it's a black box essentially in terms of how they're interpreting variants, whether they're doing it correctly or incorrectly. Of course, they will argue from a marketing point of view that they have more data and so therefore they have better interpretation of data. It's hard for any of us to know or assess that because they haven't been transparent about that process. So, I do think that's unfortunate for patients as a whole. I think if people are trying to serve patients in the best way, they should make data from patients available and patients should be able to, in the aggregate, help each other by this pool of de-identified information. But obviously that's a business decision that they've made. And I understand why they've made it, I just think it's unfortunate. *(Laura, Clinical Geneticist)*

Moreover, while sharing data and following the ACMG-AMP guidelines are helpful in resolving conflicting interpretations, these practices, on their own, are not a panacea. The ACMG-AMP guidelines are vague and broad, which means *they* can be interpreted differently, and there are no independent means for assessing actual laboratory practices or adherence to the guidelines (Nykamp et al., 2017; Thomas P. Slavin et al., 2016). In addition, as Steve, an oncologist, explains, "The idea that if everybody just puts all of the variants we've ever seen into the database, that somehow magically everything is going to become clear, is a conceit…. What's

helpful is when people put their variant classifications and their *reasoning* behind their variant classifications in to a central database." Yet, while multiple databases exist for sharing variant calls, they are not linked, and many labs do not provide the specific evidence they draw on to form their variant interpretations (ClinGen, 2018; Thomas P. Slavin et al., 2016).

Given this combination of thin data, disagreements in scientific judgement, and obscured, siloed interpretation practices and sources of evidence, laboratories sometimes generate discordant classifications of variants (Amendola et al., 2016; Balmaña et al., 2016; Lincoln et al., 2017).[15] Alyssa, a genetic counselor who works for a testing laboratory, shared how conflicting interpretations of variants has become a bigger issue in recent years. "I think we're all trying, it's just that they're called guidelines because they're guidelines. And for some variants, two groups of really smart people could look at the exact same evidence and come to different conclusions. So, I think that the ACMG guidelines are really great and they provide us all framework, but I have heard a lot of chatter recently around discrepant interpretations." Stacy, a genetic counselor who works at an academic medical center, recalled a recent case in her group practice that involved conflicting interpretations of the same variant:

> There's one case that comes to mind at our institution, it wasn't even mine, but this has also happened to me, where a family member came in with two reports from, like, her sister and her mother. And they were both done at separate labs, and it was the same variant that was found, but one lab called it a VUS and one lab called it likely pathogenic. So basically, the counselor here got to pick which labs she sent it to to figure out how it would be called, which is a tough situation. *(Stacy, Genetic Counselor)*

[15] In this analysis of discordant classifications, I am only referring to conflicting interpretations of variants that would result in a change in medical management (e.g., between likely pathogenic and uncertain, but not between pathogenic and likely pathogenic). Laura, a clinical geneticist, noted that even though variants with discordant classifications that would change medical management constitute a small proportion of overall variants, they are concerning. "The thing that I get more worried about is the small percentage, which is five percent, I believe, where they actually are meaningful differences that impact clinical care. But five percent is like not a small number to me. It is something that has to be resolved."

Similarly, Jackie, who also practices at an academic medical center and has been working in cancer genetics for over 20 years, stated, "I've had families, we all have here, where you do two family members and because of their insurance situation we use different labs. And it's the same finding, again, but it was found in one lab where they called it likely pathogenic, yet the relative's lab is going to call it an uncertain variant."

There were also striking examples of discordant results among the women who participated in this study. For example, Deena, who has a CHEK2 variant with conflicting interpretations, was treated at two different clinics for her colon and thyroid cancers. Both clinics asked her to do genetic testing, and each one used a different laboratory. Both labs identified the same CHEK2 variant, but they classified them differently.

> Now, [the private clinic] told me I have the CHEK2 gene mutation. [The academic clinic] told me I have an unknown variant of the CHEK2 mutation. They came up with different readings on the CHEK2. They came up with the same variant. But one of them classified it as unknown and of them said it is. I went right to my [private clinic] geneticist and talked to her, she said it's based on labs, that each lab knows, has different knowledge, and she felt their lab knew more than [the academic clinic's] lab did. I'm thinking [the academic clinic] is supposed to be cutting edge of research, so I would think they know more, but…. *(Deena, Age 45, CHEK2)*

Three other women I interviewed had the same variant as Deena, which is listed in ClinVar as having conflicting interpretations. One of the women was told it was a VUS, while the other two were issued "positive" results.[16] Interestingly, one of the women who was told it was positive chose not to have surgery, while the other three all had mastectomies.

Penelope, who by age 32 had been diagnosed with both ovarian and kidney cancer, had

[16] For any participant who had a variant with conflicting interpretations in ClinVar, I noted the conflict in my data. However, I categorized the women as either having a mutation or VUS based on the determination of their testing laboratory. Since the women's decisions and the responses of their medical teams were based on the conclusions provided in their genetic testing reports, those conclusions were critical context for understanding their medical management.

genetic testing done with *three* different laboratories,[17] and like Deena, she received discordant results.

> The first time happened when a genetic counselor came to the hospital while I was still admitted from the [ovarian] surgery. They submitted the genetic blood work to a company called GeneDx. There was a breast and ovarian cancer panel. That came back with two different results. I had a CHEK2 gene labeled expected pathogenic and I had a BRCA2 gene that they labeled unknown significance…. [Then] I did Myriad because of the BRCA2 variant of unknown significance. [The doctors] said that Myriad has the most information about BRCA2 and they wanted me to find out what Myriad had to say about the BRCA2 mutation…. [Myriad] came back and said that my CHEK2 was of uncertain significance instead of expected pathogenic. They said that BRCA mutation was negative and there was no clinically significant mutation detected…. So then after I had the kidney cancer, my geneticist…sent my information to Ambry Genetics and expanded it to a 49 gene analysis associated with hereditary cancer, and that came back with *three* results. That was CHEK2 variant likely pathogenic, BRCA2 variant of unknown significance, and SDHA variant of unknown significance. *(Penelope, Age 32, CHEK2, BRCA2 VUS)*

Similar to Deena's experiences, the three labs Penelope tested with all identified the same variants on BRCA2 and CHEK2, but they had discordant interpretations of them. While only Ambry identified the SDHA variant, that was the most expansive panel, and based on the information Penelope shared and the constitution of various panels at the time of her original tests, it was unlikely that Myriad and GeneDx sequenced that gene.

When laboratories generate conflicting interpretations of variants on BOC genes, it reflects disagreement about whether or not that variant increases a person's risk for developing cancer. But being "at-risk" for cancer is, itself, a state of uncertainty, and therefore discordant classifications layer uncertainty on top of uncertainty, a magnification that generates challenges for both patients and providers. For patients, the discrepancies are frustrating and confusing.

[17] Importantly, for women like Deena and Penelope who have already been diagnosed with cancer, genetic tests do more than identify levels of risk. Test results are increasingly used to guide cancer treatment decisions and can determine eligibility for certain medications and clinical trials.

When I asked Penelope how she felt after receiving so many conflicting interpretations, she said, "Pissed!" Then, toward the end of our conversation, Penelope explained that she wished labs would share data and try to reach resolution. "It's a little frustrating. I'd love if they could all share their information so if you get genetic testing results, you get *results*."

As Stacy noted, discordant classifications put genetic counselors and clinicians in a "tough situation" because they, not the scientists, then have to make judgements about whether to counsel patients to treat those variants as harmful or uncertain, which in turn impacts medical management. Most often, genetics professionals leaned toward treating those variants as likely pathogenic, which were interpretations that they perceived as cautious, but might, in practice, be harmful. For example, Stacy recalled a patient whose ATM variant had conflicting interpretations.

> It came back as a VUS at the lab that I sent to, and then in ClinVar, two other reputable labs that we do send to regularly were calling it pathogenic. One was pathogenic and one was likely pathogenic. And then I did ACMG guidelines on it and had our geneticist look at it, and she thought that it looked pretty pathogenic, also. So, in that case, we did tell her to follow the ATM guidelines, if possible. It's just hard for these people getting insurance coverage for it sometimes. *(Stacy, Genetic Counselor)*

Jackie also shared that typically she sides with the interpretation of higher risk when there is disagreement. "If somebody's leaning towards it being pathogenic, I need to counsel that we have to err in that direction, or lean in that direction…. So, we're going to do more frequent screenings rather than not enough screening. Put it that way. We'd go in the direction of more rather than the routine average screening." If the guidelines for risk management were regularly being followed and additional screening was the only intervention that women with moderate-risk mutations (MRMs) were receiving, erring on the side of classifying variants with conflicting interpretations as pathogenic would be the cautious approach. However, as I will illustrate in

Chapter Two, most women with MRMs are being offered risk-reducing mastectomy, and many of them are opting for the surgery, which notably alters the risk-benefit calculation of managing women according to the "riskiest" interpretations of variants with discordant classifications.

***Inconsistent Risk Information***

Once variant interpretations are made, laboratories produce a report that they issue to clinicians and/or patients, and even when their classifications are concordant, the content of those reports varies across labs. The ACMG-AMP guidelines provide some standards for reporting, and most laboratories adhere to the technical recommendations, such as using consistent variant nomenclature and providing descriptions of sequencing methods and citations for risk estimates. All of the five major US laboratories that conduct BOC genetic testing—Ambry, Color, GeneDx, Invitae, and Myriad—report variants classified as pathogenic and likely pathogenic; those are labeled "positive" results. Conversely, none of the five major labs report on variants that they have classified as likely benign or benign. When scientists judge a variant to be harmless, that variant remains invisible outside of the testing laboratory; the report sent to doctors and patients simply communicates that the genetic test was "negative." Thus "negative" does not mean "no variants," but rather "no variants that have been judged to have clinical significance." In addition, none of the major laboratories provides variant-specific risk estimates, despite research showing that risk is mutation-specific and varies by mutation type and location, even for pathogenic variants on the same gene (Rebbeck et al., 2015). Instead, all five labs report risk estimates at the level of the gene. However, laboratories vary considerably in how they organize their reports, what types of risk estimates they use, and what information they highlight, including whether and how they report VUSs. Moreover, their reports often contain strikingly different cancer risk information, even for pathogenic mutations on the same gene.

I analyzed and compared the content of five genetic test reports—one from each of the five major BOC genetic testing laboratories in the United States—that identified pathogenic CHEK2 mutations. The reports were provided to me by women I interviewed and were issued between 2015 and 2017. Table 1 provides a summary of the content included in each report, stratified by lab, and Table 2 charts the CHEK2-associated cancer risks mentioned in each laboratory's report. Because four of the five laboratories follow the ACMG-AMP guidelines on reporting, they mostly included similar content sections, such as descriptions of their sequencing and classification methods and a list of scientific references; only Myriad did not include sources or methods (Table 1). However, despite those uniform features and the fact that all of the reports were for pathogenic CHEK2 mutations and therefore should have contained similar risk information, not one of the reports was consistent with another in either the range of potential cancer risks it identified (Table 2) or in the specific estimates provided for those risks (Table 1).[18]

[18] As noted earlier, the risk information provided in laboratory reports is gene-level, not mutation-level, data. Once a variant is classified as a mutation (i.e., it is considered pathogenic or likely pathogenic), people with that variant are cited broad ranges of the risks of having a mutation on that gene. While research on BRCA mutations has shown that risks are mutation-specific (Rebbeck et al., 2015), for most MRMs, there is not enough data on each specific variant to calculate mutation-specific risks. But even when those calculations are possible (e.g., for BRCA founder mutations), mutation-specific risk information is not provided on lab reports. This simplification of risk information on laboratory reports is one example of how clinical applications of genetics lag behind scientific knowledge.

| Report Features | Ambry | Color | GeneDx | Invitae | Myriad |
|---|---|---|---|---|---|
| **Year** | 2017 | 2015 | 2016 | 2016 | 2016 |
| **Summary Results** | "Positive" | "Pathogenic" in Red Banner | "Positive" in Red Font | "Positive" in Beige Banner | "Positive" in Red Banner |
| **Risk Estimates** | | | | | |
| Type of Estimate | Relative | Absolute (by age 70) | Relative | Absolute (by age 70) | Absolute (by age 80) |
| CHEK2-Associated Risk of Female Breast Cancer | 2 fold increased | 20% - 44% | Odds Ratios: 2.3 - 3.3 sporadic 3.1 - 4.2 familial | 25% - 39% | 23% - 48% |
| Reference Group Risk of Female Breast Cancer | None | 7% (US women) | None | 8% (white US women) | 10% (US women) |
| **Reference Sequence Nomenclature** | Coding DNA | Coding DNA & Protein | Coding DNA & Protein | Coding DNA & Protein | Coding DNA & Protein |
| **Recommendations Provided** | Aligned with NCCN Guidelines* | Aligned with NCCN Guidelines | Breast MRI, Earlier & Annual Mammography | Directs patients to NCCN's website | Aligned with NCCN Guidelines |
| **Sequencing and Classification Methods Explained** | Yes | Yes | Yes | Yes | No |
| **Citations and Reference Lists Provided** | Yes | Yes | Yes | As PubMed IDs (PMIDs) | No |

*Recommendations are provided in Ambry's "Clinician Management Resource for CHEK2," an attached supplement to their report.

**Table 1: Content of Pathogenic CHEK2 Test Result Reports, by Laboratory**

| Cancers | Ambry | Color | GeneDx | Invitae | Myriad |
|---|---|---|---|---|---|
| **Breast** | X | X | X | X | X |
| **Colorectal** | X | X | | X | X |
| **Prostate** | X | | X | X | X |
| **Thyroid** | X | | X | X | X |
| **Ovarian** | X | | X | | |
| **Kidney** | X | | | | |
| **Leukemia** | | | | | X |
| **Lymphoma** | | | | | X |
| **Gastric** | | | | | X |
| **Endometrial** | | | X | | |

**Table 2: Cancers Associated with CHEK2 Mutations in Test Results Reports, by Lab**

Color and Invitae were the most conservative among the five labs in providing information on the cancer risks associated with pathogenic CHEK2 mutations. Color only highlighted the two types of cancer—breast and colorectal—that have been robustly connected to CHEK2 mutations in previous research, and their report explicitly noted no known connection between CHEK2 and ovarian cancer. It states, "Testing positive for a likely pathogenic mutation in the CHEK2 gene

means your chance of developing breast cancer is greater than that of the average US woman. Your chance of ovarian cancer is not known to be affected by this mutation." Invitae's report also provided a limited range of possible increased cancer risks, but their scope was slightly wider than Color's. Directly under the large "positive" summary result banner that was highlighted in beige, Invitae's report states, "The CHEK2 gene is associated with an increased risk for autosomal dominant breast, colon, thyroid and prostate cancers."

While Ambry and Myriad also emphasized the associations between CHEK2 mutations and breast and colon cancers, their reports added information about other potential cancer risks with far weaker bases of evidence. For example, Ambry stressed the risk of breast and colorectal cancers, noting both of them more prominently on the first page of their report. However, on the second page, they added, "Studies indicate that mutations in the CHEK2 gene may confer an increased risk of developing many types of cancer including breast, prostate, colon, thyroid, ovarian, and kidney." Myriad *literally* highlighted the connections between CHEK2 mutations and increased risk of breast and colorectal cancers in their report, which features a table underneath their dark red "positive" result banner that states "HIGH RISK: Female Breast" in a bright red cell and "ELEVATED RISK: Colorectal" in a bright orange cell (Figure 3). In addition, in the section titled "CHEK2-associated Cancer Risk," the Myriad report notes a range of other cancer risks, stating, "Some studies have described a possible increased risk for a wide range of cancers in patients with CHEK2 mutations, including prostate, leukemia, lymphoma, gastric cancer, thyroid cancer, and other malignancies."

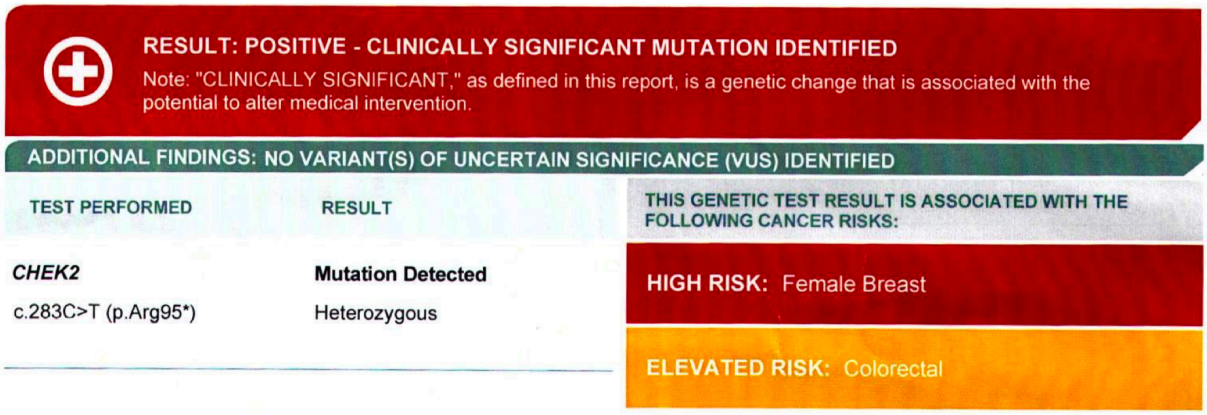


**Figure 4: Positive Results Banner and Table from Myriad Report**

GeneDx's report stood out among the five laboratories because it challenged the general consensus in the field that CHEK2 mutations confer an increased risk of colorectal cancer. The report stated that while a 2003 study had "observed a higher frequency of this pathogenic variant among families with Hereditary Breast and Colon Cancer than families with Hereditary Breast Cancer alone," the most common pathogenic CHEK2 variant "does not appear to confer a higher risk of sporadic colon cancer." Instead, GeneDx's report focused on the association between CHEK2 mutations and female breast cancer, and it was the only one to highlight women's increased risk of developing a second primary breast cancer. But like Ambry and Myriad, GeneDx also mentioned various other cancers that one or more previous studies had found to be associated with CHEK2 mutations, including prostate, endometrial, ovarian, and thyroid cancers.

In total, 10 different cancers were mentioned across the five reports as possibly associated with CHEK2 mutations, but only an elevated risk of breast cancer was identified in all of them (Table 2). Four of the five laboratories stressed the relationship between CHEK2 mutations and increased risk of colon cancer, which is consistent with the screening and risk management recommendations issued by the National Comprehensive Cancer Network (NCCN), the leading professional organization in the United States that develops and regularly updates guidelines for cancer prevention and care (National Comprehensive Cancer Network, 2018b). Four out of five

of the lab reports also mentioned studies showing elevated risks of thyroid and prostate cancers, yet NCCN mentions neither of those cancers in their CHEK2 screening and management recommendations (National Comprehensive Cancer Network, 2018b). Two laboratories noted a possible increased risk of ovarian cancer, but that information contradicts Color's report and the NCCN guidelines, both of which assert that ovarian cancer is *not* known to be associated with CHEK2 mutations (National Comprehensive Cancer Network, 2018b). The remaining five cancers that some studies have suggested may be connected to CHEK2 mutations were each noted by only one laboratory. Among the five laboratories, Myriad identified the greatest number of potential cancer risks linked to CHEK2 mutations, but they also qualified their long list by noting that the studies demonstrating those risks "are not conclusive and there are no medical management guidelines to address these possible risks." It is possible that scientists at Myriad chose to err on the side of over-informing patients. However, as I will illustrate later in the chapter, the problem with such an approach is that patients often imagine the worst possible outcomes even when potential risk information is downplayed.

In addition, even though the laboratories were consistent in associating CHEK2 with an increased risk of breast cancer, the specific risk estimates for breast cancer that they provided varied (Table 1). Both Ambry and GeneDx presented relative risk estimates, but the values were incongruent. Ambry indicated that women with a CHEK2 mutation have "*up to* a 2-fold increased risk" (emphasis added), while GeneDx presented odds ratios that suggest women have *at least* a twofold risk and up to a fourfold risk, depending on their family history. In addition, neither Ambry nor GeneDx provided data on baseline breast cancer risk among US women. Color, Invitae, and Myriad all presented absolute risk estimates that varied slightly but were fairly consistent with one another. All three labs also all provided data on breast cancer risk

among women in the general US population. However, the data they cited suggest that women with CHEK2 mutations are somewhere between three and six times more likely to develop breast cancer than average US women, which is higher than the estimates presented by both Ambry and GeneDx. Interpreting risk estimates always requires some degree of statistical literacy and numeracy skills, but when those estimates have wide ranges, are incongruent, and/or are presented without baseline data, they become even more challenging to interpret.

***Inconsistent VUS Reporting***

Another critical way in which the laboratories' reports differ is in how they communicate VUS results.[19] There is an ongoing, lively debate in US cancer genetics communities about the ethics of VUS reporting and what should be considered "best practices" for the field. Some people believe that VUSs, like benign variants, should not be reported because several previous studies show that VUSs increase patients' fears and are often misinterpreted as positive results, which can lead to potentially unnecessary interventions that carry their own risks (Eccles, Copson, Maishman, Abraham, & Eccles, 2015; Allison W. Kurian et al., 2017; M. L. Murray et al., 2011; Ray, 2017; Ready et al., 2011; Zuppello, 2018). Others feel that patients have a right to know and control their personal genetic information and are concerned about withholding VUS results because, while it happens infrequently, they are sometimes upgraded and reclassified as likely pathogenic or pathogenic. Some advocate for a middle ground—reporting the presence of a VUS and the importance of maintaining contact information for follow up, but not providing detailed information about the location of the VUS in order to minimize patient anxiety and the

[19] Data on VUS reporting were gathered through copies of test results that study participants with VUSs shared and through sample reports provided online by the laboratories. No women in the study who shared their reports and were tested by GeneDx had a VUS, and GeneDx does not share sample reports online. Thus, GeneDx is not included in this part of the analysis.

possibility of unnecessary interventions. In addition, some experts advocate for different approaches to reporting in different populations, both because the prevalence of VUSs varies across populations and because any genetic findings, including VUSs, may affect treatment pathways or clinical trial eligibility for women who already have cancer (M. C. King, Levy-Lahad, & Lahad, 2014; T. P. Slavin et al., 2018).

Consistent with their conservative reporting of associations with various cancers, Color takes a cautious approach to reporting VUSs that is closest to the middle-ground position. When they classify a variant as uncertain, in the "Genes Analyzed" section of their report they include a paragraph with the header "Genes with Variants of Uncertain Significance" that states:

> A "Variant of Uncertain Significance" (VUS) was identified. This is a genetic change whose impact on breast and ovarian cancer risk is not yet known. This is a common finding and does not change screening guidelines. To date, most VUS's [sic] have been found to be harmless (benign), and if it is further classified, we will try to contact you at [patient's phone and email.] If you would like to know the technical details of this VUS, contact us.

The text is printed in the same size font as the rest of the main report content and is not bolded or highlighted in any way. I interviewed a Color employee at a national meeting where I was doing fieldwork,[20] and she explained the reasoning behind their VUS reporting strategy:

> If you or your provider would like to have the actual VUS, the gene, the allele, the supporting evidence, you can request that by phone or e-mail. And then we send an addendum to the report. And providers can actually select, by default, "I just always want to see those details on the reports." And so that way there's a little bit of a gate so that if we find a VUS someone can absolutely access it—we totally believe your data is yours. But first we put a little bit of a gate there to help explain and prevent the possibility that it could be accidentally interpreted as a positive result and someone would act on it.

[20] All five of the major BOC genetic testing laboratories in the United States have exhibit booths at the national cancer genetics meetings I attended during my fieldwork.

The Color employee further explained that they made this decision, in part, because their reports are uniquely directed to patients, not providers. As she stated, "the YOU in the report is the person being tested," and they designed their report content considering the question, "What do people want to know when they get these results?"

Myriad provides more detail on VUSs than Color, as they identify the gene and variant sequence. However, these findings are visually and substantively muted compared to any positive findings communicated in their reports. Underneath the giant red and green banners Myriad uses to communicate whether test results are positive or negative for mutations, there is a much thinner gray banner included in all reports that says "Additional Findings: (No) Variant(s) of Uncertain Significance (VUS) Identified." When there are no VUSs, the word "No" is included, and when they interpret variants as VUSs, the word "No" is removed and the list of genes and reference sequences for the variants follows (Figure 4). By separating VUS information from any positive findings and including the green negative banner in the absence of other positive results, Myriad communicates that VUSs are not "clinically significant" and should not alter medical management. In addition, all of Myriad's reports, even ones with no VUSs, include the following paragraph in the "Additional Findings" section titled "Details About Non-Clinically Significant Variants":

> All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants (Favor Polymorphisms) and benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

Finally, Myriad provides no information in their reports about the cancer risks associated with

mutations on the genes in which VUSs are located, which further conveys that the VUSs do not confer known risks.

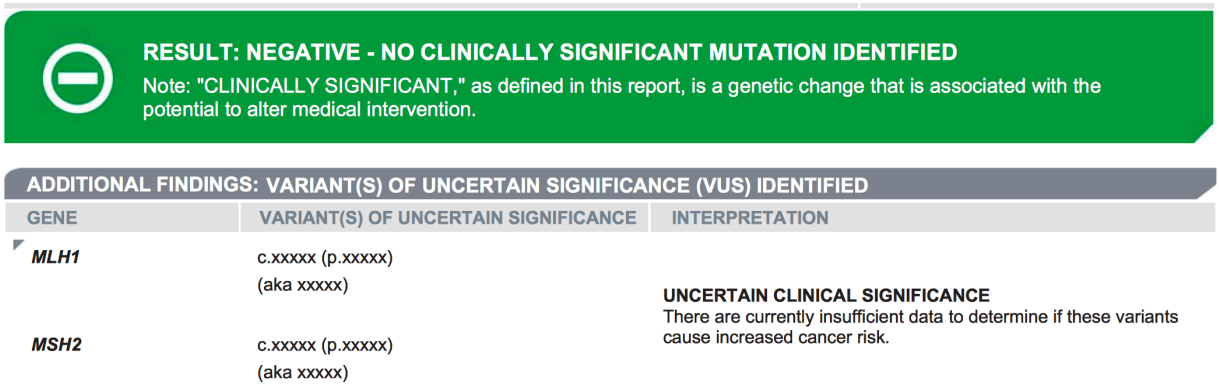


**Figure 5: Negative Results Banner with VUSs from Myriad Report**

In contrast to Color and Myriad, Ambry and Invitae both prominently feature VUS results. In fact, VUSs in Ambry's and Invitae's reports are listed in the same sections and highlighted with the same graphic features as pathogenic mutations. Figures 5 and 6 show positive and VUS results reports from Ambry and Invitae, respectively, and they illustrate that the genes and variant sequences for VUSs are identified in large banners on the front pages of their reports, just like pathogenic mutations (Figures 5 & 6). Ambry and Invitae differ, however, in the details they provide that are relevant to interpreting VUS results. Ambry's report highlights that the VUS should not affect medical management, stating in bolded text, "**No known clinically actionable alterations were detected.**" The report then clarifies that estimates of risk "should be based on clinical and family history, as the clinical significance of this result is unknown."

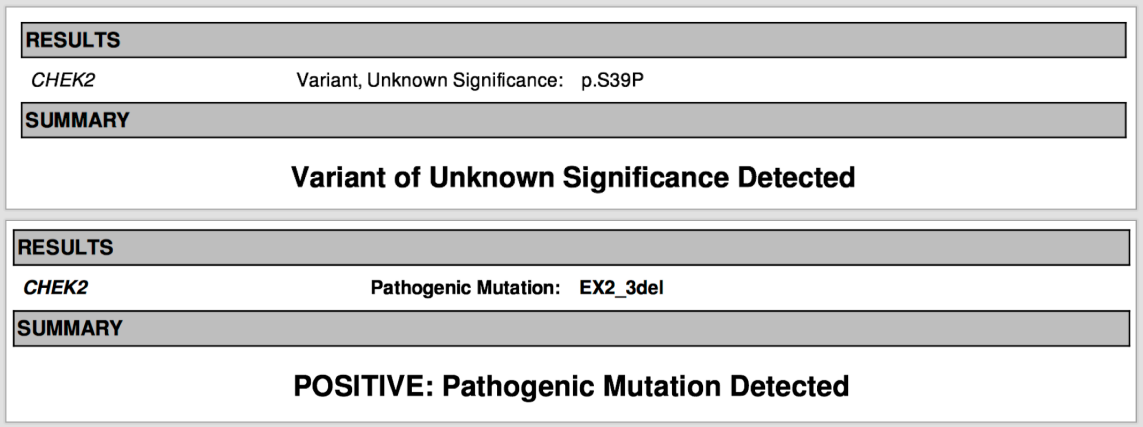


**Figure 6: Positive and VUS Results from Ambry Reports**

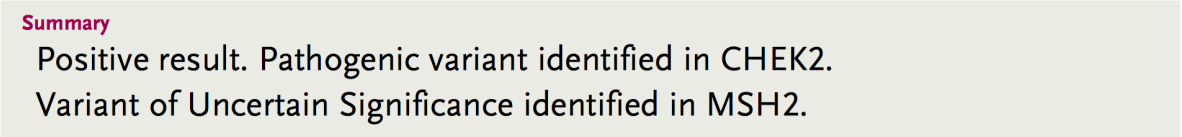


**Figure 7: Positive and VUS Results from Invitae Report**

Invitae stood out among the four laboratories by providing risk information for all genes with reported results, including ones with only VUSs. For example, the report that Figure 6 was taken from identified a mutation on the CHEK2 gene and a VUS on the MSH2 gene, but listed the risks and associations of pathogenic mutations on both CHEK2 and MSH2. Directly beneath the bulleted risk estimates for mutations in CHEK2, the report includes a section on MSH2 that states, "The MSH2 gene is associated with autosomal dominant Lynch syndrome (also called hereditary nonpolyposis colorectal cancer syndrome, or HNPCC) (MedGen UID: 423615) and autosomal recessive constitutional mismatch repair deficiency syndrome (CMMR-D) (MedGen UID: 78553)." Invitae then qualified that risk information, stating, "The clinical significance of this variant is uncertain at this time. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions." Unlike the other three laboratories, which communicated that VUSs should *not* alter clinical care, Invitae only urged "caution" in using VUS results to inform medical management.

The images and quotes from reports issued by Color, Myriad, Ambry, and Invitae reveal important differences between the laboratories in how they emphasize VUS results. Color and Myriad minimize the importance of variants they classify as VUSs and mark them as distinct from pathogenic mutations by separating those results into different report sections and clearly labeling reports without any pathogenic findings as "negative." They clearly distinguish between the risks posed by pathogenic mutations and the uncertainty of VUSs. In contrast, Ambry, and especially Invitae, highlight VUS results and present them with pathogenic mutations in their summary results banners, which conveys importance and suggests parity between the pathogenic and VUS classifications. Their reports make VUSs appear to be at least in part connected to cancer risk, which, in turn, makes those reports more likely confuse or alarm patients.

The distinctions between laboratory reports illustrated in this section might not be noteworthy if testing results were always interpreted and translated by genetic counselors or clinicians with genetics expertise in genetics, as those professionals could minimize patient misinterpretations (Culver et al., 2013). However, an increasing number of patients are having tests ordered by primary care doctors, OB/GYNs, or breast surgeons, and a recent study shows that only half of patients who undergo genetic testing meet with a genetic counselor at any point in the testing process (Allison W. Kurian et al., 2017). Given previous literature that documents VUS misinterpretation among both patients and providers without genetics training (Eccles et al., 2015; Allison W. Kurian et al., 2017; M. L. Murray et al., 2011; Ray, 2017; Ready et al., 2011; Zuppello, 2018), these differences in framing and presentation of VUSs matter, and as I will illustrate later in the chapter, can have a notable impact on patient understandings and care.

### *Black Boxes and Cancer Fatalism*

Taken together, stories from patients and providers about discordant results and the

variable content in laboratory reports illustrate how genetic testing is what STS scholars refer to as a black box (Latour & Woolgar, 1979). From patients' perspectives, when they undergo testing, they provide a blood or saliva sample that gets sent off to a lab. That "input" then passes through the black box of testing, and at the end they receive an "output"—a report—that tells them whether they are "positive" or "negative" for a mutation. The various components of genetic testing described in this chapter—DNA sequencing, variant classification, and results reporting—each involve complex scientific and social practices that are obscured from patients and other non-scientists. The obfuscation and complexity of the decisions and processes that occur between the moments of input and output make the outcomes of genetic tests appear to be preexisting, natural "facts" that were discovered rather than interpretations that were produced.

In highlighting that genetic test results are constructed, I am not arguing that they are not *real*. What science studies scholar Donna Haraway argues about other corporeal entities and processes also applies to genetic variants: "Cells, organisms, and genes are not 'discovered' in a vulgar realist sense, but they are not made up" (Haraway, 1997, p. 142). Whether a variant identified during DNA sequencing exists is rarely in question. I never encountered an example of discordance in sequencing results between the major labs in over three years of fieldwork. However, as Deena's and Penelope's stories reveal, how a variant is classified and whether scientists believe it is likely to result in the development of an illness is a matter of interpretation, and information about the health impact of a variant is typically what people are seeking when they decide to do genetic testing. For some variants, such as the three Ashkenazi BRCA founder mutations,[21] there is a high degree of consensus in the field about the scope and severity of risk

[21] Founder mutations are pathogenic variants that are found in higher-than-average frequencies in populations that share a small, defined ancestral group. There are three BRCA founder mutations that are ten times more prevalent among Ashkenazi Jews than in the general population: BRCA1 185delAG,

that they pose. But the analysis in this study of genetic test results reports reveals how patients receive curated, filtered information about their variants that is sometimes inconsistent or even contradictory. Hence, the binary outcomes of genetic tests (i.e., whether people are told they are "positive" or "negative" for mutations) are not preexisting, objective facts that are discovered through biomedicine. Rather, knowledge about cancer genetic risk is coproduced through both technoscientific and social processes (Jasanoff, 2004; Reardon, 2001), but the black boxes of testing make them appear to be natural, firm, and conclusive.

In his book *Biocapital,* Anthropologist Kaushik Sunder Rajan refers to this process of making scientific knowledge appear natural as "epistemic fetishism." Rajan argues that epistemic fetishism is only possible because the processes involved in the production of genetic knowledge are obscured. He states, "The ideological power of epistemic fetishism comes from the fact that the mystification that elevates a statement established by rigorous scientific method into that natural thing-in-itself, the Scientific Fact, is invisible." Rajan then explores a critical tension that is linked to the black-boxing of the scientific processes involved in genetic and genomic testing: that the produced and interpreted outcomes of tests for genetic variants are simultaneously portrayed as "facts" and "probability statements." For example, as I illustrated in the previous sections, individual results on genetic tests are communicated in laboratory reports as firm "facts" that are discovered. Testing clients are informed through those reports whether they are "positive" or "negative" for a mutation, and reports typically include information about the genes on which pathogenic or uncertain variants are located and the health implications of variants on those genes. However, when test results are "positive," the "fact" of the mutation is also qualified, as it only confers an elevated risk of developing breast or ovarian cancer. Hence,

BRCA1 5382insC, and BRCA2 6174delT (Levy-Lahad et al., 1997).

positive BOC genetic test results are oxymoronically communicated as factual probabilities, or certain uncertainties.

Yet, for several women in this study, developing breast cancer felt like their fate rather than a possibility. Women were almost always aware that the relationship between their positive test result and breast cancer was "stochastic, open and not closed… probabilistic rather than deterministic" (Rose, 2007, p. 51), but they still felt destined for cancer. For example, Alicia, who is 42 years old and has a BRCA1 mutation, shared, "Just kind of knowing about my family history, I kind of approached my 20s as like, 'Ahhh, probably eventually I'll get breast cancer.'" Josephine, who has a CHEK2 mutation and is also in her early 40s, said, "I definitely felt like cancer was in my future. I felt that it was inevitable." For women who already expected to develop breast cancer, receiving a positive result on their genetic test only served to reinforce the sense that cancer was inescapable. As Nora, who was 32 years old when she learned about her BRCA2 mutation, explained, "When I found out, automatically I was just convinced in my head that I had cancer. I was a ticking time bomb."

The feeling among women that cancer was inevitable was not simply a result of inaccurate information or misunderstandings of risk statistics. There were several women in the study who, through their professional training, were knowledgeable about risk estimates, yet they also felt destined to develop cancer. For example, Jill, a nurse with a BRCA2 mutation, shared that she expected to develop breast cancer, and because she was still in her 40s, she did not want to spend decades of her life undergoing surveillance and waiting for it to happen. "It felt like it was just a matter of when it was going to come. Like I couldn't take that stress of like thinking, 'Is it going to be this time, is it going to be?' I wasn't willing to, mentally, I don't think I could have done that. Not at 45. Maybe if I was 65 or 70, it would be a different choice, but not at this

young of age and so much time to just do surveillance." Marci, a 39-year-old public health researcher who also had a BRCA2 mutation, expressed, "Even as someone that understands population-based risk, I still feel like most days that I'm suddenly going to get cancer."

Previous studies have illustrated that women's perceptions of their breast cancer risk are shaped by various familial, relational, and contextual factors in addition to the numeric risk estimates they are provided with, such as whether they have children, how many close relatives have been affected, and whether those relatives survived their cancers (Dean, 2016; Nina Hallowell, Statham, & Murton, 1998; Hesse-Biber, 2014). When multiple family members have been diagnosed with or died from cancer, women often expect a similar future for themselves. As I will illustrate in Chapter Two, among the women in this study, being a mother or experiencing the death of a mother or sibling unquestionably shaped their feelings about risk. Yet those familial-level factors provide only a partial explanation for why women often *feel* that breast cancer is inevitable even if they cognitively understand that BOC mutations only confer a higher likelihood of disease. Opening the black box of genetic testing and exposing positive results as certain uncertainties sheds new light on *structural* elements that influence why and how genetic mutations are "likely to be treated—by others and by themselves—as if they were, now or in the future, certain to be affected in the severest fashion" (Rose, 2007, p. 75).

Rajan explains how concealing the active construction of the results of genetic tests and presenting them as naturalized "facts" helps to transform "probability" into "prophecy":

> The irony—and power—of epistemic fetishism is that probability statements start operating with determinate legitimacy. Probability statements therefore acquire performative force. When confronted with the question of what one *does* when confronted with a probability statement, the absence of an obvious response allows the probability statement to harden into a reified statement of prophecy. Therefore it is a fetishism that is at once an operation of naturalization (the detail of the history of construction of a statement) and an operation that, while naturalizing the statement, shifts

it from being a statement of *association* to one of *causality.* (Rajan, 2006, pp. 167-168)

What Rajan points to in this passage is how black-boxing the production of genetic risk directs attention toward what is made visible and tangible through testing—the "fact" of the positive result and information about the likelihood that cancer *will* develop—rather than what is obscured in the process, which is the social, human production of that test result and the potential that cancer might *not* develop. Rajan's passage also illuminates why positive genetic test results make cancer risk feel more "real" to women even when that risk has been visible for many years through family history. Positive results on genetic tests transform the subjective knowledge of familial risk into (dis)embodied knowledge and "facts," thereby making risk seem less probabilistic and a cancer outcome feel more certain.

Moreover, after cancer risk has been transformed and made "factual," patients and providers understandably turn toward how to respond to that risk by either preventing cancer or detecting it early. But embedded in questions about how to effectively manage cancer genetic risk is an assumption that there is a definite, looming "thing" to respond to and an unavoidable cancer outcome to beat or catch. Specific risk percentages become irrelevant because the structures of genetic medicine discourage the imagination that one might *not* get cancer. The "fact" of the positive test result makes the probabilistic "maybe" of risk feel instead like a deterministic "not yet," regardless of gene penetrance. In turn, as I will illustrate in subsequent chapters, these fatalistic feelings about the inevitability of cancer have contributed to the medicalization of genetic risk and medical over-management of VUSs and MRMs.

**Making Risk Manageable: Medicalizing BOC Genetic Risk**

Once BOC risk has been geneticized and made to feel more factual and tangible, women are thrust into making decisions about how to manage and respond to their risk. Their situation is

unusual, because while people with BOC mutations are not ill, they also are not viewed or treated, by themselves or their providers, as fully healthy. In fact, when people at BOC genetic risk first began collectively organizing and advocating for research and access to clinical care, they created a term—"previvor"—to refer to their unique in-between status and distinguish their experiences and identities from those of people managing or surviving cancer. Researchers have generated their own terms to describe genetically at-risk individuals: "pre-patients" (Rose, 2007), "pre-symptomatic ill" (Lock, 1998), "anticipatory patients" (Gibbon, 2007), "beings-at-risk" (Scott et al., 2005), and "patients-in-waiting" (S. Timmermans & Buchbinder, 2010). While the precise definition of each scholar's term varies, their frameworks share several unifying features. Each one examines and describes genetic risk as a liminal state of pre-patienthood that is located between sickness and health. In addition, social science risk scholars generally agree that genetic pre-patienthood is generated through clinical interactions, produces both social and biological uncertainty, and focuses attention on individual-level causes of and solutions for risk rather than on social or structural ones.

My findings in this study expand on the important work of these researchers, showing how high BOC genetic risk has been transformed from a state of pre-patienthood to one of full patienthood since the widespread adoption of panel tests. Unlike women in previous research, very few women with BRCA mutations in this study were treated or saw themselves as inhabiting an "in-between," unclear health status. Instead, once genetic testing validated their high-risk status by making their breast cancer risk tangible and "factual," their risk was nearly always viewed and managed as if it was an illness that required medical intervention. In other words, their cancer risk was first geneticized, and then having a BOC mutation—particularly one on a high-risk gene such as BRCA1/2—was medicalized.

The concept of medicalization took root in the 1970s, when several sociologists examined the increasing expansion of medical jurisdiction and medicine's role in social control (Conrad, 1975, 1979; Freidson, 1970; Illich, 1976; Zola, 1972). Peter Conrad, the sociologist often identified as the author of the medicalization thesis, emphasizes that medicalization is a *definitional process* in which "a problem is defined in medical terms, described using medical language, understood through the adoption of a medical framework, or 'treated' with a medical intervention" (Conrad, 2007, p. 5). Conrad notes that medicalization is not inherently a negative process that is imposed on patients or problems, despite a heavy focus in the scholarly literature on medicalization's harmful consequences, social control, and overmedicalization. Rather, Conrad and other scholars have stressed that the fundamental processes of medicalization—"the creation, promotion, and application of medical categories (and treatments or solutions) to human problems and events" (Conrad, 2007, p. 13)—are collective efforts that involve collaboration between patients and medical professionals (Conrad, 2007; Figert, 2011; Lupton, 1997).

Previous studies of the medicalization of cancer risk have explored how the process created new categories of disease and brought an increasing number of people under the jurisdiction of medical treatment for breast cancer. For example, in her study of the clinical trials for the drugs Tamoxifen and Raloxifene, medical sociologist Jennifer Fosket argues that the emergence of chemoprevention as an option for reducing women's risk of breast cancer transformed their risk from a state between sickness and health into its own new illness category that required pharmaceutical treatment (Fosket, 2010). Building on Fosket's arguments about how classifications of breast cancer risk are constructed, mutable, and contingent, I explore how the combined processes of geneticization and medicalization have not created *new* categories of

illness, but rather have reconfigured the boundaries between *existing* categories of risk, disease, and patienthood.

Other researchers have examined the relationships between medicalization and geneticization, illustrating that while the two processes sometimes co-occur, they do not have an inherent relationship. Using case studies of depression, homosexuality, and chemical sensitivity, science studies scholar Sara Shostak and her colleagues showed that geneticization and medicalization do not inevitably lead to one another, nor are they always outcomes of the identification of genetic risk factors for conditions (Shostak, Conrad, & Horowitz, 2008). Yet, in the domain of BOC risk, this study highlights that the identification of genetic risk factors and processes of geneticization and medicalization have had a mutually constitutive relationship. In the following sub-sections, I will illustrate how geneticization and medicalization have worked together to shift the zones of risk and reshape understandings of and responses to being "at-risk" for breast and ovarian cancer.

***Reconfiguring Risk and Patienthood***

Talcott Parsons' concept of the "sick role" is a theoretical tool that medical sociologists use to illuminate the social expectations involved in illnesses and examine the lived experiences of having a disease. Parsons viewed illness as a form of deviance, and he argued that two pairs of social rights and responsibilities were a means for managing that deviance. According to Parsons, sick individuals are not held responsible for their illnesses because they did not choose to develop or contract the diseases they have, and while they are ill they are exempt from their normal social obligations. However, these two benefits are tied to two expectations of individuals occupying the sick role: that they seek out expert assistance for their illnesses and actively try to get better (Parsons, 1951).

Several of the scholars who have argued that the "at-risk" status is a liminal space between illness and health have, in part, supported their arguments by showing how individuals at genetic risk are typically not subject to the rights and obligations of the sick role (Dagan & Goldblatt, 2009; Kenen, 1996; Scott et al., 2005). However, my findings in this study illustrate that individuals with BOC mutations now have the full rights and obligations of the sick role. They neither see themselves, nor are viewed by others, as responsible for their condition because they cannot control their genes. For example, Katarina described how she felt after learning about her CHEK2 mutation. "In some ways I felt vindicated. Like, ok, this wasn't my fault, it's you know, it's hereditary." Similarly, Naomi said about her PALB2 mutation, "It is not my body's fault. It just inherited this mutation." Even Janet, who had a CHEK2 variant with conflicting interpretations, felt absolved of any blame for her risk because of the potential genetic link. "It's like, factors were not necessarily in my control to have this, right?" In addition, like most other surgical patients, women are temporarily excused from their normal social obligations during and after they have any prophylactic surgeries to manage their risk.

Moreover, similar to when a person has an illness and occupies the sick role, having knowledge about genetic risk generates social demands for action. As I will illustrate in detail in Chapters Two and Four, women are expected to take active measures to do "whatever is possible" to reduce their risk and to cooperate with medical experts in that "treatment" process. While genetic counseling as a field may espouse a non-directive ethos, genetic tests are not neutral technologies that simply provide people with knowledge about their DNA. Rather, as anthropologist Rayna Rapp argues in her ethnography of prenatal genetic testing in the late 1970s and early 1980s, genetic technologies are infused with values that encourage certain responses:

> It is hard to argue for the neutrality of a technology explicitly developed to identify and hence eliminate fetuses with problem-causing chromosomes (and increasingly, genes) … The very existence and routinization of the technology implies anything but neutrality. It assumes that scientific and medical resources should be placed in the service of prenatal diagnosis and potential elimination of fetuses bearing chromosome problems. (Rapp, 2000, p. 59)

In this passage, Rapp highlights how one cannot separate prenatal genetic screening technologies from the potential actions taken in response to them. The likelihood and potential value of terminating a pregnancy in which the fetus has a chromosomal abnormality is implied in the resources committed to prenatal genetic testing and the decision to do the test.

Similarly, the "very existence" of BOC panel testing implies that sizable biomedical resources should be devoted to understanding and preventing hereditary breast and ovarian cancer. Thus, women who test positive are encouraged to adopt approaches to breast cancer *prevention* that involve high-tech *interventions,* such as mastectomy and drug therapies, all of which carry their own risks. As I will examine in detail in Chapter Two, prophylactic breast surgery is typically framed as the "best" medical choice for US women with BOC mutations, and women's desire for the procedure is influenced by these discourses and practices. While women in this study actively participated in their decisions to have mastectomies, an important influence on their choices was what physician and medical historian Robert Aronowitz refers to as "anticipated regret" (Aronowitz, 2009)—the guilt they imagined they would feel if they developed cancer but had not acted on their genetic knowledge and done "everything within their power" to prevent cancer. As Amy, who has a BRCA1 mutation, expressed, "I'm in control of this to an extent…. So, I think that's my relief, is just I did what I was capable of doing to prevent this." Currently, mastectomy is the only effective means of *preventing* breast cancer; intensive surveillance can catch breast cancer early and improve women's odds of surviving the disease, but it does not prevent breast cancer from developing.

Moreover, another issue I will further examine in Chapter Two is that when women choose not to reduce their risk and instead opt for monitoring that risk with surveillance, they sometimes face resistance and judgement. While a couple of respondents shared stories of people criticizing their decision to have prophylactic surgeries, more expressed the opposite—feeling judged and unsupported if they chose screening over surgeries. In addition, there is debate within hereditary breast and ovarian cancer (HBOC) communities about whether women can call themselves "previvors" if they have not had risk-reducing mastectomy, which reveals how risk identity is intertwined with medicalized interventions. Marci, who has a BRCA2 mutation, was frustrated by how her providers and other women in HBOC communities treated having a mutation like a clearly defined disease rather than a state of uncertainty or possibility:

> I think words like "previvor" make it very, like there's a thing, this clear thing that we're dealing with and we're overcoming. And it's *not* a clear thing, because we don't have anything. Like, you know, my sister could say, "I have breast cancer. I'm focused on that. I'm going to get better." Mine is like, "I'm focused on this nebulous thing that may or may not happen and making decisions based on a complete unknown." And to me that's a really, that choice is a little harder, and comparing these feels a little awkward, like it's a harder choice than my sister had to make. She got her diagnosis, it was like, "This is what I'm going to do." There's a clear road. The road for people with BRCA is not clear. It's just not, and it's complicated and I feel like people are trying to make it, put it in this box: "This is what you should do." And it's like, what's right for me may not be right for the person next to me or the person down the street. *(Marci, Age 39, BRCA2)*

Rather than viewing cancer as a certainty, Marci took seriously the possibility that she would *not* develop cancer. She was one of the few women in this study who actively resisted the medicalization of her risk status, but her refusal to view risk as a disease and have mastectomy required tremendous effort. Marci felt she had to constantly remind her doctors and other women of the *uncertainty* of BOC mutations, which underscores how genetic medicine treats them like diseases and structures responses to BOC mutations around the worst possible outcomes.

Thus, while previous studies framed genetic risk as a gray zone in which the course of

action was unclear, this project reveals that having genetic risk for cancer is now defined, viewed, and treated like an illness. Raina, who has a BRCA2 mutation, summed up the current state: "People look at it like a disease, not a condition." Steve, an oncologist who specializes in cancer genetics, noted that the medicalization of genetic risk has been nearly complete among US women with high-penetrance mutations like BRCA1/2. He explained, "I mean, because of BRCA and because of the high-penetrance predispositions, people have kind of thought of genetic risk as being similar to a diagnosis of disease, at least in the United States. It's not necessarily that way everywhere, but at least in the US."

Steve singled out the BRCA mutations among the BOC mutations because they are the most prevalent, have been the most extensively studied, and pose the greatest risk. But his comment alludes to how "[m]edicalization need not be total" (Conrad, 2007, p. 6), and much like risk itself, instead often occurs in degrees or along a spectrum. In the following sections, I will examine that spectrum for BOC genetic risk, revealing how, in contrast to the full medicalization of BRCA mutations, MRMs have only been partially medicalized and VUSs are mostly not medicalized. Because "treating" BOC mutations with interventions is a key component of the medicalization of genetic risk, illuminating these varying degrees of medicalization first requires an understanding of the current risk management recommendations for different groups of BOC variants. Thus, I begin with a summary and analysis of a document that has played a critical role in the medicalization of BOC genetic risk and has become one of the most important tools in genetic medicine: the "Genetic/Familial High-Risk Assessment: Breast and Ovarian" Guidelines ("*NCCN Guidelines*") issued by the National Comprehensive Cancer Network (NCCN).

### *NCCN Guidelines*

NCCN is the leading professional organization in the United States that develops and

regularly updates guidelines for cancer prevention and care. In countries with nationalized health care systems, there are clear and uniform protocols that specify under what circumstances different services will be provided and covered. However, the privatized, fragmented health care system in the United States lacks centralized protocols, and therefore medical providers often rely on clinical guidelines from professional associations like NCCN to assist them in providing up-to-date, evidence-based care. Similarly, insurance companies in the United States often use professional society guidelines to help them determine medical necessity and coverage for services.

The *NCCN Guidelines* are developed by an expert panel of genetic counselors, surgeons, clinical geneticists, and oncologists.[22] They provide evidence-based recommendations for both BOC genetic risk *assessment* and risk *management*. The first version of the *NCCN Guidelines* was released in 2006, and they were subsequently updated in 2010 and 2014. Those earlier versions of the *NCCN Guidelines* only included information on high-risk mutations, such as BRCA1/2, TP53, and PTEN, that were robustly associated with well-established cancer syndromes (National Comprehensive Cancer Network, 2006, 2010, 2014).[23] In 2015, NCCN began updating the *Guidelines* at least once per year, added information on multi-gene panel testing, and provided brief, general recommendations for MRM management (Daly et al., 2016). By 2018, the *NCCN Guidelines* contained specific recommendations, supported by extensive citations, for mutations on 19 genes that are associated with elevated BOC risk.

[22] There is also one patient advocate on the panel.

[23] TP53 mutations are associated with Li-Fraumeni Syndrome, and PTEN mutations are associated with Cowden Syndrome. These two cancer syndromes include a high-risk of developing breast cancer, but also are associated with a high-risk of developing a wide range of other cancers, including those of the brain, colon, and stomach. Because the health implications of TP53 and PTEN mutations are much broader and more severe than those of other BOC mutations, individuals with those mutations were not eligible to participate in this study.

For breast cancer surveillance in women with BRCA mutations, the current *NCCN Guidelines* recommend annual breast MRI between ages 25 and 75 and annual mammograms between ages 30 and 75(National Comprehensive Cancer Network, 2018b). Women are typically advised to stagger their appointments for MRIs and mammograms six months apart so that they are seen by a clinician and imaged twice per year. For risk-reducing surgeries, the *NCCN Guidelines* instruct providers working with BRCA-positive women to "*Discuss* [emphasis added] the option of risk-reducing mastectomy" with patients, including a "discussion regarding degree of protection, reconstruction options, and risks" (National Comprehensive Cancer Network, 2018b, pp. BRCA-A1). But the *NCCN Guidelines* provide firmer guidance for reducing the risk of ovarian cancer, telling providers to "*Recommend* [emphasis added] risk-reducing salpingo-oophorectomy (RRSO), typically between 35 and 40 y[ears] and upon completion of child bearing" (National Comprehensive Cancer Network, 2018b, pp. BRCA-A1). The *Guidelines* further clarify that RRSO counseling should include a "discussion of reproductive desires, extent of cancer risk, degree of protection for breast and ovarian cancer, management of menopausal symptoms, possible short-term hormone replacement therapy, and related medical issues" (National Comprehensive Cancer Network, 2018b, pp. BRCA-A1).

The recommendations in the *NCCN Guidelines* for managing MRMs are less intensive than those for BRCA mutations but more involved than the breast screening guidelines for women at average risk in the general population. The recommendations for PALB2 mutation-carriers are similar to those for BRCA mutation-carriers but suggest beginning screenings at age 30 rather than age 25. The *Guidelines* recommend that women with CHEK2 and ATM mutations begin annual mammography screening even later, at age 40, and they are less firm on the benefits of adding breast MRI, stating instead that clinicians should "consider*"* the procedure for

these women. But where the *NCCN Guidelines* most clearly differ for carriers of MRMs is in their recommendations for risk-reducing surgeries. The *Guidelines* do not indicate that providers should either *recommend* or *discuss* mastectomy with women with CHEK2, ATM, or PALB2 mutations. Rather, for women with these mutations they state, "Evidence insufficient, manage based on family history" (National Comprehensive Cancer Network, 2018b, pp. GENE-2-4). For ovarian cancer risk management among women with MRMs, the *NCCN Guidelines* do not recommend RRSO. Instead, they note that there is "No increased risk of OC [ovarian cancer]" for ATM and CHEK2 mutation carriers and "Unknown or insufficient evidence" for PALB2 mutation carriers (National Comprehensive Cancer Network, 2018b, pp. GENE-2-4). Yet, as I will illustrate in Chapter Two, all but one of the 38 women in this study with MRMs reported that mastectomy was offered to them, and they often reported that surgery was strongly recommended.

***MRMs: Uncertainty about the Extent of and Responses to Risk***

Because testing for BRCA mutations and research on their cancer associations has been ongoing for over two decades, they have clearly established screening and risk management recommendations and robustly established risk profiles. In addition, most people, especially clinicians, have at least heard of BRCA mutations, both because BRCA1 and BRCA2 were among the first cancer risk genes to be identified and because Angelina Jolie generated widespread awareness about them. In combination, the public visibility of BRCA mutations and broad scientific consensus about the severity of their risks have contributed to their near-complete medicalization. While there is an inherent uncertainty in any "at-risk" health status because no one can predict the future, the other aspects of having BRCA mutations—what they mean in relation to people's health and the interventions available to "treat" them—are nearly

indistinguishable from having an illness. Going back to the notion of positive test results as certain uncertainties, BRCA mutations are the *most* certain among the BOC mutations, and therefore people who are BRCA-positive are likely to be viewed and treated as if they are patients with a disease.

Likewise, the partial medicalization of MRMs is connected to their vague risk management recommendations, conflicting cancer-risk profiles, and inconsistent risk estimates. Similar to BRCA mutations, MRMs are also certain uncertainties—people with MRMs receive positive results and are therefore "diagnosed" with the "disease" of genetic risk for breast cancer. However, MRMs produce far less certainty than BRCA mutations. Most of the moderate-penetrance genes were discovered at least a decade after the BRCA genes; hence, the science around MRMs is less conclusive, fewer people have been tested for them, and clinicians are less likely to have heard of and understand them. As Colette stated, "There is a lot of information out there about BRCA1 or BRCA2, but there is not much about CHEK2." In addition, according to the *NCCN Guidelines*, while women with MRMs may receive additional breast surveillance, they should not be considered eligible for "treatments" or surgical interventions because of the uncertainty about the scope and severity of their risks. Thus, women with MRMs are sometimes treated as "qualified patients" with limited sanctioned access to medical management or interventions. The *existence* of their risk is certain, but the *extent* of their risk is not, and as a result women's experiences with having MRMs reflect some of the confusion and uncertainty that previous studies have argued were characteristic of women with BRCA mutations.

Range of Cancers Is Unclear

I asked every participant in this study to reflect on what, among all of the things we had discussed, was the most important thing that they wanted me to understand. The most common

answers among women with MRMs centered on the feelings of confusion and frustration they experienced because the cancer risk profiles and risk-management recommendations for MRMs were unclear. As Fiona lamented, “I don’t know what is CHEK2-related and what isn’t.” Megan, who also has a CHEK2 mutation, said, “There's no consistency. There's no straightforward answers, and that's been super frustrating.” June shared Megan’s and Fiona’s frustrations with the absence of standardized information and care:

> I think for me it’s just the lack of knowing and understanding, really, what CHEK2 actually does. I mean, DNA's confusing, it's not you know, something simple to understand. You know, so when you're told that you've got this—and you know, he did show me all the little squiggles and where it could come from and all that, but it doesn't really mean very much, to be honest. I think I'd just like to know a concrete, “Yes, CHEK2, definitely affects this, this and this. This is what you need to now do.” *(June, Age 51, CHEK2)*

Josephine also wished there was more clarity on CHEK2 risks and management. “It is pretty overwhelming that the doctors cannot just tell you what needs to be done because it is not a super high risk. It is an elevated risk and a moderate risk. There are two cancers and then all of these other cancers that we do not know.” Holly, who also has a CHEK2 mutation, summarized these sentiments: “The thing that stands out the most is the uncertainty, the unknown.”

Many women were especially concerned about the inconsistencies in information about the cancers for which they were at risk. Several of them shared stories about receiving different information from their health care providers, in research articles, and from women in their social networks of mutation carriers. For example, Deena, who has a variant with conflicting interpretations on CHEK2, shared how the risk information she received from her geneticist, on the internet, and in her social media group varied:

> With my first geneticist, I was told that typically breast cancer, colon cancer, and prostate were linked for the CHEK2. And then, when I talked to the other geneticist, she said

> those were the three that they knew of but she said they were finding more thyroid. That there was a lot more thyroid in there, as well. When I've looked it up, I've seen—granted, this is on the computer, so I know you can't rely on that very much—I've seen where even lung is a possibility, kidney is a possibility, and then prostate, colon, and thyroid. Couple of the other ladies on the CHEK2 group have talked about even other cancers: pancreas, liver, and one of them I *know* has had lung cancer. So, lung, you know, has all been mentioned through them. I was never told that widespread of cancers—I was told that primarily it was a breast, colon—because they had said that's what it's even called, it's the breast-colon cancer. That typically the woman will get both of those and that's not uncommon, that you will get two primaries with it. (Deena, Age 45, CHEK2 VUS)

Megan's doctors also emphasized that breast and colon cancer were the risks of CHEK2 mutations. She described the information sheet she was given after her visit, and how overwhelmed she felt when she began learning more about the mutation through her own research and in her CHEK2 social media group.

> On that paper, it specifically talked about breast cancer and colon cancer and the need for screening, so colonoscopies and the breast screenings. And it didn't speak to any other risks associated with it, or increase of risk. But then of course, as I read my own stuff, I'm finding out, we're kind of just on the edge of learning about CHEK2 and what it all means. And I'm seeing in this group that I very carefully only go to when I definitely feel like I can handle it, over and over again, I'm seeing thyroid cancer. Over and over again. And you know, my head goes, "This can't be a coincidence!" This is a group of women, it's all women in this group who have been diagnosed with CHEK2, and over and over again, they were saying "ultrasounds on thyroids." And my paper didn't say anything about thyroid. And then people have talked about lung cancer, the paper didn't say anything about lung cancer. (Megan, Age 35, CHEK2)

Emily, who like Megan has a CHEK2 mutation, also described the "fuzziness" of CHEK2-associated risks and how they were constantly changing:

> The goalpost is moving all the time with CHEK2 regarding other cancers that are involved. So, the main one that she was concerned about was colon. But then, she talked about some other stuff that she said may be related and she said it was the—the blood cancers, is what she mentioned. Like the lymphoma and the leukemia. She also mentioned the skin cancers, and then, well, testicular wouldn't apply to me. And then, so it was the question of, is it, you know, is it ovaries or uterine? And do we do something about that? You know, and so that's where everything gets really fuzzy, because the only

> thing she really came down and said was, definitely, you have to get the colonoscopy. But like, like I'm talking to other women in these groups, and in some of their cases their genetic counselors told them and their doctors told them that they needed to get thyroid screens, you know, every year. So, it gets really kind of fuzzy as far as what really is included in the CHEK2 gene besides the breast cancer and the colon cancer. *(Emily, Age 51, CHEK2)*

Finally, Josephine shared how the variability and uncertainty about the risks posed by MRMs was stressful because it created uncertainty about how to most effectively respond. "It seems like they do not quite know how to handle you. There is nobody to coordinate the information because CHEK2 is such an emerging area. The information is not all the same; it depends on which source you are getting it from. It has been very overwhelming."

Not only were women overwhelmed by the steady stream of information about *new* risks, but also, they were frustrated by conflicting information about established risks that left them even more bewildered about the best way to manage their health. For example, a few women shared stories about other women in their social media groups who had been told by doctors that CHEK2 was not linked to breast cancer. For example, Fiona said, "There are things like, 'My doctor said that CHEK2 doesn't increase the chance of breast cancer.' Everyone is like, 'That is not true!' There is that. It is always very surprising to me." Holly recalled a similar story:

> It's just confusing. One of them went to their doctor about prophylactic mastectomy, and the doctor said there's no proof that CHEK2 is related to breast cancer and she wouldn't be able to get it done. Which is crazy because that's what it has the most high chance of getting. You get all these mixed things, and of course everybody in the group is saying, "That's not true! You need to go to a different doctor." *(Holly, Age 44, CHEK2)*

Marsha, who has a CHEK2 variant with conflicting interpretations, described her personal experience with receiving contradictory information from her doctors. "I'll tell you what the providers provided me with, which was confusing. My surgeon said it was related to colon cancer, but my oncologist said it was related of the ovarian cancer. Maybe they're both right, but

they were confused, and one said one was wrong." Marsha then explained how that inconsistent information made it challenging for her to figure out how to respond to her risk. "Your first inclination is to act. And your next thing is you go through all this information, which is mind-boggling and hard to make a decision. And as a matter of fact, when you make a decision, the next day there's more information that changes the decision from the previous day. So, there's a lot of confusion."

Marsha's story also illustrates confusion that several women had about whether MRMs increased their risk of ovarian cancer. For example, most of the genetics literature does not link PALB2 mutations to ovarian cancer, but Millie firmly believed that her PALB2 mutation increased her ovarian cancer risk. She said, "So, pancreatic cancer is a risk for this mutation. Obviously, breast and ovarian. Those are the only ones that are clearly identified at this point with the percentage referred to in the literature in these reports, but the increase screening for pancreatic is not—there is not screening for pancreatic cancer. Ovarian, at this point, is not covered by insurance to do anything more than to see your gynecologist every year." Millie believed that she was at increased risk for ovarian cancer because numbers for the relationship between PALB2 and ovarian cancer were "clearly identified" in her laboratory report. While Millie was unsure who did her testing, it was likely GeneDx because they are the only one of the five major laboratories that provides any risk data or statistics for ovarian cancer in their PALB2 reports. NCCN also does not identify a relationship between PALB2 and ovarian cancer, most likely because the data supporting the relationship are thin to non-existent. The 2011 study that GeneDx cites found that people with PALB2 mutations were 1.3 times more likely to have a *relative* with ovarian cancer (Casadei et al., 2011). Not only is that a fairly low odds ratio, but also the p-value for that relationship was 0.18, far from the 0.05 threshold typically considered

statistically significant.

In contrast to Millie, several women with CHEK2 mutations were at least aware that there was a debate about the link between CHEK2 and ovarian cancer. As Katarina, who has a CHEK2 mutation, stated, "You know, some people say ovarian. I believe ovarian cause it's in my family, but some of the, you know, CHEK2 literature doesn't link it with ovarian. There's—there's so much that isn't known." Women without family histories of ovarian cancer found the lack of certainty about the relationship frustrating and frightening. For example, Josephine shared:

> Then there is this whole discussion in the CHEK2 group about ovarian cancer because apparently one of the genetic testing companies lists that as a possible but the other companies do not. There doesn't seem to be a whole lot of science connecting those two, but there are several women in this group who have had their ovaries removed because they are CHEK2 positive. I don't even think they had family members. I think family history would help lean a little more that way, but it is kind of alarming to hear women who have had no family history of ovarian cancer having ovaries removed because of CHEK2. Science isn't there yet but maybe it is coming or maybe it is not. It is kind of scary. *(Josephine, Age 41, CHEK2)*

Importantly, Josephine's fears were not just about developing ovarian cancer; she was also afraid because she observed other women in their social media group having prophylactic oophorectomies they might not need. Among women with BRCA mutations, multiple studies have found that RRSO significantly decreases all-cause mortality (S. M. Domchek et al., 2010; A. P. Finch et al., 2014; Ingham et al., 2013; A. W. Kurian et al., 2010; Parker et al., 2013). However, as I will illustrate in Chapter Four, this study shows that women who have risk-reducing salpingo-oophorectomies (RRSO) are frequently un- or under-informed about potentially enduring and disruptive side effects of the surgery. Moreover, those side-effects often are un- or under-treated. Given those findings, Josephine's concerns are warranted, as women with MRMs who have RRSO when it is not clinically indicated are subjecting themselves to

risks with minimal or no established benefit.

Several women with CHEK2 mutations also felt scared and confused about whether they were at increased risk of thyroid cancer. Megan shared how unsettling it was to learn about the potential links between CHEK2 and thyroid cancer from the other women in her social media group rather than from her health care providers:

> The thyroid thing is kind of terrifying. There's just been a lot of people talking about finding these nodules and then having to have things removed and tested and biopsied and like... in the beginning of this whole journey, nobody was like, "Hey, also, thyroid cancer!" That was never a thing, and so it's like, kind of being thrown one more thing. But the thing about that is, I don't feel I have anybody to turn to for that information. (Megan, Age 35, CHEK2)

Marlene had a similar experience to Megan. She explained, "I posted a question about my thyroid maybe because I was shocked to learn so many of these women have thyroid cancer. But they're all like, 'Me too!' We're all super confused and we all don't—we all need more information." Marlene noted that until she gets more information, she is insisting on annual thyroid ultrasounds, a request with which her clinicians have complied. Margaret noted her confusion about what exactly she should do to monitor her risks for thyroid and colon cancer. She said, "Again, there are no guidelines for the thyroid. The colon cancer screening—I am still confused about that. Sometimes I hear three years and sometimes I hear five. And since my gastroenterologist knew nothing, I don't feel like I could ask him."

Responses Are Unclear

Margaret's comment that she could not turn to her gastroenterologist (GI) for guidance illustrated another common frustration among women with MRMs: that many of their doctors—especially ones who did not specialize in genetics, such as primary care physicians, OB/GYNs, and GI specialists—knew little to nothing about their mutations. Fiona shared that women

frequently discussed other clinicians' lack of knowledge in their CHEK2 social media group. "I would say that the number one thing I notice gets mentioned is just how few doctors—particularly outside of an academic setting, so in more clinical realms—have no idea what to advise people when it comes to having a CHEK2 diagnosis." Megan, who learned about her CHEK2 mutation after her sister with premenopausal breast cancer tested positive, shared how her sister's OB/GYN had never heard of CHEK2:

> It is very frustrating; the lack of knowledge is intense. My sister actually, she had an OB appointment coming up in, it was like, I think four months after she got her positive diagnosis. She called her OB and left him a message and said, "Hey, listen, I just want to give you a heads up, I just got this back, I'm positive for something called a CHEK2 mutation. I know it's not very well known, that's why I'm giving you a heads up, cause I'm gonna want to talk to you about it." So, then she went and talked to her OB, and her OB was like, "Yeah, I've never heard of it." *(Megan, Age 35, CHEK2)*

Heather had a similar experience when she went to see her primary care clinician and OB/GYN. She said, "I would actually walk into my doctor's and be like, 'I have the CHEK2 gene. Do you think I should be doing this?' And they'd say, 'I don't even know what that is.' Some of the doctors, just had no clue about the gene."

Some women even told stories about clinicians in the Risk Management field of practices (Figure 2), such as breast and plastic surgeons, who had never heard of their mutations or had very limited knowledge about them. For example, Sylvia, who has an ATM mutation, shared a comment she overheard her plastic surgeon make to a nurse: "When I went to the plastic surgeon, he was talking outside. He said, 'Oh my god, I cannot keep up with these new genes.' I was like, 'That is interesting.' I just thought I'd share that because it is like, god, they really don't know about this." Megan recalled how multiple clinicians involved in her breast screenings knew nothing about CHEK2:

> I mean even just, after I had my mammogram, the two ultrasound techs and two radiologists asked me what that CHEK2 was on my chart. Which is fine, like "Thank you for being honest and asking." But, like, also, how crappy to be cursed with something that the people you would have turned to for help go, "What's this?" …. I can't trust my healthcare professionals, because they don't—I mean, I trust them, but I can't trust them to inform me, cause they don't know about it. *(Megan, Age 35, CHEK2)*

Margaret shared that even her genetic counselor had trouble keeping up with new findings about MRMs. She stated, "Not even the genetic counselors. I think that they follow the NCCN guidelines, but those are ultra-conservative from what I can tell. So, the things like thyroid cancer, which seems to be starting to be connected. Or, I had melanoma nine years ago. I went to my yearly check-up and I mentioned this to him and he said that he didn't think it was involved with this. And then I go, 'I find research that says they think it is.'"

Margaret's story also reflects how many women with MRMs felt that they had to take responsibility for educating their providers. She recalled a conversation with her GI specialist, whom she felt should know about CHEK2 mutations since there is general consensus that they elevate risk for colorectal cancer:

> I had a screening colonoscopy because it was time, and I mentioned it to the doctor then. I told him that I have 1100delC[24], and he goes, "Well, gosh that is specific." And I asked, "Do you know that they showed a higher increase?" He responded, "No," and I'm like, "Dude! This is colon cancer!" The same with my family physician. She doesn't know anything about it, so I keep feeding her research papers. I feel like I am educating the doctors. *(Margaret, Age 60, CHEK2)*

Similar to Margaret and Megan, Marlene also felt that she had to "be on top of" current research and screening recommendations because she could not trust her doctors to be informed:

> It's hard. It sucks because you read something online and you see actual women who have your mutation that, you know, have thyroid cancer and breast cancer, and so you

[24] 1100delC is the most common CHEK2 variant and the one on which there is the largest body of research (Leedom et al., 2016; Schmidt et al., 2016).

> know the risk is real and you know it's out there. But then you see these people, these providers and they just don't know anything about it. So, I think the biggest, the scariest thing for me is I feel like I have to be on top of it in order to demand testing from my general practitioner who doesn't know anything about it…. most family doctors don't know anything about these mutations unless it's BRCA. *(Marlene, Age 35, CHEK2)*

A couple of women with BRCA mutations also shared stories about having to educate their health care providers. For example, Lily, who has a BRCA1 mutation, recalled having to teach her new OB/GYN that not only was it safe for her to be on hormonal birth control, but also it was recommended as a form of chemoprevention for ovarian cancer. "But mostly, my experience has been I am teaching my doctors about BRCA. And I'm like, 'You are doctors, you should know about this!' But as soon as I got this new doctor who was excellent, she says, 'Well, you can't be on that birth control. Blah, blah, blah, you can't be on this birth control.' So, I had to go online and pull up all these studies." However, such stories were considerably less frequent among women with BRCA mutations. Moreover, the fact that women with BRCA mutations sometimes had to inform their clinicians about their risks and appropriate medical management only underscores the challenges faced by women with MRMs. For while there has been over two decades of research on the BRCA mutations and there is regular media coverage of women who have them, there are far fewer studies on MRMs and media stories on women with MRMs are almost nonexistent.

Qualified Patienthood

Marlene's comment that doctors "don't know anything about these mutations unless it's BRCA" highlights a feeling shared by several of the women with MRMs: that they were second-class citizens in the world of BOC genetics. For example, Maya, who has a PALB2 mutation, stated, "It feels as though the other mutations are just kind of afterthoughts." Holly, who was working as a receptionist at a clinical breast center when she tested positive for a CHEK2

mutation, said her colleagues in reception were not empathetic, and instead they reacted like, "You don't have BRCA!" Rose described feeling different and marginalized: "I don't know, sometimes I feel with this mutation that I'm like an alien of some sort. It's not the BRCA gene and it's, you know, this weird mutation, this CHEK2. It's like, it's not mainstream at all." Riki explained that she felt BRCA mutations were taken more seriously because of greater awareness of them. "I also think that BRCA1 and BRCA2 have a lot more clout because of just the way that came out…. I feel that the medical community and the general populace is more aware of what BRCA is. It is just out there."

In drawing these contrasts between how MRMs and BRCA mutations are regarded, women were juxtaposing the partial medicalization of MRMs against the full medicalization of high-risk mutations. Like women with BRCA mutations, women with MRMs are told with certainty that they are positive for a mutation and have the "disease" of genetic risk for breast cancer. But women with MRMs subsequently face uncertainty that women with BRCA mutations do not about both the extent of their breast cancer risk and the range of other cancers for which they have elevated risk. Moreover, unlike for women with BRCA mutations, there are no recommended "treatments" for the "disease" of risk among women with MRMs. While current guidelines indicate that women with MRMs should have access to additional screenings, such as more frequent mammograms and breast MRIs, evidence currently does not support their access to interventions that reduce their risk and/or prevent cancer, such as prophylactic surgeries. Bailey, a 30-year-old woman with a CHEK2 mutation, shared her frustration with the inability to act on her risk knowledge:

> You know, the thing that was probably the most frustrating about all of this is that they have these tests that tell you you're a moderate risk mutation for cancer, but there's just still not all that much information out there in terms of what you can do to lower your

> risk….Or, you know, the studies some places say 25%, some places say 35%, so the range of risk even varies in the information that's out there. And I know it's because it's so new, but that's a bit frustrating, is that they know this mutation's out there, but they don't necessarily know what to do with the information. *(Bailey, Age 30, CHEK2)*

The vexation that Bailey conveys in this passage emerges from being a qualified patient—she was issued a "diagnosis" and thrust into the sick role, and she sought expert guidance, but they could not provide her with sanctioned "treatments" or ways to take action and try to get better.

Megan explicitly pinpointed the partial medicalization of MRMs when she referred to having one as "half a diagnosis." She shared Bailey's frustration but also expressed how the uncertainty of qualified patienthood made her feel sad and isolated:

> Giving somebody half a diagnosis with half a recommendation and a big question mark can be pretty heavy for a lot of people. So, you know, you're given a diagnosis, without really being told exactly what to do. We start screening at 30, or maybe 40, and insurance will pay for it, or they might not. And we think that it affects breast and lung—or, breast and colon cancer, but apparently there's also some other cancers that are identified. So, the big question mark is infuriating and it—you just feel lonely. *(Megan, Age 35, CHEK2)*

Like many of the women in this study with MRMs, what Megan desired was clarity about the extent of her risk and a clear set of steps she could follow in order to manage that risk. "Like, am I supposed to get an ultrasound on every organ in my body? Like, what do I do? There's a point when this is ridiculous. So, I just wish that there was factual evidence-based information on, 'This is what you need to do and these are what your concerns are, and this is the screening that you need at this age.'" In other words, what Megan and other women with MRMs often want is to move from qualified patienthood to full patienthood. In the final sections of this chapter, I will illustrate how women with VUSs share that desire to transform their uncertainty into certainty, and I will examine the ways in which women with MRMs and VUSs both attempt to do so.

**Transforming Uncertainty**

In contrast to the uncertainty about the *extent* of risk generated by MRMs, VUSs reflect uncertainty about the *existence* of elevated cancer risk. Women who have VUSs and no other pathogenic mutations do not receive a positive result, and therefore they have not been "diagnosed" with the "disease" of genetic risk like women with BRCA mutations or MRMs. In fact, as I illustrated earlier in the chapter, some of the major laboratories use "negative" results banners in their VUS reports to emphasize this distinction. In addition, there is widespread agreement among genetics experts that VUSs have not been determined to confer risk and therefore should *not* be treated with interventions. Clinicians without genetics training sometimes misinterpret VUS results, but throughout my fieldwork I heard providers with training in genetics religiously repeat the phrase "VUSs should not affect medical management." Hence, while BRCA mutations and MRMs are "certain uncertainties"—it is certain that they elevate women's risk of breast cancer, yet they also generate uncertainty because risk is a state of probability—there is no certainty in a VUS result. Rather, VUSs are "uncertain uncertainties" because whether or not they even pose additional cancer risk is in question.

As "uncertain uncertainties," VUSs have mostly not been medicalized by genetics experts. Professional society guidelines and laboratory reports do not define VUSs medically, describe them with medical language or frameworks, or recommend treating them with medical interventions. In addition, most genetic counselors and clinicians with genetics training do not view or treat women with VUSs as either full or qualified patients. Women with VUSs share some experiences with "patients-in-waiting" (Stefan Timmermans & Buchbinder, 2013), such as occupying a liminal state of scientific uncertainty. However, pre-patients usually face clinical uncertainty and are treated like patients in their medical encounters, but genetics experts

explicitly advise against the use of surveillance or interventions in response to VUS results. The sanctioned standpoint within genetic medicine is that women with VUSs should not be considered patients at all because there is no established risk that should be managed or treated.

Despite that official position, previous studies have illustrated that, in practice, women with VUSs sometimes do become patients who access screenings and interventions (Culver et al., 2013; M. L. Murray et al., 2011; Ready et al., 2011). Genetics experts refer to this practice of regarding VUSs as similar to positive results and "treating" them with surveillance or surgery as "VUS mismanagement." The findings of this study support prior research documenting VUS mismanagement in genetic medicine. Genetic counselors and clinicians shared stories with me, both in interviews and during fieldwork at conferences, about women with VUSs being mismanaged. In addition, three of the four participants in this study with just VUSs or variants with conflicting interpretations were offered prophylactic breast surgery, and two of them opted to have the procedure. Yet what this study can reveal about the *existence* of VUS mismanagement is limited given how few women with only VUSs participated. However, by combining those four women's experiences with stories from genetics professionals, data from fieldwork at cancer genetics conferences, and the experiences of ten women who had both a mutation *and* a VUS, the following sections shed light on how VUS mismanagement happens and why it, but not MRM mismanagement, is a focus of concern in genetic medicine.

***Producing Gray Answers***

Providers who have training in genetics all stress the uncertainty of VUS results, and most of them adhere to professional society guidelines that indicate that VUSs should not affect clinical management (Richards et al., 2015). For example, Linda, a genetic counselor who has been working in cancer genetics since the 1990s, described how she explains VUSs to her testing

clients. “So, a VUS is exactly what it says. We don't know whether or not it is connected to cancer risk. And it should not be used for medical management decisions.” Similarly, Jackie, a genetic counselor who works for a BOC genetic testing laboratory, shared what she says to clients about the possibility of VUS results before they are tested. “I say, pre-test, that there is this possibility that we're going to find something, one or more somethings that we do not yet know how to interpret. And we don't make medical decisions based on if it's a true variant of uncertain significance. We don't use that finding to, as I say, to color medical management.” Alexandra, a cancer genetic counselor at a community hospital, said that in recent years she had changed her explanation to emphasize that VUSs should be treated like negative results since most of the time they are reclassified as benign. She conveyed what she says to patients:

> “For practical purposes, you should act as if this test result is totally normal…. You have not been shown to have a mutation. You shouldn't say to yourself that you have a mutation. You have what's called a quirk in the genes. You have this quirk. What does it mean? Probably nothing.” So, I feel like I really try to talk down a patient, just to normalize the situation and to do my best to not allow them to act as if they have a mutation that they're not known to have. *(Alexandra, Genetic Counselor)*

Lisa, a genetic counselor who works at a regional cancer clinic in a mid-sized city, noted that she even emphasizes in her clinical notes and letters to other providers, such as breast surgeons, that VUSs should not affect medical management. “Our phone notes say, you know, ‘Patient had a VUS. This should be treated clinically as negative. This does not indicate any medical management changes or surgeries should happen based on that result.’ Our letter will say the exact same thing.”

Unfortunately, Lisa also shared that despite the “best efforts” of genetic counselors at her clinic to minimize VUS mismanagement, she knew of several women with VUSs who ended up having mastectomy. She recalled two recent cases in which the breast surgeons either did not

understand the uncertainty of VUSs or chose to ignore that uncertainty:

> We are at a cancer center with three certified genetic counselors working with providers that are cancer surgeons, and we have had two patients who have had their breasts removed because of a VUS. And that's here with experts…. I think part of the issue is sometimes the surgeons interpret that as a positive result, despite what we say, despite what our phone notes say, despite what our letters say, they think they know better. *(Lisa, Genetic Counselor)*

Hence, even at a clinic where there were genetics experts and all of the providers met weekly and had excellent coordination, surgeons and patients were uneasy with the uncertainty of VUS results and sometimes responded to those results as if they were sufficient to justify an intervention. Lisa further commented about the detailed letter that she and other genetic counselors provide to surgeons and their clients, "Sometimes I think they don't even read it."

However, most women with VUSs whom I spoke with *had* heard and read the recommendations from their genetics providers. The problem was not that they were unaware that VUSs are scientifically uncertain results that should not affect medical management, but rather that they did not fully believe that explanation. Most women who seek out genetic testing do so because they are trying to determine the cause of their personal or family's history of cancer; there is an existing phenotype, either in their own bodies or their family members' bodies, that is in search of an explanation. Thus, several women believed that there "had to be" a causal link between their VUS and their own or their relatives' cancer(s) despite being told by genetics experts that their VUS results should be treated as negative until otherwise informed. For example, Heather, who was diagnosed with breast cancer at age 34 and subsequently learned she had VUSs on the CHEK2 and MUTYH genes, shared her reaction to women's posts in the CHEK2 social media group:

> I was keeping a close eye on the board, and thyroid, breast, cancer, mastectomy, all the

> words that I know are coming up. And I'm like, "Oh my god! This has to be connected! It just has to be!" I know I don't have the known variant. And then knowing that the CHEK2 is related to the BRCA genes? I mean, that just sealed it for me. I mean, I'm not a scientist, I have no idea how they're related, but if they're connected in any way, that is something. That *must* be something. *(Heather, Age 35, CHEK2 VUS, MUTYH VUS)*

Similarly, Marlene who has a CHEK2 mutation and PALB2 VUS, said that her VUS made her feel even more certain about her decision to have a mastectomy:

> I went to a surgeon, I think, that's pretty reputable and had other CHEK2 patients. Like she has seen—I wasn't her first one. I felt like I was the first one with everyone I saw. And she kind of made it, like, a definite yes in my head, especially with the PALB2 unknown. They tell you, "Oh don't—we're not going to worry about that one because we don't know." But I'm like, "Even having that unknown significance is still significant, right? That's why it's unknown significance!" *(Marlene, Age 35, CHEK2, PALB2 VUS)*

Both Heather and Marlene reinterpreted their VUSs, transforming the uncertain results produced by the black boxes of genetic testing into certain ones I call "gray answers." Rather than seeing their VUS results as scientific unknowns or questions like their genetics providers did, women bestowed those results with explanatory power.

Even women with high genetic literacy sometimes felt nervous about VUSs and transformed them into gray answers. For example, Jessie, who like Marlene has a CHEK2 mutation and PALB2 variant, demonstrated sophisticated knowledge about BOC risk, particularly for a non-scientist, during our interview. Yet she was still concerned about her PALB2 VUS. "The doctor gave me the spiel on variants, and I was fine on the variants until I found out I was PALB2 variant." Jessie was concerned because PALB2 mutations are associated with an increased risk of pancreatic cancer, which is extremely difficult to detect and has, by far, the lowest five-year survival rate of any type of cancer (National Cancer Institute, 2018f). Similarly, Naomi, who has a PALB2 mutation and a CDH1 variant, is a biology professor, and her understanding of genetics made her *more* concerned about her VUS. She said, "It's an

unknown variant, you know, how common is that? To find something, a mutation, some kind of nucleotide substitution, it's probably fairly common. But then I went back in and read the report and then I was like, 'Oh my god! CDH1 is like the worst!' You know, so like panic set in for a little bit." Mutations on CDH1 are associated with multiple cancers, including an 80% lifetime risk of developing stomach cancer, and understanding the science of how a variant could affect protein function added to Naomi's anxiety about having one on the CDH1 gene. Thus, it was not only women with less education or lower genetic literacy who were concerned about the potential risks of VUSs, and having one on a gene in which pathogenic variants are linked to serious cancers heightened women's anxiety.

Much like the "fact" of a positive result encourages women and clinicians to envision the "worst possible outcome," thereby helping to transform the probability of risk into prophecy of an inevitable future (Rajan, 2006), these women's responses to their VUSs illustrate how *any* reported variants, even ones formally labeled "uncertain," are "things" that people can point to as potential causes of their or their family's history of illnesses. While variants labeled pathogenic and highlighted in reports are more factual and have more credibility than variants that are classified as uncertain, once variants are identified and information about them is distributed outside of the laboratory, scientists cannot control how people respond to them. Anyone, not just genetic scientists, can interpret VUSs as harmful and transform them into gray answers. In fact, in contrast to positive and negative results, which are presented as firm facts, the uncertainty of VUSs highlights how risk classifications are constructed rather than preexisting and discovered. By calling attention to the active production of risk classifications that is usually made invisible by the black boxes of genetic testing, VUSs and variants with discordant classifications invite reinterpretation outside of the laboratory in a manner that the firmer "facts" of positive and

negative results do not. By publicly admitting that they do not know how to classify VUSs, scientists open the door for people to view that "unknown significance as significant."

Linda, the cancer genetic counselor who has been practicing for over two decades, noted how people tended to view and treat VUSs like mutations: "There's a bias toward acting upon a VUS as if it's a mutation or a deleterious mutation. There's kind of a bias toward that. So somehow people put more weight on that possibility than the fact that, whatever you do, there's a 50/50 chance you're doing the wrong thing, whichever way you treat it." What Linda meant by this statement was that VUSs treated as benign might end up being reclassified as harmful, and conversely, VUSs treated as harmful might be reclassified as benign. But the probability of "doing the wrong thing" is, in fact, not "50/50." Rather, previous studies have demonstrated that over 90% of VUSs that get reclassified are downgraded to benign or likely benign (Balmaña et al., 2016; Mersch et al., 2018; T. P. Slavin et al., 2018). Thus, the bias toward treating VUSs as if they were mutations is more likely to be "wrong" than treating them as harmless.

Importantly, while women with VUSs and women with MRMs experience different types of uncertainty, their discomfort with their uncertainty often centers on the same problem: not knowing how to effectively respond to their uncertain risk and not having access to screenings or treatments they may want or need. Many BOC genetic testing clients are what anthropologist Sahra Gibbon refers to as "anticipatory patients"—women who have evidence of familial risk but are seeking proof of their high-risk status in order to gain insurance-covered access to increased surveillance and/or risk-reducing surgeries (Gibbon, 2007). Being issued a genetic "finding," even if that finding is characterized by uncertainty about the existence or extent of their cancer risks, only underscores women's concerns about developing cancer and, in turn, their desire to take action to manage those potential risks. Hence, both women with MRMs and those

with VUSs sometimes desire further medicalization because they are uneasy with the liminality of being a qualified patient or a maybe-in-the-future patient. In response, they challenge, negotiate, and reinterpret the significance and meanings of their MRMs and/or VUSs by drawing on knowledge shared in their social networks or gathered through their own research. In addition, similar to individuals with emergent or contested illnesses, women with MRMs and VUSs also develop and share tactics for accessing clinical management services that exceed recommendations in current guidelines (Barker, 2008; Dumit, 2006).

***Gaining Access and Coverage***

As I highlighted earlier in the chapter, there were considerable variations in the risks that women with MRMs were informed about and the screenings that were recommended to them. That unevenness in information and care is characteristic of the private-profit heath system in the United States, in which there are no official protocols for providers of genetic medicine to follow. There are clinical guidelines, but those are suggestions, and health care providers are not required to adhere to them. The fragmented, insurance-based US system, combined with the lack of clinical protocols, produces inconsistency and inequality in BOC genetic medicine, particularly in the Risk Management field of practices. While navigating that uneven terrain, many women in this study turned to online social media groups for information and support. Women shared how finding other women like them helped them feel less isolated and scared. For example, Holly said about her CHEK2 group, "It's like, 'Wow! All these people have the same thing.' And that's helpful to me—it's not just my sister and I. There are all these people across the country who have it too."

Likely because less is known about MRMs than BRCA mutations, women with MRMs, in particular, noted that these groups were not just venues for emotional support, but also vital

sources of medical and scientific knowledge. As Jessie stated about the CHEK2 group she helps to moderate, "I don't think the literature has caught up with the patient…. I don't go there as much for emotional support so much as I do looking for the clinical trends of my 200 people in my tribe that have the CHEK2 mutation that I have." Josephine echoed Jessie's feelings about her CHEK2 group helping women "get ahead" of the scientific literature. "These patient groups are where a lot of knowledge is. They can talk about things and family history and you have to take it with a grain of salt. Sometimes science follows the experiences being shared by the patient population. You cannot always wait for the guidelines." Marsha shared how she thought of the women in her CHEK2 group as part of an extended scientific and clinical care "team." She said, "People at the grassroots level who have this knowledge, now, because of the computer, can be connected to help figure out the puzzle…. I have all these people on my team now that are working to figure out what they can." What Jessie, Josephine, and Marsha were pointing to with these statements is how some women at BOC genetic risk engage with these topics as lay experts (Susan E. Bell, 2009; Epstein, 1996). That lay expertise was also evident in the responses of several women in this study who demonstrated sophisticated genetic knowledge and had put considerable effort into reading and understanding their results.

Several women with MRMs shared how they learned through their social media groups about additional screening tests and/or surgeries to request from their doctors. For example, Marlene was advised in her CHEK2 group to ask her primary care doctor to scan her thyroid even though that screening is not recommended in the current NCCN guidelines (National Comprehensive Cancer Network, 2018b). "I am now getting a thyroid ultrasound in a couple weeks because I demanded it," she explained. Jessie also began insisting that her doctors order

thyroid screenings, and she requested more frequent colonoscopies[25] after learning more about her risks from women in her group:

> Everybody will do what I ask. As far as, I told my GI I'm having annual colonoscopies. He's not giving me a hard time. Otherwise it's either make stuff up or I find a GI that would give me annual colonoscopies. My thyroid doctor is going along with my every-six-month thyroid ultrasound. That is about as benign of a procedure that you can get, and now I'm going to beat thyroid cancer to the punch. *(Jessie, Age 48, CHEK2)*

Jessie's comment that she would have either faked symptoms or searched for another doctor if her GI specialist had denied her requests highlights two other things women indicated they had learned through their social networks and advocacy groups: strategies for accessing screenings and/or surgical services that their providers initially denied and how to get those tests and procedures covered by insurance.

The first tactic women described learning about and using was feigning symptoms. For example, Margaret described how women in her CHEK2 group had listed specific symptoms they could relay to their doctors in order to get thyroid ultrasounds covered. "Interesting enough, women are sharing that on the CHEK2 site—that you are hoarse or that you have pressure there." Margaret then used those symptoms to justify getting an ultrasound, but she let her doctor in on the ruse. "I shared with her why I wanted one, and then we figured out how to get around the insurance problem. I had some symptoms suddenly." Jessie also described feigning symptoms to get her screenings covered while ensuring that she made what she was doing clear to her clinicians:

> Look, the first thing you have to do is lie to a physician. I actually—if I'm going to lie to my physician, my Gyn/OB, I kind of make it clear that she kind of knows that I'm about

[25] NCCN currently recommends that women with CHEK2 mutations have colonoscopies every five years beginning at age 40, which is 10 years earlier and twice as frequent as the recommendations for women in the general population (National Comprehensive Cancer Network, 2018c).

> to lie to her. So, we're still kind of on the same page, she's still doing her due diligence of whatever she needs to do for her medical stuff. But if I had insurance that did not cover my colonoscopy unless I was having rectal bleeding, I'm telling you right now my butt is bleeding. *(Jessie, Age 48, CHEK2, VUS-PALB2)*

Margaret was angry that she and other women with CHEK2 mutations had to pretend to have symptoms in order to get insurance companies to cover the costs of screenings for cancers for which they were told they had higher-than-average risk. "Also, it is frustrating sometimes. Like, the thyroid thing. In the CHEK2 support group, there are a lot of women popping up on there that have thyroid cancer and they are finding it because they demanded that somebody pay attention. And so that makes me angry. It's like, a thyroid screen is an ultrasound. It is very low cost and has no side effects. Why don't they give it to everybody who has a CHEK2 mutation? How hard is that?"

The second tactic women shared with one another in their social networks was "doctor shopping"—the practice of seeing multiple clinicians until finding one who agrees to perform a desired test or procedure. For example, the first two surgeons Penelope saw refused to perform mastectomy to manage her CHEK2 variant, one that has conflicting interpretations, because they said that it was not clinically indicated. However, she had other doctors who had recommended the procedure to her. Buoyed by women in her CHEK2 group, she continued to seek out a doctor who would perform the surgery:

> The first doctor was like nope. Two times [the risk] is not enough. Have a good day. My gynecologist, oncologist, and urologist recommended that I get a mastectomy, and in my CHEK2 support group there is another person who has my exact mutation—there is only 300 of us in there—and she had stage four metastatic breast cancer. So, I was like, "Nahhh! I do not care what your paper says." Once I found out that—originally, I think I just wanted some information. But the more I looked into it, the more I wanted the surgery. I do not care if I have a 2% risk. It is a low-risk surgery and it reduces my risk. I am not removing my colon and living with a bag. It is a low-risk surgery. Let us get it done so I do not have to worry about it…. The third doctor that I met with agreed to do

> the surgery. It is relatively—especially given my age, and aside from cancer, I am pretty healthy—a low-risk surgery. I would ten times rather have a low-risk unnecessary surgery than wait and have to have the surgery because I have breast cancer down the road. *(Penelope, Age 32, CHEK2, conflicting interpretations)*

Penelope acknowledged that she might be having an "unnecessary surgery" but felt strongly that surgery was a better option than potentially developing cancer. Deena, who has a CHEK2 VUS, also did not want to risk getting cancer, so she met with multiple surgeons until she found one who was willing to perform mastectomy. She explained, "I do know that supposedly my CHEK2 is linked less—more likely colon and less likely breast, but I figured I didn't want to take the risk." Likewise, Heather, who has VUSs on the CHEK2 and MUTYH genes, shared how her first surgeon advised against contralateral prophylactic mastectomy (CPM) of her healthy breast, but she subsequently found a doctor who would perform the procedure. "I looked into it, and I asked the breast surgeon, and they didn't know. No one could give me information. They said, 'We don't know. It's not connected. You shouldn't take the other breast because of it. It's not a big deal.' So, I thought, 'I *gotta* take the other breast.' It was my first instinct. So, I did a double mastectomy."

Jessie combined feigning symptoms with doctor shopping in order to gain access to services she desired. She wanted to have a hysterectomy because, based on her own research and what she had learned through her CHEK2 social media group, she was concerned about a possible link between CHEK2 mutations and ovarian cancer. Because there is general consensus around CHEK2's associations with female breast and colon cancer but not ovarian cancer, the first couple of doctors Jessie met with adhered to the NCCN guidelines and refused to perform the procedure because it was not recommended. But she was persistent and continued to seek additional opinions until she found a responsive doctor whom she trusted. She recalled their conversation:

> I said, "I need to let you know that I'm going to have a hysterectomy. I want you to be my surgeon. So, I guess what I need to know is, if I walk out the door today and go home and have extreme heavy uterine bleeding that doesn't go away after a day or two, can I call you for my hysterectomy?" And she looked at me like, "Seriously?" And she said, "Yeah, if you call me and tell me you're having really heavy, abnormal bleeding, we'll do your surgery." So, I waited until the end of December, and called and said, "Hey! I'm having really heavy bleeding, it won't stop after two days, I want a hysterectomy." *(Jessie, Age 48, CHEK2, VUS-PALB2)*

Jessie also went to see five different breast surgeons in order to have CPM. She explained why she was tenacious and continued searching for a doctor who would perform the surgery:

> The first four surgeons that I got opinions from, all four said they would only do a single mastectomy, and they would not take off the healthy breast. And I said, well I'm not keeping the healthy breast, it's going. I mean, I saw pictures of reconstruction. Two things: 1. I'm not going to be a unicorn. So, if I don't get reconstruction I'm not going to have one breast. And 2. I saw reconstruction of one new breast and one healthy breast, and my new breast was going to be happy and my old breast was going to be a normal 48-year-old breast, and I'm not going to do that either. The fifth surgeon that I saw, I said, look—same story with the GYN-Oncs: "Look, you're going to be my surgeon. I already know this, and I'm having a bilateral mastectomy. And I understand that you have a dissertation to give me on why I don't need my right healthy breast removed. But I want to confirm you are comfortable with taking it anyway." She said, "Yup. You're the patient. Let's do it."

Together, these stories highlight how in the fragmented, fee-for-service US health system, women who are persistent and either have financial resources or insurance coverage that allows them to see a broad network of providers can usually find doctors who will surgically manage their risk regardless of the penetrance or pathogenicity of their variants.

However, women's stories also reveal that there are a variety of complex reasons why they advocate for themselves and seek services that are not formally recommended. Some women and their clinicians without genetics training were unaware of the current guidelines for managing MRMs and VUSs. However, many women in this study were fully aware of those recommendations but actively challenged them because they felt that getting certain screenings

or surgeries was what was best for their bodies and lives. When women with MRMs and VUSs engage in practices like feigning symptoms and doctor shopping, they are seeking what sociologist Kristen Barker refers to as "physician compliance" in her study of women with contested illnesses —the willingness of doctors to concur with their assessments of their risks and the best ways to monitor those risks (Barker, 2008, p. 31).

The response Jessie's breast surgeon provided—"You're the patient"—sheds light on why some providers are willing to "comply" and respond to symptoms they know are feigned or perform surgeries they know are not clinically indicated. The clinicians in genetic medicine whom I interviewed and encountered over more than three years of fieldwork were largely motivated by a desire to help their patients. Many of them were actively striving to provide patient-centered care and to employ a model of shared decision-making—to listen to their patients wants and needs and factor them into the decision-making process. In addition, health professionals, like patients, are human beings with their own feelings and life experiences. Some clinicians I met who worked in genetic medicine had chosen to pursue their medical specialties because of their own family's experiences with hereditary BOC cancers. Given that many health professionals both care about their patients and witness the unevenness of care in the insurance-based US health system, it is not surprising that some are willing to, as Jessie said, "be creative" in order to help their patients navigate those varying insurance restrictions and obtain coverage for their care.

I observed one provider, during a breakout session at an advocacy conference, openly encourage a woman to deploy creative tactics in order gain insurance coverage for a desired screening. The session was devoted to cancers other than breast and ovarian that are associated with BOC mutations, and the conversation had turned toward pancreatic cancer. One patient

shared her frustration that she had been unable to get her insurance company to cover the cost of endoscopic ultrasounds (EUSs) even though she had a BRCA mutation and a brother who had died of pancreatic cancer. The current screening guidelines state that EUS is indicated when two first degree relatives have had pancreatic cancer, not one (Canto et al., 2013). A genetic counselor in the room responded to her, "They don't check. All I'm saying is, when you give a family history, they don't verify it." While subtler than Jessie's explicit directive to lie, this genetic counselor was suggesting that the woman say she had two relatives with pancreatic cancer rather than one so she could gain access to insurance-covered screenings. And her strategy would, indeed, be effective for women whose insurance companies base their coverage for services on current guidelines because clinicians and insurance companies cannot legally demand proof of family history due to patient privacy protections.

***Boundary Work***

The previous section illustrated how women employ various tactics to manage the uncertainty of MRMs and VUSs, and in the uneven and unequal terrain of the US health system, some health care providers are willing to partner with them in that process. However, whether these practices are interrogated and critiqued by genetics experts or are largely overlooked and sanctioned by the field varies both by the type of service provided and who is seeking that service. For example, providing women with additional screenings that are not recommended among women in the general population, such as MRIs and ultrasounds, is barely discussed among professionals in genetic medicine, either at scientific conferences or in the literature. Given that most types of surveillance are low-risk, the absence of critique or examination of screening mismanagement in the field, whether it occurs among women with MRMs or VUSs, is unsurprising. While screening procedures can generate false positives that lead to more invasive

follow-ups, and they occasionally have risks of their own, such as reactions to MRI contrast dye, most surveillance is fairly benign.

In contrast, surgical mismanagement is widely examined and critiqued by genetics experts, but, importantly, *only when it occurs among women with VUSs*. Several studies have investigated surgical mismanagement of VUSs, and commentaries and reviews that grapple with the issue have also been published in the medical literature (Culver et al., 2013; S. Domchek & Weber, 2008; Miller-Samuel et al., 2011; M. L. Murray et al., 2011; Ready et al., 2011; Vos et al., 2012). In addition, sessions that focused on minimizing VUS misinterpretation and mismanagement were regularly offered at medical genetics conferences during the three years I conducted fieldwork, and discussions in other sessions sometimes veered toward the topic. Yet "MRM mismanagement"—providing mastectomy or RRSO to women with MRMs, which is not supported by current evidence-based recommendations—remains largely invisible in the discourses of genetic medicine, despite, as I will illustrate in Chapter Two, the practice being exceedingly common. Other than a few individual conversations with health professionals, in over three years of research, I never encountered articles or conference sessions focused on MRM mismanagement.

In her study of prenatal genetic screenings, medical anthropologist Rayna Rapp highlights how the US medical system tends to classify women as "good" or "bad" based on their health behaviors. "In the United States, multiple iterations of our sex/gender system index our medico-legal system: We have normative and deviant reproducers, just as there are justified and selfish aborters, or good women and bad women" (Rapp, 2000, p. 307). While Rapp was examining reproductive medicine, the same patterns are evident in BOC genetic medicine. Some women are considered "good," adherent patients, while others are "bad," noncompliant ones, and there is

"appropriate" and "inappropriate" medical management of BOC genetic risk. Given that mastectomy is not clinically indicated for either women with VUSs or MRMs, why are experts within genetic medicine concerned about the former but not the latter? Both women with VUSs and women with MRMs who have surgeries are being subjected to the risks of procedures that may provide them with limited to no benefit to their physical health; yet, managing VUSs with surgery is criticized, while managing MRMs with surgery is not only ignored, but often encouraged.

The disparity between the responses to surgical mismanagement of VUSs and MRMs is, in part, a reflection of boundary work performed by the scientists and health professionals in BOC genetic medicine who are considered genetics experts. Sociologist Thomas Gieryn first used the phrase "boundary work" to describe how scientists demarcate their work from non-scientists in order to protect their credibility and authority in their professional domains (Gieryn, 1983). As I have highlighted throughout the chapter, VUSs reflect uncertainty about the *existence* of risk, and that uncertainty is identified within the Risk Production field of practices (Figure 2). The professionals in that field who are most directly involved in the interpretation of variants and the production of VUS results are genetics experts: clinical geneticists, laboratory scientists, and genetic counselors. Among those experts, there is widespread consensus that since VUSs have not yet been classified as "risky" they should not affect medical management. When there is uncertainty in the field of practices that produces genetic risk, the individuals with the expert knowledge on variant classification have not issued a "positive result" and declared that any risk exists. Therefore, those experts agree that there should be no change in actions in the Risk Management field of practices because *there is no risk that warrants a response*. As I illustrated earlier in the chapter, genetics laboratories and genetic counselors often engage in discursive

practices that minimize the visibility of VUSs in order to prevent testing clients and non-genetics providers from "treating" VUSs as risk.

When women and providers without training in genetics disregard the cautions of those experts and seek or provide surgery in response to VUSs, they are reinterpreting the meaning of those variants and thereby challenging the expertise of the scientists and practitioners involved in the initial interpretations. Whether or not that challenge is intended, having or performing mastectomy for a VUS indicates that the patient, surgeon, or both believe that the VUS is *not* uncertain and poses some risk. Lisa, a genetic counselor, discussed surgical VUS mismanagement that she had witnessed at her cancer clinic, and she framed the issue as a struggle over authority between the genetics experts on the clinical team, most of whom were not physicians, and the members without expertise in genetics, who mostly were physicians:

> Part of the issue is if I tell a patient that they don't need a surgery, and I'm not a doctor, and then they go see a breast surgeon who says they are a perfect candidate for a surgery, and they're an MD and they're a breast surgeon, who is the patient going to listen to? The doctor. So, I don't think that the patient is getting all of the info that they should be getting, and the balanced discussion that they should be getting, from some of our breast surgeons. Despite our best efforts. *(Lisa, Genetic Counselor)*

By noting that patients were not receiving the "balanced discussion that they should be getting" from breast surgeons about VUSs, despite the "best efforts" of the genetics team, Lisa's statement highlights how individuals with expert genetic knowledge, such as genetic counselors and laboratory scientists, are sometimes perceived as having less credibility and authority on variant interpretation and management than non-experts because they are not medical doctors. In response, genetics experts engage in boundary work—they attempt to reassert their jurisdiction over variant interpretation and (mis)management and to protect their domains of expertise by conducting studies, writing articles, and actively discussing VUS mismanagement during

scientific meetings (Abbott, 1988; Gieryn, 1983).

But these discourses in genetic medicine that are critical of VUS mismanagement are not solely about the risks to patients; if they were, experts would also critique MRM mismanagement. Rather, as science studies scholar Steven Epstein stated in his study of the politics of AIDS activism and knowledge, "debates *within* science are simultaneously debates *about* science and how it should be done—or who should be doing it" (Epstein, 1996, p. 3). Hence, the ongoing debate over VUS reporting, misinterpretation, and mismanagement in genetic medicine is both a debate about patient care and a debate about *scientific expertise*. Genetic experts are contesting the reinterpretations of and challenges to expert knowledge that are required for VUSs to be conceptually reclassified as "risky" and thus become medically mismanaged in the first place.

In contrast to VUSs, there is no uncertainty about whether MRMs are classified as risky in the Risk Production field of practices (Figure 2). The scientific and clinical experts who produce genetic risk have firmly interpreted MRMs as harmful and made them clearly visible to patients as "positive" findings. The *degree* to which MRMs elevate breast cancer risk and the other cancers with which they are associated may be in question, but *whether* MRMs increase women's risk of breast cancer is not. Once variants are classified as pathogenic or likely pathogenic and labeled mutations by experts, women have been "diagnosed" with genetic risk for breast cancer. That risk may be either moderate or high, but the risk "exists;" it is a "fact" according to scientists, and therefore a clinical response in the Risk Management field of practices is not only sanctioned, it is often expected. Since no reinterpretation of risk is required to "treat" MRMs, neither the women who seek surgical responses to them nor their surgeons are encroaching on the authority of genetics experts. In fact, determining optimal courses of

treatment for patients with clear diagnoses falls squarely within clinicians' and surgeons' domains of expertise, not genetic scientists' or counselors'. Hence, women and breast surgeons may be exceeding the recommendations in current guidelines for managing MRMs, but that mismanagement is only a matter of degree and does not challenge the jurisdiction of the genetics scientists and providers who make risk factual. In turn, there is no need for genetics experts to perform boundary work around MRM mismanagement, which helps to explain the absence of a collective discourse or professional response to the issue, despite it being, as I will illustrate in the following chapter, a pervasive phenomenon with potentially serious health implications for women.

**Conclusion: How Risky? Which Responses?**

This chapter examined how, in the wake of the transition to multi-gene panel testing, risk for breast and ovarian cancer was geneticized, genetic risk was medicalized, and in turn, these shifts have reconfigured the boundaries of risk, illness, and patienthood. Drawing on stories from women and providers and test results reports from the five major BOC genetic testing laboratories in the United States, I argued three main points. First, that the geneticization of cancer risk and practices that black-box the active production of genetic risk make cancer seem inevitable because testing directs attention toward the seemingly certain "facts" of mutations rather than the uncertain probability of developing cancer that those mutations signal. Second, in contrast to literature that has theorized genetic susceptibility as a liminal space between sickness and health, I argued that panel tests have contributed to a spectrum of medicalization of BOC genetic risk. Women with high-risk mutations have patienthood experiences that are almost indistinguishable from those of people with diseases, while women with MRMs are "qualified patients" who have also been "diagnosed" with the "disease" of genetic risk but lack formally

sanctioned access to "treatments" like surgical interventions. VUSs, however, are contested sites of medicalization; some women with VUSs actively seek medical management and patienthood status, while genetics professionals actively work to prevent the clinical management of VUSs. Finally, I argued that professional boundary work accounts for the discourses in genetic medicine that critique surgical VUS mismanagement but mostly overlook surgical MRM mismanagement, despite the pervasiveness of the latter.

Collectively, the stories and examples shared in this chapter reveal that there is no static, preexisting, objective "truth" about people's cancer risk that gets discovered by panel tests. Rather, BOC genetic risk is a moving target. Not only are the results of genetic tests actively coproduced through social and technological processes, but also the scientific and clinical relevance of mutations are constantly in flux, and patients and providers are agents who reinterpret those results and negotiate their responses to them. Clinicians and genetic counselors may provide women with specific numeric risk estimates, as Angelina Jolie's doctors did when they informed her that she had an "87 percent risk of  breast cancer and a 50 percent risk of ovarian cancer" (Jolie, 2013). However, even those seemingly firm risk numbers are constructions, as they are statistical abstractions of data from populations in previous studies that have ascertainment bias.[26]

Yet even if accurate individual-level risk estimates could be generated, the experiences of women with MRMs and VUSs shared in this chapter illustrate how people's responses to genetic

[26] Ascertainment bias is bias generated by the selection criteria or data collection methods for a study. Risk estimates in cancer genetics are broadly acknowledged to suffer from ascertainment bias because they are mostly generated from studies of women who either already had cancer or came from extremely high-risk families. Since the proportions of people in those populations with mutations are likely to be higher than in the general population, the selection criteria of the populations in the studies distorts the estimates (Obeid, Hall, & Daly, 2017; Sorscher, 2018).

test results are not rational or calibrated according to the specific numeric percentages of risk that get communicated to them. Whether they are told they are 23% likely to develop cancer or 87% likely, once any findings are made tangible and reported—sometimes even if those findings are uncertain—people often envision the worst outcome and want to take action to prevent that outcome from occurring. The "facts" of "positive" results make risk seem more real even among women whose risk was visible through their family histories prior to testing. Moreover, as genetic risk is increasingly medicalized, one of the consequences is that medicalization generates a desire among patients to "treat" that risk. As Nikolas Rose stated, risk thinking "denotes a family of ways of thinking and acting that involve calculations about probable futures in the present followed by interventions into the present in order to control that potential future" (Rose, 2007, p. 70). In the following chapter, I will examine how the structures and architecture of US genetic medicine encourage women to seek one of those "interventions into the present" that can "treat" their risk: prophylactic risk-reducing mastectomy.

## Chapter 2: "Risk Is Continuous, and yet Responses Are Dichotomous": Risk-Reducing Mastectomy in US Genetic Medicine

> "There seems to be a huge movement in the country to do this prophylactic surgery." *(Ingrid, Age 62, PALB2)*

> "It's the *when* you're going to have it, not *if* you're going to have it." *(Marci, Age 39, BRCA2)*

> "So, it's only kind of more recently with next-gen panel testing and also a more broad acceptability, if you will, of genetics that we have had to wrestle with this idea that the risk is continuous, and yet responses are dichotomous. So, you have to pick a point at which somebody stops doing the average and starts doing something more than average…. And how you determine where that point is, is, I think, a societal question." *(Steve, Oncologist)*

### Introduction

The factors that shape whether and why women with BRCA mutations undergo risk-reducing mastectomy (RRM), along with the outcomes of their surgical experiences, have been widely examined in the fields of genetic counseling and clinical genetics (D. G. Evans et al., 2009; Gilbert et al., 2017; Glassey, Ives, Saunders, & Musiello, 2016; Howard, Balneaves, & Bottorff, 2009). However, few social scientists have explored women's experiences with prophylactic breast surgeries, and those who have typically have focused on psychological, familial, or interpersonal dimensions of women's decisions (Dagan & Goldblatt, 2009; Nina Hallowell, 2000; Hamilton, Williams, Bowers, & Calzone, 2009; Hesse-Biber, 2014). This chapter, instead, examines the social and structural factors that constrain and enable women's medical management options and facilitate the selection of certain choices over others. Drawing on three years of fieldwork at cancer genetics conferences and interviews with 75 women with breast and ovarian cancer (BOC) mutations and/or variants, I analyze how and why uptake of prophylactic breast surgery is high in the United States. I illustrate widespread departures from the risk management guidelines for women with moderate-risk mutations (MRMs), revealing

how US genetic medicine financially and socially incentivizes mastectomy and frames it as the bravest and best medical choice, regardless of the penetrance of women's mutations.

I argue that the practices of cancer panel testing and risk-reducing mastectomy mutually justify, sustain, and define one another. Pathogenic findings on genetic tests legitimize breast cancer risk and have become required for insurance-covered access to prophylactic breast surgery—without genetic knowledge, mastectomy would be considered drastic, not brave. At the same time, prophylactic breast surgery validates the utility of cancer genetic testing by providing a mechanism for transforming its abstract, molecular knowledge into action and power—without the treatment of surgery, genetic knowledge would not be power, it would merely generate anxiety. Through a close examination of the mastectomy experiences of women in the United States with both high- and moderate-penetrance mutations, this chapter sheds light on how and why risk-reducing mastectomy has become the standard and preferred treatment for the "disease" of BOC genetic risk.

***Departing from the NCCN Guidelines***

As I explained in the previous chapter, the *NCCN Guidelines* recommend discussing the option of mastectomy with BRCA1/2 mutation carriers but not with women with MRMs. Most of the health professionals I interviewed indicated that they followed the *NCCN Guidelines* when counseling and treating patients. For example, Linda, a genetic counselor, said, "I find myself reviewing the medical literature often. But also the NCCN guidelines. Those are a really nice summary of what do we know right now, and they get updated at least once a year. And they have some guidance in there." Similarly, Steve, an oncologist, stated, "NCCN in particular has become a bit of an arbiter." Jackie, a genetic counselor at an academic medical center who began working in cancer genetics at the field's inception, explained how she utilizes the specific

language in the *NCCN Guidelines* when discussing risk management.

> I explain what the current guidelines are. For example, if we're talking BRCA, I will explain bilateral mastectomy as an option. It's one of the *options*. Whereas removal of the ovaries and tubes is a *recommendation*. I explain there's a difference in the wording there, and there's a reason there's a difference in that wording. So, we fall back on what the current guidelines are. And NCCN is constantly tweaking even BRCA guidelines and then coming up with more information for some of these other genes as well. *(Jackie, Genetic Counselor)*

However, the guidance patients reported receiving and risk-management options presented to them rarely aligned with the nuanced recommendations in the guidelines. As I will illustrate in Chapters 3 and 4, very few women reported being counseled about the full range of surgery-related issues that the NCCN guidelines recommend discussing; instead, many conveyed that they were un- or under-prepared for the side-effects of RRSO and breast reconstructive surgeries.

In addition, the nuanced distinctions between "no risk" and "insufficient evidence" and what clinicians should "recommend," "discuss," or "consider" are murky in practice and rarely had an impact on women's understandings of the guidance they received. For example, Marci recalled her initial conversation with her genetic counselor after discovering she was BRCA2-positive.

> So, I said, "Well, what's the recommendation?" And she said, "Well, you know, we recommend that you have a double mastectomy and we recommend that—" either recommend or consider. I think they were—they couldn't recommend it. She's not a doctor; she's a genetic counselor. So, she was very clear on the boundary. What I heard was a little different. What I heard was, "Cut off your breasts and cut out your ovaries" was what I heard. *(Marci, Age 39, BRCA2)*

Like Marci, nearly all the women I interviewed, whether they had high- or moderate-risk mutations, indicated that mastectomy had been presented not only as a possible option, but also often as the recommended and desired option.

In fact, of the 38 women I interviewed who had MRMs, all but *one* were offered the

option to have either contralateral prophylactic mastectomy (CPM) or bilateral prophylactic mastectomy (BPM).[27] Among the 37 women offered mastectomy, nearly two-thirds of them had already had the surgery or were planning to have it in the near future (Table 3). In addition, all three[28] women who learned they had VUSs prior to undergoing any interventions were offered mastectomy, and two of them chose to have surgery (Table 3). The high prevalence of RRM among carriers of genetic mutations is unique to the United States. Other countries have much lower prevalence of BPM among unaffected[29] women with high- and moderate-risk mutations and CPM among mutation carriers with breast cancer (Laitman et al., 2014; Mamtani & Morrow, 2017; K. A. Metcalfe et al., 2008; K. A. Metcalfe, Goel, Lickley, Semple, & Narod, 2002; Nash et al., 2017). So why is mastectomy a consistent practice in the otherwise uneven landscape of US genetic medicine?

[27] CPM and BPM are both forms of risk-reducing mastectomy. CPM is the removal of an unaffected breast in a woman with cancer and BPM is the removal of both healthy breasts. Some women who have breast cancer have genetic testing to help them determine whether they should have CPM, as a higher risk of a second primary breast cancer is associated with some mutations. However, genetic testing is only recommended in a limited subset of breast cancer patients since most breast cancers are not genetically linked. In addition, some women who have mastectomy and CPM are candidates for lumpectomy, and therefore they are choosing both treatment mastectomy and a risk-reducing surgery.

[28] There were four women who participated in this study who had no pathogenic variant and only a VUS in a gene associated with breast cancer risk. However, in 1982, over a decade before the discovery of any mutations associated with breast cancer, one of those women, Marsha, had a prophylactic mastectomy based on her family history. Because her VUS was not known at the time of her RRM, I do not include her in the group of women with VUSs who were offered mastectomy.

[29] I use the phrase “unaffected women” as a concise way to refer to women who have never experienced cancer in their own bodies. I recognize that many, if not most, of the women whom I describe with this phrase have loved ones who have experienced cancer and therefore have lives that have been deeply affected by the disease.

| Breast Surgery | BRCA1/2 | Moderate Risk Mutations | VUS or Conflicting | Family History | Total |
|---|---|---|---|---|---|
| **Not Offered** | | **1** | | | **1** |
| **Had/Having RRM** | **25** | **24** | **2** | **1** | **52** |
| BPM | 13 | 6 | 1 | 1 | 21 |
| CPM | 5 | 11 | 1 | | 17 |
| Scheduled/Planning | 7 | 7 | | | 14 |
| **Declined/Undecided** | **8** | **13** | **1** | | **22** |
| Undecided | 4 | 4 | | | 8 |
| Not Planning | 4 | 3 | | | 7 |
| Lumpectomy | | 6 | 1 | | 7 |
| **Total** | **33** | **38** | **3** | **1** | **75** |

**Table 3: Number of Women Offered Breast Surgeries, by Decision and Variant Type**

**Desiring Mastectomy**

Previous social science scholarship has examined a complex array of individual and relational factors that affect the risk management decisions of women at high risk for breast and ovarian cancer. For example, studies have shown that the breast cancer experiences of women's mothers—in particular, whether their mothers survived—and being a mother both notably influence women's feelings and decisions about risk-reducing surgeries (Dagan & Goldblatt, 2009; Gibbon, 2007; Nina Hallowell, 2000; Hamilton et al., 2009; Hesse-Biber, 2014). In this study, I move beyond an individual-level analysis of women's decisions and instead explore the social and structural dimensions of US genetic medicine that shape those decisions and encourage certain choices over others. Analyzing the system-level factors that encourage high uptake of prophylactic breast surgery in the United States requires an understanding of both why women at BOC genetic risk desire mastectomy and how the procedure has become widely accessible to women, even when many of them do not meet the criteria specified in clinical guidelines. In this section, I illustrate, through women's voices and stories, the four most common reasons they shared for wanting prophylactic breast surgery: to prevent chemotherapy

and other difficult treatments, to reduce their stress and anxiety about developing cancer, to "be there" for their children, and to save their lives.

### *Preventing Breast Cancer and Intensive Treatments*

Mastectomy is extremely effective at reducing women's risk of developing breast cancer. Women who have the procedure reduce their lifetime risk of developing breast cancer to approximately 5%, which is less than half of the 12% lifetime risk of women in the general population (S. M. Domchek et al., 2010; Kuchenbaecker et al., 2017; A. W. Kurian et al., 2010; Li et al., 2016; Razzaboni et al., 2012). In addition, mastectomy is relatively quick and safe when compared to many other major surgeries. The procedure takes, on average, two hours, and the most common risks and side effects are ones associated with any major surgery, such as pain, infection, swelling, numbness, and/or scar tissue formation (Breastcancer.org, 2013; Eisemann & Spiegel, 2018). Mastectomy is also a relatively straightforward decision, as there are limited options to weigh. Women who desire reconstruction are sometimes offered the option of nipple-sparing surgery, which removes the glandular breast tissue but leaves the breast skin and areola intact in order to create a more "natural" reconstructed look. Current estimates for women's lifetime risk of breast cancer when they have nipple-sparing mastectomy is 8%, so slightly higher than that of women who have RRM without nipple-sparing surgery but still below the lifetime risk of women in the general population (Galimberti et al., 2017; Jakub et al., 2018). A similar option that is sometimes offered is skin-sparing mastectomy, which preserves all of the skin around the breast except for the nipple and areola, which are more connected than other skin to the underlying glandular tissue and therefore are the most likely areas to contain some cancer cells (Galimberti et al., 2017).

The alternative to mastectomy for women at high risk of breast cancer is to undergo semi-

annual breast screenings that typically include clinical manual breast exams and alternate between breast MRI and mammography. The goal of breast surveillance is early detection. By examining and imaging women's breasts every six months, if breast cancer develops, it is usually caught in its earliest stages of growth, when it most likely to be curable. However, curing breast cancer, even when it is detected early, at minimum involves surgery (either mastectomy or lumpectomy) and may also require other intensive treatments, such as radiation, chemotherapy, immunotherapy, or other drug therapies. For example, women who have low-stage, low-grade[30], hormone-receptor-positive cancers are often candidates for lumpectomy, which removes only the area directly affected by cancer, thereby conserving a majority of the breast. But the standard of care for women who have lumpectomies also includes several weeks of localized radiation treatments in order to ensure that any dormant cancer cells that were missed during surgery are killed. In addition, women with early-stage, hormone-receptor positive breast cancers are typically prescribed anti-estrogenic drugs (either a selective estrogen receptor modulator or an aromatase inhibitor) for 5 - 10 years post-surgery. These drugs have a range of side effects, including increased risks of blood clots, bone loss, joint pain, hot flashes, vaginal dryness, and endometrial cancer (National Comprehensive Cancer Network, 2018a). Hence, women who have mastectomy undergo a more invasive *surgical* procedure than they would require if they developed a low-grade, low-stage, hormone-receptor-positive cancer, but they avoid radiation treatments and ongoing drug therapies.

In addition, there are circumstances in which clinicians will recommend chemotherapy

[30] The *grade* of a cancer indicates how abnormal the cells appear and behave at a molecular level. It is distinct from the *stage* of a cancer, which refers to how extensively the cancer has penetrated tissues in the body (i.e., the tumor size and how far the cancer cells have spread). At any stage, low-grade cancers appear similar to normal cells and are slower-growing; high-grade cancers look atypical and are faster-growing and harder to treat (National Cancer Institute, 2018c).

and/or immunotherapy even when a breast cancer is caught early and localized. For example, approximately 25% of breast cancers test positive for HER2 protein[31] overexpression. HER2-positive cancers tend to be more aggressive—they grow quickly and are more likely to metastasize and recur than HER2-negative cancers (Onitilo, Engel, Greenlee, & Mukesh, 2009; Parise, Bauer, Brown, & Caggiano, 2009). However, certain immunotherapy drugs are extremely effective at targeting the HER2 growth pathway and killing those cells. As a result, women with early-stage HER2-positive cancers are usually treated with immunotherapies in order to reduce the likelihood of recurrence or spread. Similarly, breast cancers that are negative for HER2 overexpression *and* for estrogen and progesterone receptors, which are called "triple-negative" breast cancers, are also aggressive and more likely to metastasize and recur. But they are even harder to treat than HER2-positive cancers because they do not respond to immunotherapies or hormone-blocking drugs. Therefore, regardless of stage, oncologists almost always recommend that women with triple-negative breast cancers be treated with chemotherapy.

Women with BRCA1 mutations are disproportionately likely to develop triple negative breast cancer. Approximately 70% of BRCA1-associated cancers are triple-negative, compared to only 12-14% of total breast cancers(K. N. Maxwell, 2015). In addition, a recent study found that the absolute risk of developing triple-negative breast cancer was 18% for carriers of BRCA1 mutations, 10% for women with PALB2 mutations, and 6% for women with BRCA2 mutations, which range from five to 16 times greater than the absolute risk in the general population (Shimelis et al., 2018). As a result, even when surveillance is effective at detecting breast cancer early, a majority of women with BRCA1 mutations and a sizable proportion of those with mutations on PALB2 and BRCA2 will likely require chemotherapy treatments if they develop

[31] HER2 proteins are receptors on breast cells that control cell growth, division, and repair.

cancer. Nina's story provides an example of such a case.

Nina discovered her BRCA1 mutation relatively young, at age 26. Despite being encouraged to have mastectomy by clinicians, family members, and other women with mutations, she elected to continue with surveillance. Surveillance was effective for Nina—when she developed breast cancer nine years later, it was caught at an early stage. However, she explained that no one had ever informed her that as a BRCA1 mutation carrier she was at high risk of developing a triple negative cancer and therefore of needing chemotherapy.

> I knew the goal was early detection. But the only thing I guess I was frustrated about was that no one said triple negative is a thing, and if you get triple negative, no matter if it's Stage 1, you're still gonna do chemo. Like, I didn't have any concept of that part. That part I was like, "Well wait. So early detection, you know, wouldn't have changed a thing?" Well yeah, I mean, I guess it changes the risk of it metastasizing, but other than that, the treatment would still have been the same. So, it would have been helpful to know that information in advance. *(Nina, Age 35, BRCA1)*

Nina clarified that she was not upset that chose surveillance over mastectomy. "I don't regret doing surveillance anyway. I got to keep my healthy breast tissue for quite a while." But she wished she had been informed about her disproportionate likelihood for needing chemotherapy treatment even when surveillance achieved its "goal" and detected cancer early.

Nina's story reveals an important, but often under-emphasized, benefit of mastectomy—that by reducing women's risk of developing breast cancer, it also reduces women's risk of needing toxic treatments. Beverly, a woman with a BRCA1 mutation whom I met a conference, explained that avoiding the painful and difficult treatments she had witnessed family members endure was one of the many reasons she chose mastectomy. "The way I saw it was, I can either have a mastectomy, or I can have a mastectomy with a side of chemo. I'll take mine without the chemo, thanks." Similarly, Eleanor, an ATM mutation carrier who had a unilateral mastectomy to treat her breast cancer, expressed that her desire to avoid a second round of chemotherapy was

why she was strongly considering prophylactically removing her remaining breast.

> I think the thing informing most of my personal decisions is that I don't want to go through chemo again. I'm not a vain or even very feminine person, but I do like having hair on my head. I've read that people who've done chemo multiple times reach a point where their hair doesn't come back. And I can live without my chest; that doesn't bother me even remotely. But it is nice to be able to pass as a healthy person by having hair on your head and having eyebrows and all that silly stuff. *(Eleanor, Age 42, ATM)*

Eleanor's, Beverly's, and Nina's stories illustrate that, for some women, the risks and recovery from mastectomy are preferable to potentially needing ongoing, uncomfortable treatments or therapies that could severely impact their daily quality of life.

***Reducing Stress and Anxiety***

Many of the women I interviewed and spoke with at conferences discussed the beneficial effects that risk-reducing surgeries had on their mental health. They expressed how the stress and anxiety of ongoing surveillance, which is sometimes referred to as "scanxiety," was difficult for them to manage. Once women undergo mastectomy, they no longer have annual MRIs or mammograms because their lifetime risk of breast cancer is even lower than among women in the general population. The possibility of eliminating the cyclical stress of breast screenings motivated some women to consider and eventually have surgery. For example, Joan, who was 24 when she discovered her BRCA2 mutation, explained how her anxiety about her surveillance appointments was what led her to pursue surgery.

> Once I found I was positive, and I started doing the every six months mammograms and breast MRIs—I just hated it. I hated it! I mean, I was so young, I had such dense breast tissue, they always saw stuff, had to come back for ultrasounds and, "Oh, we think that might be something, we're not sure, that could be something." And I just couldn't deal with it. It was just making me so anxious and worried, I dreaded these appointments and I just was terrified they were gonna find something, so I was like, "I just want to do it. I want to do it now!" *(Joan, Age 34, BRCA2)*

Similarly, Colette, a 34-year-old woman with a CHEK2 mutation, shared that the stress from

repeated screenings was why she had scheduled her mastectomy. “All of this surveillance—this is on my mind. If I have to have another MRI and then a follow-up biopsy every six months, that is a lot of emotional, physical, and financial stress every six months.”

Like Joan, several women mentioned that their regular screenings often required follow up visits or additional imaging, which compounded their stress. Mindy, who has a CHEK2 mutation, chose to have a lumpectomy after being diagnosed with early-stage breast cancer. She recalled the intense stress of waiting for the results after one of her mammograms when her doctor thought she saw something suspicious.

> Every six months I have to think about having these tests, which involve radiation, and think about the fact that I may have to go back and have the mastectomy later on. The fear that you have that the test might include the results. I just had my six-month mammogram after completing radiation, and the way it works at the center, you have your mammogram, and if they don't need more pictures and everything is fine, they tell you to get dressed and you go home. If the radiologist has to look at your pictures, they escort you into this lovely room where they have soft lute music playing, and bottled water, and a blanket warmer where you sit down on this very comfortable chair and wait for the radiologist to come out and talk to you. You know that if you're going to this lovely room, you're screwed. After they had the mammogram and escorted me into that room, it took the radiologist a good half-hour to go over my films. And in that half-hour, I had myself dead, buried, my children in mourning, my house sold, and me just trying to imagine how I am going to handle hospice. It only took half an hour to go through this grief process. *(Mindy, Age 59, CHEK2)*

Mindy did not have cancer—the suspicious spot the radiologist saw was a calcification. But she was shaken when she shared her story and was clearly still feeling the reverberations of the anxiety she experienced in that visit.

Summer also shared a story about suspicious results that ultimately were found to be benign. After waiting months for a conclusive finding on those images and biopsies, she felt she did not want to endure that stress on a regular basis.

> I went in for my very first mammogram and of course they found something. So, I went through an MRI guided biopsy and they found flat epithelial atypia [FEA]. My understanding is that can occur in close proximity to an actual cancer. They were concerned that maybe they hit the FEA and not the cancer. So, I had a lumpectomy. The lumpectomy did not find any cancer. After three months of thinking, "Oh my god, I already have cancer, it is too late for me!" and the stress of going through the procedures and waiting, I decided that going through that every six months was not for me. It seemed almost inevitable anyway because of my risk, so why not get it over with when I have decent insurance and I am young? *(Summer, Age 35, ATM)*

Summer's experience with suspicious imaging and follow-up procedures made breast cancer feel like less of a risk and more of a certainty, which propelled her toward surgery. Similarly, Fiona, who was 33 when she discovered her CHEK2 mutation, decided to have CPM rather than a unilateral mastectomy or lumpectomy to treat her early stage breast cancer because she did not want to feel perpetually anxious about developing it in her other breast. "It came down to the peace of mind mentally. I am very much a worrier and Type-A. I knew that I would be paranoid even more so than I already am."

Eliminating constant worry was also a major reason that Hannah and Amber, the two youngest women to participate in the study, chose to have mastectomy at age 23. Amber, who has a BRCA1 mutation, explained, "I feel like I would stress too much about when I'm going to get breast cancer by not having it done. So, by going ahead and getting it done, then I can stop worrying about it all the time." Like Joan, Hannah, who has a BRCA2 mutation, did not want to live a majority of her life worried about when she might develop cancer. "Honestly, by the time I had seen the genetic counselor I had already had my surgery scheduled and I met with surgeons…. I just realized that they were ticking time bombs sitting on my chest. I have my whole life ahead of me, and I don't want to wait every year to think, 'Is this my year?' I was like, 'No. That is not for me.'"

Women were often aware that having a mastectomy would not eliminate 100% of their

risk, but they still noted how relieved they would feel once they had their surgeries. For example, Adele had already been diagnosed with early-stage endometrial cancer and kidney cancer by age 40. She was eagerly awaiting breast surgery in order to avoid developing a third cancer:

> I will feel much better. I feel like I'm walking—I feel like I did when I had cancer.[32] I feel like I'm walking around with cancer in my body and I just want to get it out. And I understand that if I have the mastectomy, that that doesn't mean that I'm never going to get cancer, that they can't get all the breast tissue out and it can go elsewhere. And even the ovarian cancer, there could be ovarian cells right now inside me that have turned cancerous. I get all that. But I'm going to feel much better when the bulk of it is gone. *(Adele, Age 42, BRCA2)*

Megan, a pregnant CHEK2 mutation carrier who was delaying mastectomy until she was done breastfeeding, was also eager to have her surgery. She explained how the mental health benefits of RRM mattered more to her than the risks of the surgery to her physical health:

> I want to understand the risks associated with surgery, but I have to weigh the mental health part of it. Every six months, with the screening and the question mark… I guess if I went a few years and everything was fine, I would almost feel different. But I've read a lot of stories where things have been missed, and to me, you know, if my boob's gonna kill me, take my boob off! My mental health is very important to me, and if I can take away 97% of the anxiety of the breast cancer part, then, heck! Take it away. And it sounds terrifying, like I know it's a major surgery and you know, it can have its own complications. But that's the whole kind of cost-benefit analysis that I want to speak to a surgeon about. *(Megan, Age 35, CHEK2)*

While Megan was aware of potential surgical complications from mastectomy, she felt that on balance, removing her anxiety about developing breast cancer was worth the physical toll of the surgery and the risk of additional complications.

Women who had already had mastectomies confirmed that the procedure had reduced

[32] Adele had genetic testing because she was diagnosed with endometrial and kidney cancer by age 40. She did not discover any mutations that are significantly or robustly associated with endometrial or kidney cancer, but instead learned she had a BRCA2 mutation and therefore elevated risk for many other cancers.

their stress and anxiety, just as Adele and Megan anticipated. For example, Veronica, who had no family history of breast cancer and discovered her BRCA1 mutation through a genetic ancestry test, explained how prophylactic breast surgery helped her regain a feeling of "control" in her life:

> When I first got diagnosed or tested positive, I felt like I had no control over my life. Like, this had been determined from conception. From the moment I was conceived, I was mutated. Just, you know, I felt like I had no control. And now I feel like I have more control than ever, in that I feel like I, in some ways, have more control than people in the general population, because I took this step to reduce my risk, and now the risk is so low…. And I feel like, you know, there's always gonna be some kind of risk out there, but I am personally doing everything that I can. And it feels very empowering. *(Veronica, Age 32, BRCA1)*

Amy also shared how mastectomy removed her constant stress and worry about developing cancer. Like Veronica, she felt reassured by taking action and doing "everything possible" to manage the factors that she felt were within her "control":

> I've done what I'm in control of. So, I don't have that stress of, "Oh, I'm not going to do this and then I'm going to have to wait, and then they're going to have to do a breast MRI every other year, and I'm going to have to have mammograms, and I'm going to be nervous about that every time." Like every time my mom had one we all held our breath, you know? … And if anything else happens, I mean I'll deal with it, but I didn't want to sit and wonder, "Like okay, I could have done this and I didn't! I could have minimized my chances down to the same risk as everyone else has." Or I'm going to sit and worry, "Great, I have this and now I'm just going to wait for it to develop into something." I didn't want to do that. So, I think that's my relief, is just I did what I was capable of doing to prevent this. *(Amy, Age 41, BRCA1)*

Veronica and Amy both knew that having a mastectomy did not completely eliminate their risk of developing breast cancer, but they were glad they had the procedure because it reduced their anxiety and helped them feel more in control of their bodies and lives.

Marsha was the only woman in the study who could reflect back on decades of living with a reduced risk of breast cancer after having a prophylactic mastectomy. She was 74 when

she learned about her CHEK2 variant, but based on her strong family history, she had a prophylactic mastectomy over 30 years earlier—in 1982, long before the discovery of the BRCA genes. Marsha acknowledged that it was impossible to know, with certainty, whether her mastectomy was the primary reason that at age 75 she had not yet developed breast cancer, which had affected many of her female relatives much earlier in life. "So, the thing is, you know, did I forestall the inevitable? Would I have gotten premenopausal breast cancer like everybody else and did this help me live a longer life? Or maybe it wouldn't have mattered." Yet even with her uncertainty about how surgery had affected her outcomes, Marsha expressed that she was glad she had prophylactic surgery. "For me, I think it was the right decision because it helped me live all those years without that—I was able to tolerate the uncertainty much better than if I would have had my breasts and would have kept bringing my breasts to doctors who would wring their hands and say, 'Well, we don't know about the changes.'" For Marsha, an important benefit of mastectomy was that it helped her cope with the "uncertainty" of risk.

Together, women's stories illustrate that breast screening and surveillance often focuses and intensifies their anxiety about developing cancer, while mastectomy relieves their fears. This difference in women's feelings about their risk management options helps to explain, in part, why they seek out prophylactic surgeries regardless of the penetrance of their mutations. As the previous chapter illustrated, by making risk tangible and "factual," positive results on genetic tests can make their cancer risk feel more "real" even when the specific probabilistic risk estimates women are provided suggest otherwise. In turn, what women often seek to reduce through mastectomy is not their overall risk of developing cancer, but rather their *anxiety* about developing breast cancer. Mastectomy removes them from the perpetual state of uncertainty and fear generated by being "at-risk" and "waiting for cancer to come" (Hesse-Biber, 2014). Nina

Garcia, the Editor-in-Chief of *Elle* and *Project Runway* judge, shared this perspective with the public in her recent essay in *Elle* about her decision to have a prophylactic mastectomy:

> [F]or three-plus years, I've been closely monitored, getting regular mammograms and breast checks. Throughout this time, I've had numerous biopsies, two lumpectomies, and countless follow-ups…. I was living in a loop of testing, every day waking up thinking: Is today the day I will get cancer? I no longer wanted to have these scary thoughts, and I knew the only way they would stop was to schedule the surgery. The answer was clear. (N. Garcia, 2019)

Garcia had been following the high-risk screening protocol for her BARD1 mutation, but the continuous screenings and false alarms heightened her anxiety, as they did for many women in this study. Hence, while clinicians may divide women at genetic risk according to their lifetime risk estimates, from the perspective of patients, what prophylactic mastectomy responds to and reduces is not that abstract numeric risk. Instead, mastectomy ameliorates women's lived experiences of stress and fear that are generated by their genetic risk for cancer, and those feelings are not directly proportional to the penetrance or pathogenicity of their specific variants.

The scientific literature on RRM rarely emphasizes the mental health benefits of removing the stress and anxiety that women experience from breast screenings and being at elevated genetic risk for breast cancer. In contrast, among women in the general population, the stress caused by suspicious breast imaging results and the follow up exams they require is often emphasized as a negative outcome of over-screening. For example, scientific literature on the anxiety and invasive biopsies associated with false positives on mammograms was among the evidence that led to recent controversial changes in the US Preventative Services Task Force (USPSTF) mammography guidelines. These revisions included raising the age threshold for mammography screenings for women in the general population from 40 to 50 and reducing the recommended frequency of screenings for women between the ages of 50 and 75 from annual to

biannual (Pitman et al., 2017; Squiers et al., 2011; Witten & Parker, 2018). If the stress from false positives on breast screening tests are cited as reasons to limit the use of those tests in the general population, then *avoiding* the stress of those screening tests should also be cited as a benefit of risk-reducing surgeries among women at moderate-risk or high-risk.

***Being There for Your Kids***

This study supports previous research that has documented the influence of motherhood on the risk-management decisions of women with BOC mutations. One of the earliest themes that emerged from women's stories about choosing prophylactic mastectomy was the impetus of "doing it for your kids." Several women shared how becoming a mother and forming a family altered their perspectives on risk, making them less tolerant of uncertainty and therefore more inclined to choose surgery. For example, Alicia, who has a BRCA1 mutation, explained:

> I want to do everything that I possibly can to be around for my kids. And I think having children made that decision a lot easier to make. I think it would be a totally different decision, like if I were single, or if I didn't have kids. Like, you know, once you become a mother, you're like, your kids become the focus of everything. And it's like I don't want to leave my children without a mother. And, you know, I may still get cancer. But at least everybody knows I did every damn thing I possibly could to not get it. *(Alicia, Age 42, BRCA1)*

Anita, a BRCA2 mutation carrier who was nursing her infant during our interview, was planning to have a mastectomy once she was done breastfeeding. She shared a similar sentiment: "Now that I have a family it's just like, I don't want to take that risk and leave them behind…. You don't want to leave your spouse behind. And then also your baby, it's like I can't imagine not being able to be there for him, and raising him." Similarly, Veronica, a BRCA1 mutation carrier, had recently adopted her foster daughters and explained how becoming a mother was the catalyst for her decision to have surgery:

> Once I started meeting with them and knew that we were going to adopt them, I said, "I just wanna have the surgeries!" I don't want to die young or have cancer and put them through more loss and more sadness and trauma in their lives. And prophylactic surgery kind of sucks and I was really nervous about the surgery, but for me, as soon as I was matched to the kids, and as soon as I met them, my risk tolerance plummeted to like, zero. *(Veronica, Age 32, BRCA1)*

The stories shared by Alicia, Anita, and Veronica illustrate how the process of becoming a mother can transform women's feelings and decisions about prophylactic breast surgery and alter their timelines for the procedure.

Being a mother also made women less tolerant of the prospect of chemotherapy, radiation, and the stress generated by ongoing screenings. For example, Megan, who has a CHEK2 mutation, was in her third trimester of pregnancy during our interview. She had suffered a previous pregnancy loss, and she felt that becoming a mother and wanting to be there for her daughter had changed what felt acceptable to her going forward:

> We've tried really hard to have a healthy baby, and I want to be around. And so, I don't want any part of me—my breasts, my colon, my anything—to take away that experience, or make it more difficult. I don't ever want to in my life be having to go through chemo and radiation and have a young child. So, like, it's very frustrating, and I think it's because it has changed the way that I get to look at the future. Because my future now is, every six months, I need to look at these tests and be ok with it kind of thing. And I think with... with having a child on the way, it just makes it bigger for me. *(Megan, Age 35, CHEK2)*

Joan, who inherited her BRCA2 mutation from her mother, explained how difficult it had been for her as a child to witness both of her parents going through chemotherapy. She explained that she, in part, chose mastectomy to protect her children from that pain:

> My kids. And... not wanting to be sick, not, you know. You watch a parent go through--my dad also had cancer when I was in high school, both of my parents were sick, at the same time. Both going through chemo, nobody could work. It's horrible, and I never want my kids to have to go through that. Like, never. You know, and I want to live. *(Joan, Age 34, BRCA2)*

Colette, a CHEK2 mutation carrier, also remembered how scared she was as a teenager watching her mother endure chemotherapy. She also chose surgery because she wanted to try to prevent her children from going through the same experience. “It was really hard to see her go through chemo and radiation and being scared. Even though I was a 17 year old, I was scared that I was going to lose my mom. It was hard. If I can keep that experience from my kids, I want to.”

Like Megan and Joan, other women shared how their desire to undergo mastectomy was linked to wanting “to live” so that they could “be around” to support their children and watch them grow up. For example, Jessie, who has a CHEK2 mutation and PALB2 VUS, shared, “My favorite question is—my husband’s name is Jim—when they say, ‘Well what did your husband say? What does Jim think?’ And I say ‘Jim who? I don’t give a shit about what Jim thinks. I want to be here to watch my children grow up. It’s about longevity.’” Elena also said that being a mother was a major factor in her decision to have CPM. “When [the test] came back CHEK2 positive and they knew I had this increased likelihood of having breast cancer or getting it again, I just decided with three young kids and a lot of life still left to live, I decided on the bilateral mastectomy.” Similarly, Deena, who has a CHEK2 VUS, explained that she sought out breast surgery experts who would perform risk-reducing mastectomy because she wanted to be there for her son. “I just kind of felt like, if I have this, I want to live as long as I can for my four year old, so I'm going to go to the people who know what they're doing…. I figured you can remove every body part I have, as long as I'm here for him.” Colette, a CHEK2 mutation carrier, conveyed that her certainty about mastectomy was rooted in being a mother. She stated, “I know this is the right decision for my family. It gives me more time with my kids, and as a mom that is all that I want.”

The impact of motherhood on women's decision to have prophylactic breast surgery was also illustrated by the sizable overlap between the small fraction of women who did not have children and the relative few who declined or were undecided about mastectomy. Women without children constituted 25% (19/75) of the participants in this study, yet they accounted for 45% (10/22) of the women who had declined or were undecided about surgery (Table 4). Viewed another way, among the women with children, 77% (43/56) had or were planning a mastectomy, while that was true of only 47% (9/19) of women without children (Table 4). These proportions need to be interpreted cautiously because samples in qualitative research are not designed to be representative or to generate statistical estimates or rates, and qualitative analyses do not control for other variables that might help explain these differences.[33] However, the disproportionate desire to have mastectomy among women with children and their corresponding underrepresentation among the women who were avoiding or unsure about surgery was striking, and when these numbers are triangulated with women's stories, it further reveals the importance of motherhood to women's decisions.

| | Had Children | No Children | Total |
|---|---|---|---|
| **Had/Planning RRM** | 43 | 9 | 52 |
| **Declined/Unsure RRM** | 12 | 10 | 22 |
| **Not Offered RRM** | 1 | 0 | 1 |
| **Total** | 56 | 19 | 75 |

**Table 4: Women's Mastectomy Decisions (Ns), by Motherhood**

[33] For example, an obvious potential confounder of these uneven distributions is age. In the general population, a greater proportion of younger women would be childless, and given the relative uncertainty of employment and relationship contexts at that stage in the life course, younger women might also be more likely to be undecided about surgery. However, while the median ages of women with and without children were slightly different (43.5 vs. 37, respectively), the median ages of women who were undecided about or had declined surgery and those who had chosen or planned on having RRM were nearly identical (42.5 and 42, respectively).

***Saving Lives?***

An important assumption embedded in women's desire to "be there for their kids" and "watch them grow up" was the belief that having mastectomy would increase their longevity. Similarly, the improvements in mental and emotional health that women reported after mastectomy were not independent of their belief that the procedure could help them avoid dying young. Women, in part, felt less stressed about getting cancer after having mastectomy because they believed it would "save their life." For example, Lily, a 27-year-old BRCA1 mutation carrier who was undecided about having a prophylactic mastectomy but leaning toward having the procedure, said that saving her life was her top priority. "I hate 'Save the TaTas!' That's one of the things that I really can't stand. I'm like, 'No, save *me*!' We don't say that about any other cancer. We don't say, 'Save the skin!' or 'Save the pancreas!' And I think if I had cancer, I wouldn't be worried about losing my breasts, I'd be worried about my life." Similar to Megan, Lily was explicit about her willingness to remove a part of her body if it meant that she would not die prematurely. Tara, whose sister died of breast cancer, also explained that she was much more concerned about not dying than she was about keeping her breasts. "At the time my sister was dying. There was just nothing that would ever—I mean I can't even imagine saying, 'Oh, you know, I'm not going to do this because I like my boobs or that seems scary.' Nothing was scarier than watching her do that, you know?"

Many women explicitly noted how learning about their mutation had "saved their life." For example, Alicia, a BRCA1 mutation-carrier, expressed the gratitude she and her mother felt toward her doctors.

> My mom always says that my doctors saved my life. I mean, every time, when my mom came for my surgeries, she gave my OB/GYN a huge hug. She didn't have to come, but

> she came and saw me before my surgeries and visited me in the hospital. You know, my mom was like, "You saved my daughter's life." I mean, it's a huge thing, and I hopefully am going to see my kids grow up. *(Alicia, Age 42, BRCA1)*

Veronica also felt saved by testing and surgery. She had no family history of breast cancer and discovered her BRCA1 mutation through a direct-to-consumer ancestry test that had been given to her as a gift. "I always joke around that it was the worst gift that anyone ever got, but it was also kind of great in a way, because it probably saved my life. You know, my dad is in his 60s, and for men, it's not the same type of risk. But for me and my sister, I mean, we would never have suspected. And so, knowing that, that stupid little gift probably saved our lives."

Like Veronica, Hannah had no family history of breast or ovarian cancer, so her BRCA2 mutation was also a surprise finding. She was a pre-med student working in an OB-GYN's office where women were frequently tested, and she tested herself on a whim one day because she wanted to better understand the process for her patients. When the representative from the testing company emailed Hannah the results, she did not know they were for Hannah herself and said, "Look, this 23-year-old just saved her life!" Even one of the speakers at a major professional conference on cancer genetics repeatedly referred to mastectomy as lifesaving. She was both a physician and BRCA mutation-carrier, and she told audience members that by learning their risk-status and having surgery, "You can save your life or your family's life."

While women often felt that by learning their risk status and having a mastectomy they had, as Jill said, "dodged a bullet," data do not support those feelings. High-risk women who have mastectomies reduce their lifetime risk of developing breast cancer to approximately 5%, which is a highly significant reduction and even lower than lifetime risk among women in the general population, which is 12% (Li et al., 2016; National Cancer Institute, 2018d). However, multiple studies have illustrated that prophylactic mastectomy is not associated with a

statistically significant reduction in mortality when compared to the typical protocol for high-risk breast surveillance (i.e., alternating semi-annual MRIs and mammograms), even for women with high-penetrance mutations (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010; Li et al., 2016). The increase in survival is only significant when compared to no screening (A. W. Kurian et al., 2010), and women who have the social and financial capital to access and use genetic testing services are very unlikely to do nothing in response to a positive result. If anything, as I will highlight later in this chapter, the selection bias among women who get tested for genetic mutations is toward individuals who espouse a more interventionist model of care.

Of course, most patients do not read scientific literature or medical guidelines, which helps to explain why many are unaware that mastectomy does not significantly reduce all-cause mortality. However, for researchers and health professionals, the data on prophylactic mastectomy and survival are hiding in plain sight. The meta-analyses and comprehensive reviews that illustrate the lack of a survival benefit from mastectomy are widely cited and are referenced multiple times in the *NCCN Guidelines*. In fact, the subtle language distinctions in the guidelines reflect these findings—clinicians are guided to "recommend" risk-reducing salpingo-oophorectomy (RRSO) because it *is* associated with a reduction in all-cause mortality among women at genetic risk. But the guidelines only suggest providers "discuss" the option of RRM with patients because the evidence supporting the procedure is far less robust. Similarly, countries that have universal health care systems[34] typically encourage and cover RRSO because it improves survival, but often limit covered access to mastectomy to only women at the highest risk. In contrast, women's accounts in this study illustrate that US women at BOC genetic risk,

[34] The United States stands alone among its peer nations as the only large developed country that does not provide some form of universal health care coverage (Fisher, 2012).

even those with moderate-penetrance mutations, are usually offered mastectomy and often elect to have the procedure.

Given that prophylactic mastectomy is not significantly associated with reduced mortality rates, why is the procedure frequently offered and performed among women at genetic risk in the United States? Most health care providers genuinely want to help their patients, and breast health specialists bear daily witness to the stress and complications associated with breast cancer screenings and treatments. Thus, surgeons might offer mastectomy to patients despite being aware that it likely will not extend their lives because it can improve the *quality* of their lives. As I illustrated earlier in this section, many women expressed feeling less stressed and anxious about developing cancer after RRM or shared feeling relieved that they would likely avoid toxic treatments. However, the potential for improvements in women's mental health and quality of life from mastectomy is not unique to US women, so it does not fully explain how and why the procedure is widely offered in the United States. Similarly, both this study and previous research illustrate that motherhood and women's desire to "be there" for their children are among the individual-level factors that motivate them to have risk-reducing surgeries. But a strong desire to live to see your children grow up is also not limited to women in the United States, and therefore "being there for your kids" does not explain why US women disproportionately choose mastectomy.

People's health care practices and the services they desire are not solely driven by scientific data. The recent controversy that ensued in response to the evidence-based changes in the USPSTF mammography screening guidelines illustrated the potential for disconnect between women's feelings about breast health practices and scientific evidence. A careful, comprehensive review of the scientific evidence of the benefits and risks of mammography had revealed that the

potential harms of annual mammography between the ages of 40 and 50 (and of annual rather than biannual mammography after age 50), outweighed the potential benefits among women at average risk for breast cancer (Gotzsche & Jorgensen, 2013). Yet when the screening mammography guidelines were altered to reflect these findings, women across the United States were furious that their access to mammography might be delayed and or reduced (Pitman et al., 2017; Squiers et al., 2011; Witten & Parker, 2018).

Because health-related beliefs and practices always emerge within and often reinforce broader social, economic, and cultural contexts, understanding the high uptake of mastectomy in the United States requires an exploration of not just women's beliefs, but also of the practices that shape those beliefs and facilitate certain decisions. In the following section of the chapter, I will examine how and why social discourses and the structures and architecture of genetic medicine in the United States encourage women to have mastectomy regardless of the penetrance of their mutations and despite current data and clinical guidelines that suggest otherwise. I will illustrate the financial and social incentives women encounter that encourage them to choose RRM and how prophylactic breast surgery is framed as the best medical choice for all women with BOC mutations. I argue that the discourses and practices that encourage mastectomy are both rooted in and reinforce the medicalization of breast cancer risk.

**Encouraging Mastectomy Regardless of Penetrance**

In the previous section, I illustrated why women at genetic risk, regardless of the recommendations in clinical guidelines, often desire mastectomy. However, women in other countries also want to avoid chemotherapy, reduce their anxiety about developing cancer, increase their longevity, and be alive to see their children grow up, yet their rates of mastectomy are much lower. Moreover, whether or not women want prophylactic surgery, without clinicians

who recommend and perform surgery and health insurance coverage for the costs, they would be unable to have it. Hence, in this section, I shed light on how social norms and discourses in the United States and the unique structures and architecture of the health care system encourage women, both implicitly and explicitly, to make the "strong" choice to have RRM.

***Incentivizing Mastectomy***

Both the privatized structures and fragmented architecture of the US health care system encourage mastectomy and contribute to the relatively high US rates of prophylactic breast surgeries among women at genetic risk, regardless of the penetrance of their mutations. In the United Kingdom, the National Health Service (NHS) strives to optimize public health expenditures because the costs of procedures are distributed across UK citizens. Hence, BOC genetic medicine in the United Kingdom limits access to procedures that have minimal evidence of a survival benefit or a low benefit-to-risk ratio, such as mastectomy for carriers of moderate-risk mutations. However, the fragmented, insurance-based, fee-for-service organization of health care in the United States serves to maximize profits for corporations and private medical practices,[35] not to control public or individual patients' risks or costs. In the US system, there is no consistency or transparency in billing charges, negotiated rates, or actual prices for the isolated insurance pools or individual patients who shoulder those costs.

With less public accountability and oversight and more industry control, it is not surprising that the privatized, insurance-based US healthcare system provides greater flexibility in accessing procedures with limited evidence of medical benefit. While some US doctors and clinics adhere to professional society guidelines, they are recommendations, not binding

[35] Maximizing profits for private medical practices is sometimes in tension with maximizing profits for corporations, particularly insurers. But in both cases, minimizing costs for and impact on patients is not the goal or priority.

protocols. Therefore, some health professionals might be more tentative in their guidance, particularly in a field like medical genetics where the science is changing at an accelerated pace. In turn, if patients are persistent and have the resources, they often can, as Jessie did with her hysterectomy, find ways to access the services they desire. But in addition, the financial structures and fragmented architecture of the US healthcare system sometimes actively encourage women to have mastectomy.

Diagnostic Loophole

As I illustrated earlier in the chapter, once women get tested and discover they have a genetic mutation that places them at elevated risk of developing breast cancer, most genetics providers recommend following the *NCCN Guidelines*. For breast screening in women with BRCA mutations, the guidelines indicate that women ages 25-29 should have annual breast MRI with contrast and women ages 30-75 should have both annual MRI with contrast and annual mammograms, with consideration of tomosynthesis (i.e., 3D mammography) (National Comprehensive Cancer Network, 2018b, pp. BRCA-A1). The guidance in the *NCCN Guidelines* for women with moderate risk mutations are similar—for women with PALB2 mutations, they eliminate the recommendation for MRI screening between ages 25 and 29, and for women with CHEK2 and ATM mutations, they recommend beginning annual mammography and breast MRI at age 40 instead of 30 (National Comprehensive Cancer Network, 2018b, pp. GENE-3-4).

The Affordable Care Act (ACA) requires that all *screening* tests graded A or B by the U.S. Preventative Services Task Force (USPSTF) be covered without patient cost-sharing (i.e., without copays, coinsurance, and before any deductibles are met) (Johns & Bayer, 2016). However, there is no regulated limit on cost-sharing for *diagnostic* tests. According to the most recent update to the Grade A and B recommendations list, “The USPSTF recommends screening

mammography for women, with or without clinical breast examination, every 1 to 2 years for women age 40 years and older" (US Preventative Services Task Force, 2018).[36] However, whether a test is considered and coded for billing purposes as screening or diagnostic depends on the circumstances in which it is offered. A test is deemed a screening or preventative service when it is performed in an asymptomatic individual; however, that same test would be considered a diagnostic test if it is performed in response to a symptom. Hence, mammograms are considered screening tests when they are performed as part of routine annual checkups in women ages 40 or older, but they are deemed diagnostic when they are performed in response to abnormal symptoms in women's breasts, such as lumps, inflammation, swelling, discharge, or pain.

Women who have not been affected by breast cancer but have genetic mutations that place them at higher *risk* for breast cancer are nearly always asymptomatic when they get their recommended annual mammograms or MRIs. If a person does not have breast cancer, they are not likely to have physical symptoms of the disease. Given that *NCCN Guidelines* clearly label mammography and breast MRI as "breast screening" and that mutation carriers are typically asymptomatic when they seek these tests, one would imagine that these procedures would be covered by insurance without cost-sharing. However, one of the findings I was most shocked by in this study is that breast cancer surveillance in women at genetic risk falls into what I refer to as the "diagnostic loophole": mammograms for women who know they have pathogenic

[36] The Department of Health and Human Services utilizes the 2002 USPSTF guidelines on breast screening rather than the revised 2016 final recommendation (US Preventative Services Task Force, 2018). In the 2016 guidelines, the age range for the B grade was narrowed to women ages 50-74. Mammography was issued a C grade for women ages 40-49, and for women age 75 and over the USPSTF did not assign a grade because the evidence was insufficient to evaluate the balance of benefits and harms (US Preventative Services Task Force, 2016).

mutations are no longer deemed *screening* tests by providers or insurers. Instead, screening mammograms for women at genetic risk are always coded as *diagnostic* for insurance purposes. Moreover, MRIs are *never* considered screening tests, despite the fact that breast MRIs are recommended as screening procedures in the *NCCN Guidelines*. As a result, the women for whom breast screening is likely to confer the greatest benefit also face the greatest financial barriers in accessing those screenings.

I first encountered the diagnostic loophole in my conversation with Marci, who was among the first women I interviewed. Marci had not yet made decisions about having preventative surgeries, and she was conveying her frustration with getting insurance to cover the screenings that had been recommended to her.

> The way it's been explained to me is: anything that's diagnostic is not covered, but preventative is covered. So as long as they bill it like my breast MRI is preventative, there's the *potential* to get it covered, maybe. But all MRIs are generally considered diagnostic—they're not considered preventative. In my mind, if you can consider a mammogram preventative, then you can consider a breast MRI preventative. You know, it would be the same theory. But [MRI] is a lot more expensive and the science, you know, like all the things now that are covered because they're mandated to be covered, this level of specificity for people that are BRCA2, or BRCA1 even, the insurance companies aren't there yet…. The woman I talked to at the insurance company, she was kind of like, "You can try it. They may cover one preventative MRI a year, but it's a crapshoot. *(Marci, Age 39, BRCA2)*

I initially thought that Marci's challenge with getting her MRIs covered was an exception. Annual breast MRIs have been part of the recommended high-risk screening protocol since the early 2000s, and several studies have shown that breast MRI has, on average, nearly double the sensitivity of mammography in BRCA mutation carriers and other women with familial or genetic risk. The sensitivity of MRI ranges from 77% - 94%, while the sensitivity of mammography ranges from 33% - 59%; however, MRI has only slightly lower specificity than mammography, with ranges of 81% - 98% and 92% - 100%, respectively (Kriege et al., 2004;

Kuhl et al., 2005; Leach et al., 2005; Passaperuma et al., 2012; Riedl et al., 2007; Warner et al., 2004). In a recent study evaluating the effectiveness of alternating MRI and mammography every six months, MRI detected breast cancers that mammography had missed just six months earlier (Le-Petross et al., 2011). Furthermore, the radiation exposure from mammography has been shown to increase breast cancer risk in younger women ages 25-29 (Pijpe et al., 2012). Hence, I expected most insurance companies' policies to align with current science and cover the safer, more effective screening tool in high-risk women.

Marci's story prompted me to begin researching policies on insurance coverage of breast cancer surveillance in high-risk women. Disappointingly, I learned that the fine print of the USPSTF breast screening guidelines explicitly specify that they do not apply to women who have known genetic mutations:

> These recommendations apply to asymptomatic women aged 40 years or older who do not have preexisting breast cancer or a previously diagnosed high-risk breast lesion and who are not at high risk for breast cancer because of a known underlying genetic mutation (such as a *BRCA1* or *BRCA2* gene mutation or other familial breast cancer syndrome) or a history of chest radiation at a young age. (US Preventative Services Task Force, 2016)

Hence, the diagnostic loophole was not a policy oversight; rather, it was designed. In an extension of the medicalization of carrying a high-risk mutation, asymptomatic BRCA carriers were grouped with women who had already had breast cancer and were purposefully excluded from the ACA's cost-sharing protections for breast screening. Lisa, one of the genetic counselors I interviewed, acknowledged this inequity. She explained that clinics have gotten savvy at getting genetic testing covered with minimal or no patient out-of-pocket costs, but she noted that coverage for surveillance in mutation carriers is more difficult. "The problem lies in their management moving forward. We do hit insurance barriers there. A great example of that is MRI.

Even if it's covered by a patient's insurance, typically their deductible comes into play. So, they'll have to pay $1,500 or $2,000 for that MRI for their screening. So, we do hit insurance barriers for that future management."

Financial Incentives

After speaking with Marci, I began asking all of the women I interviewed about their insurance coverage for risk management, and I was stunned at what I uncovered. Only 20 of the 75 women in this study had their recommended breast screenings covered by insurance without hassle and with annual out-of-pocket costs lower than $500. The other 55 women either encountered challenges getting their MRIs covered, incurred hundreds or thousands of dollars in out-of-pocket costs for MRIs, had sizable out-of-pocket costs for mammograms, or all of the above. For example, Diana, a young BRCA1 mutation carrier, told me that her breast screenings were not covered by her insurance and she had spent thousands of dollars on her care.

> So that's been kind of a headache because the insurance company I'm with, they won't cover the majority of it because it's an individual risk versus a population risk. And unfortunately, we have a rather high deductible before it does start kicking in. They pay a small percentage of it…the MRI was probably around four grand is my guess, if I remember right. Meeting with the Onco-OB-GYN was probably over $100…the insurance wouldn't cover the mammogram because it was labeled as diagnostic and not preventative, which is unfortunate. But that was probably a couple hundred dollars. I talked to both the insurance company and the clinic about changing the [billing] code, and neither one would budge and just said that's how it has to be. So that was a bit frustrating. And then ultrasound was a couple hundred too. Whether it was $300 or $600 I don't remember. But I know we've spent a couple thousand, I mean obviously with the mammogram, but I feel like everything together, we probably spent between $6,000 and $8,000. *(Diana, Age 26, BRCA1)*

Similarly, Eleanor shared her surprise at receiving a bill for the MRI that had been recommended to her and relayed the conversation that ensued with her insurance company.

> We were told that it was indicated that with the elevated risk with the ATM gene I needed

> to do an MRI once a year, a mammogram once a year, and that they needed to be spaced every six months. So, I went and had the MRI done. I got the bill, and I called the insurance company and explained the situation and said, “This is the recommended follow-up for this finding, why isn't the MRI covered?” She disappeared and came back and said, “Unfortunately it will never be covered because MRIs are something we don't categorize as required care.” I don't remember how she phrased it. It's something that's ordered as part of a diagnosis, and not part of prevention? So, she said they wouldn't cover the MRI. The bill on the MRI was like $10,000, and the insurance adjustment brought it down to like $1,800 which is much more manageable, but still that's a known cost that we'll have every year if we don't do a mastectomy. *(Eleanor, Age 42, ATM)*

Stories like Diana’s and Eleanor’s kept emerging, with most women citing costs of at least $1000 for their screenings in addition to their insurance premiums, which were also often high. Women like Eleanor who had “only” one to two thousand dollars in annual out-of-pocket costs often characterized their situations as “lucky” or said they felt “blessed” to have “good insurance.” They had heard stories from women like Diana and the 21 other women I interviewed who had exorbitant out-of-pocket costs ranging from $5,000 - $12,000.

Veronica, who was a leader of a local support group for women at BOC genetic risk, was furious about the diagnostic loophole. However, she was not angry because of her personal expenses; rather, she noted the injustice and potential for these charges to keep women with less privilege and fewer financial resources than her from seeking care.

> One thing that enraged me was that they charged me for mammograms—I had to pay co-insurance, and it was like $150 or something. And you know, for us, that's not a problem to pay $150. But mammograms for screening purposes are under Obamacare supposed to be free. And because we're BRCA positive, this is considered a diagnostic mammogram, so it is not covered 100%. And so, I said to the person on the phone, "So what you're telling me is a woman who is at completely normal risk goes in for a mammogram and gets it for free. But we're at extremely high risk and these mammograms could save our lives and we, I have to pay $150?” And they're like, "Yes." And I'm like, "Do you see how that makes no sense?" And she was like, "Yes, but it's just how it is. We didn't write the law." I was like, "Okay. This is stupid and it's going to prevent people from getting screening, because there are women who are single mothers or who are, you know, who are not high income, and they will not be able to afford it and so they just won't get it done. And this is, I’m sorry, this is bullshit. *(Veronica, Age 32, BRCA1)*

Veronica's concern that women might avoid recommended screenings or care because of these costs is likely accurate. Studies of health care use in the general population have shown that higher copays, deductibles, and out-of-pocket costs lead people to delay or avoid care (Ku, Deschamps, & Hilman, 2004; Taber, Leyva, & Persoskie, 2014). Likewise, several women in this study shared that they were considering skipping their recommended screenings because of the cost. For example, given how expensive Diana's MRI was, she said, "I honestly don't know if I would do it every year or if I would do every other year." Similarly, Riki, a CHEK2 mutation carrier, said, "I think that if my first mammogram comes back clean as a whistle and my first MRI comes back clean as a whistle, I may do more due diligence to see if I want to do it every six months. You know what I mean? I don't think that anything is set in stone. I understand that is their recommendation, but I also have to live my life and be aware of the costs associated."

In addition to encouraging women to sometimes skip critical breast screenings because of their high annual out-of-pocket costs, the insurance loophole also generates financial incentives for women to have risk-reducing surgery. All of the 52 women in this study who had or were planning mastectomy had their breast surgeries covered or approved by insurance. While some of those surgeries also involved high out-of-pocket costs because of large deductibles, co-pays, or co-insurance, surgery is a one-time expense. In contrast, the diagnostic loophole leaves many women who choose surveillance with annually recurring uncovered expenses or extremely high out-of-pocket costs for their MRIs and mammograms. When compared to the repeated costs of MRIs and mammograms, surgery is often the more affordable option. Several women I interviewed noted that the recurring cost of screenings was one of the factors that shaped their decision to have surgery. For example, Scarlett, who has a CHEK2 mutation, shared her reaction to learning the risk management options from her doctor:

> He said I could do MRIs once a year, mammogram once a year, and do one every six months. And they also wanted me to take Tamoxifen. I was not crazy about the Tamoxifen idea. And the MRI idea was kind of strong for me because of my $2,000 deductible. Because I knew an MRI was probably $1,000 or more. So that was really kind of a, like, “Oh no! You know, I just don't know what should I do?” Anyway, my oldest daughter is a nurse practitioner and she was with me that day. And she said, "Momma, you're probably gonna meet your deductible with this MRI." She said, "You know, I just think that you ought to just do the prophylactic mastectomy. That way you won't have to take the Tamoxifen, too. And hopefully, you know, you'll be done with this." And I pretty much agreed with her. *(Scarlett, Age 61, CHEK2)*

High out-of-pocket costs for MRIs were a concern for Scarlett, and coupled with her desire to avoid taking Tamoxifen, they contributed to her decision to have mastectomy. Her experience reveals that in addition to costing women thousands of dollars and encouraging them to skip needed screenings, another grave consequence of the diagnostic loophole is that it incentivizes risk-reducing surgery.

Social Incentives

Women’s and clinicians’ stories revealed not only financial incentives for women to have mastectomy, but also social incentives and encouragement. Media coverage of BOC genetic risk and cancer risk advocacy and support networks often praise women who have mastectomy, portraying the procedure as a brave and empowered choice. For example, Angelina Jolie stated in her Op-Ed:

> [T]here are many women who do not know that they might be living under the shadow of cancer. It is my hope that they, too, will be able to get gene tested, and that if they have a high risk they, too, will know that they have strong options. Life comes with many challenges. The ones that should not scare us are the ones we can take on and take control of. (Jolie, 2013)

Nowhere in Jolie’s Op-Ed does she mention breast screening procedures such as MRIs and mammograms. Hence, the “strong options” that she refers to that enable women to “take control” of their genetic risk for breast and ovarian cancer are the surgical ones she chose: mastectomy

and reconstruction. Because of her celebrity, Jolie's decisions about and perspectives on managing BOC genetic risk through prophylactic breast surgery were magnified by other media outlets and contributed to the positive framing of mastectomy and breast reconstruction as the brave and empowered choices for women.

Several of the health care providers I interviewed noted the impact of Jolie's first op-ed on women's interest in both genetic testing and prophylactic mastectomy. Alyssa, a genetic counselor, noticed a sharp increase in the number of patients seeking testing at her clinic immediately after the article was published. "[D]emand was extremely high, especially after Angelina Jolie published her Op-Ed in The New York Times. Our referral volume tripled that week. And I don't think it ever went back down." Laura, a clinical geneticist, shared how Jolie's 2013 Op-Ed and other celebrity publicity of BRCA mutations had a positive impact on the field and public awareness of genetic risk for cancer.

> Angelina Jolie brought this, although others had before, Christina Applegate being another one. But I think some of the celebrities bringing this into the limelight actually help to increase awareness. People started thinking through this, trying to put themselves in the situation: "What would I do? Do I want this testing?" So, the learning curve, the health literacy or the genomic literacy for hereditary cancer testing, it's like the whole community took a leap up within that six months after Angelina Jolie wrote her Op-Ed piece. And I think that was good for the public. *(Laura, Geneticist)*

Several studies have examined this potential "Angelina Jolie Effect" and have found that there were spikes in internet searches on genetic risk and requests for genetic testing and RRM following the publication of her Op-Ed (Bhatti & Redelmeier, 2015; Borzekowski et al., 2014; Desai & Jena, 2016; D. G. Evans et al., 2015; Noar et al., 2014).

However, while some clinicians and patients appreciated the awareness Jolie brought to BOC mutations and managing cancer genetic risk, others were concerned that it may have encouraged more women to have mastectomies and to perceive that decision as the best or right

choice. For example, Linda, who has been a cancer genetic counselor since the field's inception in the 1990s, stated, "Sometimes people come in and think, especially with the Angelina Jolie, that if I have this [mutation], that means I'm having a mastectomy." Steve, an oncologist who works with individuals at genetic risk for cancer, also mentioned Jolie and the impact of "celebrity culture" on uptake of mastectomy in the United States. But in addition, he discussed how celebrity influence is embedded in and predated by a broader set of "social network pressures" in the United States to have prophylactic breast surgery.

> The biggest social network pressures surround prophylactic mastectomy. I mean, I think that's where it all comes from. And interestingly—I mean, social network pressures are different in different places. In Israel the social network pressures oppose prophylactic mastectomy, right? Like, "Why would you do that?" And not only from the religious authorities—I mean, certainly within the religious authorities, but also within the secular communities there, there is significant pressure. Whereas here, people blame Angelina Jolie, or point to Angelina Jolie, and I think she had something to do with it, kind of celebrity culture. But this was going on way before she came on the scene. And I think that what happens is—and I say this from conversations I have with women in my surveillance clinic—is that they go to certain support networks which are, dominated is too strong a word, but heavily populated by people who have already made a decision to have prophylactic surgery, and feel quite strongly that that was the right one. *(Steve, Oncologist)*

Steve importantly highlighted cross-national differences in attitudes toward mastectomy, clarifying how social encouragement to have prophylactic breast surgery is particularly strong in the United States. Yet I encountered few instances or stories of direct or explicit "pressure" on women to have RRM from other women with BOC mutations. Most women with mutations exhibited respect for the complex and deeply personal nature of other women's surgical decisions and refrained from passing judgement on their choices. However, many participants shared positive feedback they had received from clinicians, family members, friends, and other previvors on their choice to have surgery. I came to understand this positive reinforcement of

mastectomy not as social *pressure,* but rather as a social incentive or encouragement to have surgery. Especially when coupled with the lack of support for the decision to continue with breast surveillance, which is an ongoing rather than acute stressful process, the affirmations surrounding mastectomy position it as the socially desirable option for breast cancer risk management.

For example, several of the women I interviewed shared that they had clinicians, family members, and friends who described their decision to have surgery as courageous. Nina, who eventually opted for surveillance over mastectomy, recalled her interaction with her genetic counselor after learning about her BRCA1 mutation. “Originally when I met with the genetic counselor, I had said, ‘I’m gonna do a double mastectomy immediately, no questions about it.’ And then she was like, ‘You’re so brave! That’s so wonderful.’” Raina, who has a BRCA2 mutation, explained that she received positive reactions from family and friends when she chose surgery. “I got a lot of encouragement of, ‘Good for you! You’re doing something proactive, and it takes courage.’ And I got a lot of pat-on-the-backs from family and friends that I was doing the right thing, which was nice at the time.” Veronica shared how a family member’s perspective that mastectomy was courageous shifted her own perception of her decision:

> My husband's aunt told me the other day when we were together, she said, "You know, I don't think I ever told you this but — when you got your surgery, but I think what you did was so brave." And she was like, "I don't know if I could have made the same decision." And it made me think, 'cause it didn't feel brave. I felt terrified. Like “Oh my gosh, I got this false positive [on a screening test], I don't want that to happen again. I'm doing this because I'm petrified.” But I started to think more and more, like, maybe she's right! And you know, now I kind of like to own that description. Like I, you know, I did something brave. I did something courageous. I did something empowering. And it feels good to know that sort of when the chips were down, I did something that was brave. (Veronica, Age 32, BRCA1)

While Veronica was motivated to have surgery because of the anxiety she experienced after

receiving a false-positive breast-imaging result, her aunt viewing her decision to have surgery as brave helped her reframe her choices and instead view them as empowering.

The associations of mastectomy with bravery, strength, and empowerment are also underscored by the debate within Hereditary Breast and Ovarian Cancer (HBOC) communities over whether women can claim the identity of being a “previvor" if they have not completed their prophylactic surgeries. Joan, who learned about her BRCA2 mutation in her mid-twenties and has been active in online and in-person BRCA support communities for over a decade, explained:

> There's always a lot of discussion on there, because when people have a surgery, they're like, "Now I'm a previvor!" You know, and then people will be like, "Well... you can be a previvor and choose surveillance.” There's always kind of that back and forth about it…. I don't know that I identify myself as a previvor, but I do think about that word when I think about having the second surgery and kind of being done with that stuff. I do think about like, “Hey, will that make me a previvor?” (Joan, Age 34, BRCA2)

Similarly, Veronica, who is also in her thirties and has a BRCA2 mutation, stated, “Some people feel like they don't wanna call themselves that until they have had prophylactic surgery and been cleared. So, I have my ovaries out. I had a mastectomy, and now I am a previvor, because now I have eliminated my risk to the extent possible. It's not like a hostile conflict, but it's something that people really wrestle over, and I think there's a layer of superstition, honestly, over calling yourself a previvor when you still have a risk for cancer.” Hence, while there is disagreement among women at genetic risk about what constitutes previvorship, for some women, becoming a previvor and fully belonging in previvor communities requires making the “strong” choice to have prophylactic surgery.

The widespread social validation of the decision to have mastectomy stands in sharp contrast to the lack of support resources for women choosing surveillance. As I highlighted

earlier in the chapter, women often experience stress and anxiety around their semi-annual breast screenings. Yet in over three years of fieldwork at patient advocacy conferences, there were only two sessions offered on the topic of "breast cancer surveillance" and none on managing scanxiety or other issues unique to the decision *not* to have prophylactic surgery. In contrast, these same conferences offered a total of 19 sessions, ranging from five to seven annually, on issues related to prophylactic mastectomy and/or breast reconstruction. These sessions on surgery covered both medical issues and the social and emotional dimensions of the procedures.

Lily explicitly mentioned the lack of social support for breast surveillance. She is a BRCA1 mutation carrier in her mid-twenties, and she was leaning toward having mastectomy in part because she felt that there was not adequate social support for the stress of ongoing screening. She expressed that her family, friends, and other women provided her with support and empathy when she first discovered her mutation, but not subsequently when she had her regular surveillance appointments. "There's, like, no support for that with the screening. There is support in the beginning, and then it's, "Okay, well, now that you know you have this, you know what you *really* should do." As I will illustrate later in the chapter, what women often felt they "should" do was have prophylactic surgery to reduce their risk.

Similarly, in online communities for women at BOC genetic risk, mastectomy and reconstruction are frequent topics, but there are far fewer discussions about choosing *not* to have surgery. In fact, Nina organized a separate group on social media for women choosing surveillance because she received very little support, and even some open criticism, when she shared her decision to continue with screenings but avoid RRM. The group Nina formed now has several hundred members, and it provides the women who find it some of that much needed social support for choosing breast screenings. However, the fact that she and other previvors felt

they needed a separate space to safely discuss choosing long-term surveillance, while information and support for prophylactic mastectomy are frequent topics in online HBOC communities, further illustrates how mastectomy is constructed as the socially normative and desirable choice. Hence, much like the diagnostic loophole creates financial incentives to have surgery, these stories from women and providers reveal that validation and praise for the decision to have mastectomy combined with the lack of support for surveillance generates social incentives to have surgery. Together, these financial and social incentives normalize and encourage RRM while constructing surveillance as the alternative choice over the long-term.

Making the Wrong Choices?

Of course, one of the central goals of advocacy groups and social networks focused on BOC genetic risk is to provide a safe space in which women can share their personal experiences, whether those experiences are positive or negative. As I illustrated earlier in the chapter, most women felt relieved after their breast surgeries because the procedures reduced their anxiety about being at risk. In addition, some women described feeling even stronger and better than before they discovered their mutation. For example, Veronica described how having surgery helped her move from feeling powerless to powerful:

> When I first got diagnosed or tested positive, I felt like I had no control over my life. Like, this had been determined from conception. From the moment I was conceived, I was mutated. [LAUGH] Just, you know, I felt like I had no control. And now I feel like I have more control than ever, in that I feel like I in some ways have more control than people in the general population, because I took this step to reduce my risk, and now the risk is so low…. There's always gonna be some kind of risk out there, but I am personally doing everything that I can, and it feels very empowering. *(Veronica, Age 32, BRCA1)*

When women like Veronica share their positive feelings and successful outcomes with their "tribe," they do so with the best of intentions. Much like Angelina Jolie expressed in her op-ed, they want other women with mutations to feel supported, to be aware of their options, and to

know that they can and will get through this experience. Tara, a BRCA2 mutation carrier who had served several times as a peer support person for other women at genetic risk, explained what she hoped to convey: “Just helping them understand that it's not a scary process and it can be really easy and it can be quick and it doesn't have to be painful. And you can live a normal life when you're done.”

However, the social discourses that frame mastectomy as the strong and empowered choice, which are rooted in positive intentions, can also contribute to the demands of genetic responsibility (Clarke et al., 2003; Lupton, 1995; Rose, 2007) and, in turn, the marginalization of women who choose *not* to have prophylactic breast surgery. For example, Lily felt that the support groups she participated in were hyper-focused on surgery and described an underlying sentiment that “you’re not brave if you don’t do it”:

> There is definitely pressure, almost peer pressure from the BRCA community that that's what you have to do or you're not brave…. Nobody has ever point blank been like, "I don't think you are brave." But even the magazines, you know, now it's sort of like a trendy subject to bring up every October. And so, they will have a spread. Glamour Magazine will say, "I was in my 20s and I had my breasts removed." That will be the byline. And I'm like, “Okay. But that's because that's more interesting than ‘I just go to the doctor every six months.’” So, there's no one actually being like, "You should do this now!” but just the general sense of “Are you finally gonna have the surgery?” I mean, people act as if themselves, they are not brave. And the groups that I went to, the few meetings, it was just like psyching themselves up to have a surgery. That was all, it felt like that was the goal. Like, "If I could just have the surgery, then all my problems will be solved.” *(Lily, Age 27, BRCA1)*

Even in the absence of direct or explicit pressure to have RRM, Lily’s experiences highlight how the discourses that describe surgery as the interesting, brave, or strong decision can indirectly position surveillance as the boring, timid, or weak one.

The social norms and incentives surrounding mastectomy also made some women feel that if they did not do “everything possible” to reduce their risk that they would be to blame if

they eventually did develop cancer. For example, Nora discovered her BRCA2 mutation after her sister was diagnosed with breast cancer at age 35 and tested positive. She said, “Everyone in my family was like, ‘Do it, do it, do it!’” regarding surgery, and she explained that she would feel at fault if she chose not have RRM and then developed cancer.

> I would feel guilty. I would feel major, major guilt if I didn't have the surgery and I was diagnosed with breast cancer and I had to call my sister and say, "I didn't listen to you and now I have it." And I'm her little sister. We all protect each other—especially sisters, we protect them—and we're super, super close, and it would break her heart. And then to know that I have to tell my children, "Mommy has breast cancer," when I could have prevented it. *(Nora, Age 32, BRCA2)*

Nora’s feelings are a salient example of feelings of genetic obligation (d'Agincourt-Canning, 2001; Dagan & Goldblatt, 2009; Nina Hallowell, 1999; N. Hallowell et al., 2006; Hamilton et al., 2009)—she felt she should have surgery to protect her sister and her children. Steve, the oncologist who works with people at genetic risk for cancer, discussed how messages that often circulate within women’s social networks were contributing to his patients’ feelings of obligation and guilt and, in turn, their decisions to have mastectomy.

> And so, it’s not exactly a shaming effect, but sometimes it is a shaming effect. Sometimes it’s a, “Don’t you want to be there for your children?” And then people come and tell me that they’ve heard that, both in support groups, Facebook groups, and from family members. So, I don’t mean necessarily social network just on Facebook, I mean it being social networks in the broadest context. And so, they feel this incredible sense of, sometimes, guilt. “Gee, of course I want to be there for my children, you know?” And those are not unreasonable points of view. I understand those points of view, I think they are legitimate points of view. I just think sometimes it is very, very difficult for people to push back against them when they are expressed that way. *(Steve, Oncologist)*

Steve emphasized that he did not feel that choosing to have mastectomy to “be there for your kids” was “wrong.” Rather, he was concerned about how such social messages might leave women feeling like surgery was the only “right” choice among their options.

Several women I interviewed who had chosen long-term surveillance did feel mastectomy was often presented as the "right" choice. This framing of RRM is relatively recent; in the initial years following the discovery of the BRCA genes, mastectomy was often labeled a "drastic" measure. Yet as BRCA-positive status has become increasingly medicalized in the new era of multi-gene panel testing, prophylactic breast surgery has become the normative choice. Overall, it was uncommon for women in this study to share experiences that reflected explicit judgement from others about their decisions. However, when women did discuss feeling judged, it was nearly always about pursuing surveillance rather than surgery. For example, Anna described how other women in Facebook groups criticized her when she shared her decision to do long-term screening with new group members:

> Whenever I tried to throw an alternate viewpoint out there for surveillance—people would ask, "Hey I just got diagnosed, what are you doing?" And I would answer, "Here's what I've been doing, I've been doing it for six years."—I would get attacked. "Why are you doing that? Why are you advising people to do that? That's a ticking time bomb! Oh my god, why would you even put yourself through that?" And it got to the point where I just closed those loops. I don't look at them anymore, I don't comment, I don't respond, anything like that. *(Anna, Age 37, BRCA1)*

Nina, who like Anna has a BRCA1 mutation, also felt judged in online groups for her decision to avoid prophylactic breast surgery. In fact, she became an advocate for surveillance and started a surveillance-only Facebook group for women with BRCA mutations as a result of her experiences. She explained, "One day I was like, 'Hey you know, I'm not doing any mastectomies, I'm doing surveillance,' and the response I got was, 'That's your death sentence!' and 'Fuck, you're stupid!' And I got like, you know, people private messaging me hate mail. So, I left the group, and I was not going back."

A few women in this study exhibited the type of criticism that Nina and Anna both experienced. These women had opted for surgery and felt bewildered by other women at genetic

risk who had chosen to avoid BPM or CPM. For example, Scarlett mentioned women in her CHEK2 support group who had been diagnosed with cancer and opted for breast conserving surgery. She referred to their decisions as "the craziest thing I've ever heard":

> You've got the CHEK2 gene and you're going to have a lumpectomy and radiation? Knowing that your recurrence rate is probably high, why would you do that? Why wouldn't you just go on and have the prophylactic mastectomy and get as much breast tissue taken off and reduce your risk down to, you know, five percent? That kind of stuff just really blows my mind…To me I'm thinking they're just set up for disaster, you know? *(Scarlett, Age 61, CHEK2)*

Similarly, Tara, whose sister died from breast cancer, was openly frustrated with women who chose not to have preventative surgery. "It's like, 'You have a choice!' My sister didn't have a choice. She just died. You know? I get angry about that. You have a choice to get new boobs and not have to think about this every six months 'cause you have to go in for an MRI or a mammogram. Why wouldn't you do that? I can't understand." Hence, in contrast to the initial years following the discovery of the BRCA genes when women felt criticized for considering the "drastic" measure of mastectomy, Lily's, Anna's, Nina's, Tara's, and Scarlett's experiences illustrate that when judgement occurs, it is now more often directed at the decision *not* to have surgery. As Marci clearly summarized, when surgery is constructed as the best and normative choice, "deciding *not* to do anything beyond just active monitoring is a challenge."

***Framing Mastectomy as the Best Medical Choice***

A central tenet of genetic counseling that has infused the broader field of genetic medicine is that providers should be non-directive with patients (Rapp, 2000; A. M. Stern, 2012). Counselors and clinicians with extensive training in genetics often see their roles as guides or "shepherds" (Rose, 2007) who provide patients with the best information available so that those patients can then make complex, personal decisions that are best for the unique context of their

lives. For example, when Steve discussed the pressures his patients experienced in their social networks to have mastectomy, particularly the emphasis on "being there for your kids," he contrasted those messages with clinical approaches to discussing options for risk reduction. "In medicine we wouldn't say that. I mean, it's a little too directive, right? But social networks don't have those historical constraints against directive counseling." However, I found that while many clinicians avoided being explicitly directive, the discourses and practices of genetic medicine encourage mastectomy by framing it as the best medical choice.

All of the women in this study indicated that their health care providers had appropriately recommended enhanced breast surveillance options with them. Yet their stories revealed that MRIs and mammograms were often presented as "bridge" procedures—tools they could use to monitor their bodies until they were ready to have mastectomy. Women described implicit and explicit assumptions amongst both doctors and their peers that at some point they would have prophylactic breast surgery. As Marci, a BRCA2 mutation carrier who was still undecided about mastectomy, stated about the procedure. "I mean, the sense I get is that with breast it's like eventually you'll want to do it…. it's the *when* you're going to have it, not *if* you're going to have it."

Right Choice for BRCA mutations

Marci's impression of people's fatalistic attitudes toward prophylactic breast surgery mirrors the experiences of other women with BRCA mutations. Many of the BRCA-positive women in this study shared stories of doctors and genetic counselors who had indicated that mastectomy was the clear recommended option for medically managing their increased risk. For example, Veronica, who has a BRCA1 mutation, stated that her doctors had told her surgery was "the right thing to do" from a clinical standpoint. "They said, you know, 'This is the right

decision medically.' Not that it ends up being the right decision emotionally for every person, but medically, they were very clear: 'This is where the road leads to.'" Anita, a young BRCA2 mutation carrier with a newborn who was planning on having mastectomy once she was done having children, explained that her breast surgeon was not neutral when she reviewed risk-management options with Anita. "I would almost say that maybe she was—it was kind of clear that her opinion was definitely very pro-PBM [prophylactic bilateral mastectomy]." While Anita was "of that opinion as well" and therefore did not personally find her doctor's position problematic, other patients might desire a less directive consultation. Tara's doctors conveyed that mastectomy was the best choice for managing her BRCA2 mutation by noting that they would recommend surgery to their family members. She recalled: "I remember asking the breast surgeon 'If you were me, what would you do?' And I think this is why I picked them. They were both like, 'I would do exactly what you're doing.' And the plastic surgeon said the same thing. He said, 'If you were my wife…'"

Several of the women who had BRCA mutations but had elected not to have mastectomy described encounters with health care providers who initiated unprompted conversations about prophylactic mastectomy with them that were dismissive of their preferences to avoid surgery. For example, Marci recalled an interaction she had with her sister's oncologist, who knew Marci was BRCA2-positive. "My sister's cancer doctor turned to me during one of my sister's visits and said, "When are you having your breasts removed?" or something to that effect. And I said, "Well, you know, I want to have kids. I want to breastfeed." She was like, "Oh, you don't need your breasts to have kids. You should just do it now." Rather than respecting Marci's expressed feelings about avoiding surgery until she was done breastfeeding, this oncologist told Marci what she "should" do without any request from Marci for that advice.

Brenda and Dorothy also encountered doctors who advised or encouraged them to have mastectomy long after they had initially learned about their BRCA mutations and without them asking for new guidance or information. Brenda is a BRCA1 mutation carrier who was planning RRSO when we spoke but was not interested in RRM, in part because she only has a family history of ovarian cancer, not breast cancer. She described how she has had mixed responses from clinicians about her decision not to have prophylactic breast surgery.

> I did meet with people who were like, "You should get a preventative double mastectomy – why are you waiting?" I've also had providers who were like, "If you do get your ovaries removed, that will give you a protected factor for the breast cancer as well" …. It is varied. I haven't found a doctor who has pushed it in a way where it seems like they are focusing on it too much. But I have had people who have been very blasé about, "Yeah, you should just get a double mastectomy preventatively" type of thing. I feel like I have had some odd experiences with providers recommending that without any other contextual information or discussion. *(Brenda, Age 39, BRCA1)*

While Brenda did not feel explicitly pushed to have a mastectomy, she faced providers who communicated that it was what she "should" do without engaging in a discussion with her about what *her* preferences and desires were.

Similarly, Dorothy is a BRCA2 mutation carrier who had her ovaries removed but was also not interested in having mastectomy. She described a recent interaction with her new breast surgeon who was monitoring her semi-annual screenings:

> The doctor that sees me, after I have my MRI, after I have my mammogram, the doctor that does my physical breast exam, is a surgeon. And the new one that they have assigned to me is very nice, but she is young. Have you ever heard the old saying: Everything looks like a nail if you're a hammer? She talked so quickly on our very first meeting about mastectomy. And this was last year in the spring, and it was the last thing on my mind. I continue to have good test results, and I was surprised by it. It's not that she was recommending it. She was saying, "I want you to know that that is an option for you, and your insurance company must pay for it. And they also must pay for the reconstruction. We can be really strong in that if we want to." It was just an odd conversation. I didn't ask for information on mastectomy at that time. I was just getting my results, and so it

was a surprise. (Dorothy, Age 53, BRCA2)

At the time of Dorothy's interaction with her new doctor, she had already had an oophorectomy and five years of MRIs and mammograms showed no suspicious findings. So, this was neither an initial conversation in which a physician was laying out Dorothy's options for her, nor was it in response to what her screenings showed. Instead, the surgeon brought up mastectomy without any prompting and without asking Dorothy about her preferences.

Safest Choice for MRMs

Clinician recommendations to have mastectomy were not limited to women with high-risk BRCA mutations. As I noted earlier in the chapter, Dana was the *only* woman out of the 75 patient-participants in this study who was never offered prophylactic breast surgery by a provider, and over half of the women I interviewed had either moderate risk mutations or VUSs. Dana was 72 when she discovered her CHEK2 mutation, and she had never had cancer but was tested after her brother discovered he was CHEK2-positive. She explained that her provider explicitly told her mastectomy was not recommended: "The woman who had done the initial testing on me, the first thing she said to me after she gave me the results, she said, 'We do not recommend bilateral mastectomy.' She said with my condition, 'We do not recommend a prophylactic bilateral mastectomy for your case.'" Notably, Dana was one of only two women in the study above the age of 70; over two-thirds of the participants were younger than age 50. Given that after age 75, even the benefits of breast *screenings* are not supported by evidence, her age was likely a factor in her genetic counselor's recommendation against surgery.

Like Dana, some women with MRMs or VUSs initially saw health care providers who informed them that mastectomy was not recommended. But Dana's provider was unequivocal when she stated that RRM was not indicated in her case. Other women's doctors noted that

mastectomy was not an evidence-based practice for their mutations, but also communicated to women that they ultimately could choose whether or not to have surgery. For example, Janet shared that her provider recommended avoiding mastectomy in her case but would not discourage her from choosing it, either.

> So, she was pretty honest in saying that she had not come across too many patients with CHEK2, and that the last patient she'd had decided to move forward with the mastectomy. There was guidance, but there was no strong recommendation to do a mastectomy. She and I had already talked, and she calls herself a "breast conservationist." She's—if at all possible, she wants to conserve, you know, the breast….What I appreciated her saying in the process was that, you know, yes, there was limited information and that she wouldn't necessarily make any changes to her recommendations, but, if based on what I could find out or had found out, if I wanted to change my mind and move forward with the mastectomy or bilateral that she wouldn't necessarily discourage me from that. *(Janet, Age 44, CHEK2)*

Similarly, Scarlett, who also has a CHEK2 mutation, met with a surgeon who emphasized that surgery was her choice and shared what his previous patients had decided. She recalled their conversation: "I said, 'What about other women that have had this gene, what did they do?' And he looked at his nurse and he said, 'Well, I think I've had four in the last year, and all four of them had the prophylactic mastectomy.' And I was like, 'Wow! I'm not going to be the guinea pig!'" Mindy, a nurse who has a CHEK2 mutation, encountered wavering, unclear advice from her surgeon, a trusted colleague who conveyed that the decision was Mindy's to make.

> It made it a very complex decision for any health care professional to give me good information. They could tell me I'm at increased risk for a second breast cancer, meaning not a reoccurrence of the current one, but a completely separate cancer. You're at risk for quite a large percentage. It's not as high as BRCA, but it's enough that insurance would absolutely cover prophylactic mastectomy on the other side and reconstruction. I guess it just made it really hard for me to know how much risk was I willing to live with? The surgeon that took care of me is somebody that I've worked with for many years, and he's a close work colleague and I really trust him. He could not tell me what the right thing to do was. He could tell me that if I never want to think about it again, the best way to go was prophylactic mastectomies. *(Mindy, Age 59, CHEK2)*

While Mindy noted that her surgeon did not explicitly tell her surgery was the "right" thing to do, he indicated that RRM would be most effective at alleviating worry and easing her mind. Hence, his guidance ultimately leaned in the direction of having prophylactic breast surgery.

Similar to Mindy, Deena had a provider who presented options to her under the guise of being non-directive while still communicating that surgery was, in his opinion, the best choice. Deena learned that she had a CHEK2 variant—one with conflicting interpretations—and a VUS on the MUTYH gene after being diagnosed with Stage 1 thyroid and colon cancer at age 42. Both the genetic counselor and the clinician she initially saw encouraged her to have additional breast screenings, but not breast surgery. Yet the genetic counselor also referred her to an oncologist who specialized in breast cancer, and the oncologist advised her to have mastectomy despite it not being a recommended practice.

> They recommended the MRIs and all that stuff. And then I went to another doctor and she kind of said, "Oh, I wouldn't go having anything removed, but let's send you to an oncologist. Let's see what he recommends" …. So, she directed me towards an oncologist and he basically, very nicely said, "I can't tell you what to do, but I'll be honest with you, if I were you, I'd just want them removed after already having two cancers. I know the recommendation is to watch, but I would rather have them removed, too." And then he said, "You take one doctor off the plate." Because they were suggesting MRIs and all that every six—what is it, like every six months? And then a mammogram every six months. Or I could go on, is it Tamoxifen? Tamoxifen or something like that, that they said I could go on for five years. But he said, "Then you're risking uterine cancer, and you're having me as a doctor." He said, "If I were you, I'd have them removed and you would eliminate a doctor." So, I went ahead and I had the double mastectomy. *(Deena, Age 45, VUSs on CHEK2 and MUTYH)*

While Deena's oncologist expressed that he could not "tell [her] what to do," he then immediately followed that statement with a recommendation about what to do. Moreover, his guidance was a clear departure from medical guidelines. According to the *NCCN Guidelines*, VUSs should not affect medical management. Neither of Deena's variants were firmly classified

as pathogenic—the MUTYH variant was considered a VUS by all labs, and there were conflicting interpretations of her CHEK2 variant. Hence, even recommending additional breast screenings for her was questionable, albeit understandable in the case of a woman who had already had two cancer diagnoses at a young age. However, neither Tamoxifen nor mastectomy are advised for pathogenic CHEK2 mutations, so even if her oncologist was cautiously interpreting the variant as likely pathogenic, those recommendations were not aligned with clinical guidelines.

Finally, there were several women in the study with MRMs who indicated that their providers had consistently and explicitly communicated that mastectomy was the "right choice" for managing their risk. Despite having quite different risk profiles, these women's experiences were very similar to those of women with BRCA mutations. Their doctors had discussed surveillance options with them, but mammography and MRI were described as effective bridge procedures, not optimal long-term options. These women's stories reveal messages from their providers that mastectomy was the "right" choice and that eventually they should undergo the procedure. For example, Summer is a 35 year old woman with an ATM mutation, and she said, "It was definitely every doctor that I have seen since finding out about my mutation, it is the first thing that they recommended to me." Similarly, Naomi, who has a PALB2 mutation and was scheduled for an upcoming mastectomy, stated, "I went to [big city] and met with this breast specialist and she said, 'Yes, I absolutely feel like you should have a double mastectomy and reconstruction…. When you are ready, I am here to talk about doing something a little more drastic for prevention.'"

Reflecting and Reinforcing Medicalization

Most often, when women shared a story about a doctor who implied or explicitly stated

that breast surgery was the best medical choice, that doctor was a surgeon. In addition, several genetic counselors and clinicians I interviewed commented that the surgeons they worked with were inclined to recommend mastectomy and did not calibrate their recommendations according to the penetrance of women's mutations. For example, Lisa, a genetic counselor, stated, "Our surgeons, they feel very strongly that risk-reducing mastectomy is the answer to everything…. Our oncologists are a little bit better about it, but definitely from our surgeons' perspectives, a positive result equals a bilateral mastectomy." Similarly, Steve explained that most of the clinicians he worked with as an oncologist tried to avoid being "too directive" about prophylactic mastectomy, but he noted that surgeons were an exception. "If you don't have a prophylactic oophorectomy at some point—I mean the issue is timing—but if you don't have one at some point, then you really are swimming against medical advice. Whereas for prophylactic mastectomy, it is a little bit more balanced in terms of the presentation, as long as it's not a breast surgeon."

Two of the women I interviewed who had elected not to have mastectomy found surgeons' pushback on their decision to do long-term surveillance frustrating, but also understood that it was well-intentioned. For example, Becky shared the ongoing tension she experienced with her medical team regarding her decision to avoid surgery.

> Some doctors, I guess, are used to their patients with this mutation to just get the preventative surgery. So, when I go in every six months for a screening, a lot of them think that it's a hassle, they're like "why would you want to travel all this way to do a screening every six months when you could just do the surgery and then you wouldn't have to worry about it?" So, that's, I feel like a disagreement that we often have, because of my personal feelings and issues about surgery. So, to me this is highly more preferable than going through that and I don't always feel like that's a doctor's perspective because they're just about prevention and maybe doing what they think is more of a sure thing. *(Becky, Age 31, BRCA1)*

As Becky noted, her doctors, including the surgeon who served as one of the primary doctors on

her team, wanted her to do the "sure thing" and to prevent cancer rather than treat it. Similarly, Marci, a BRCA2 carrier who is also a public health professional, commented on how breast surgeons' perspectives are understandably shaped by the trauma they see in their cancer patients.

> Surgeons like to do surgery. And I don't mean that negatively, but it's just—that is what they know and do. And that's what they have seen save people's lives, and so that is what they are focused on. My sense was her perspective was, "I've seen a lot of women die of cancer, and so I am going to do everything I can so you don't die of cancer." Which is fine except for the fact that I don't have cancer. And so, it's a very weird conversation to have since it's a gamble. *(Marci, Age 39, BRCA2)*

Marci's and Becky's comments are reminders that breast surgeons are people whose attitudes, beliefs, and practices are socially and culturally embedded. Just as women's perceptions of cancer risk and desire for preventative surgery are shaped by their own mothers' and close relatives' illness experiences (Nina Hallowell, 2000; Hesse-Biber, 2014), surgeons' feelings about cancer risk are affected by their personal experiences working closely and regularly with women who sometimes die from breast cancer. Of course, oncologists also regularly work with patients who die from breast cancer. However, the primary tools of oncology—chemotherapy, immunotherapy, and radiation therapy—are only capable of treating breast cancer; they cannot prevent breast cancer from developing. In contrast, mastectomy, the primary tool of a breast surgeon, can both prevent and treat breast cancer. Thus, when the option exists, surgeons may understandably be inclined to encourage women to choose surgical prevention over the potential for needing surgical treatment.

However, framing prophylactic breast surgery as the best medical choice for women at genetic risk raises the stakes of the "imperative of health" and the demands of genetic responsibility (Clarke et al., 2003; Gibbon, 2007; Lupton, 1995; Rose, 2007), much like the financial and social incentives that encourage women have surgery. The need many women felt

to "do everything possible" to prevent cancer, along with the guilt and self-blame they said they would experience if they did not have RRM and then were later diagnosed with cancer, was connected to the messages they had received about the "right" and "wrong" medical choices. For example, Marci, like Lily and Nora, felt that she would be at "fault" if she chose to continue with surveillance and then eventually developed breast cancer. She explained, "There's no *thing* here that I need to be treated for, so just not making people feel—giving the information without it being like, "But if you make the wrong decision…" Because now it feels like if I was diagnosed with cancer, it's like, 'Well, it's my fault.'" Marci's comment underscores how mastectomy is often framed as the "right choice" and discussed as if it is the standard treatment protocol for a disease rather than as one option women can consider for managing their risk.

Moreover, while Marci understood that the recommendation from her sister's surgeon that she have mastectomy was well-intentioned, Marci was also puzzled by the surgeon's response because, as she noted, unlike her sister, *she does not have cancer*. Her repeated emphasis on this difference through comments such as "except I don't have cancer" and "there's no *thing* here I need to be treated for" illustrates the extent of the medicalization of risk for breast cancer. Marci had to explicitly note the distinction between her situation—being at *risk* of developing breast cancer—and that of her sister—having actual breast cancer—because the boundary between the two has blurred. As Chapter One illustrated, risk is now treated like a disease. In addition, Marci's response provides another critical reminder that is simultaneously obvious and yet often invisible in the practices of genetic medicine: that the benefits of risk-reducing surgery are a "gamble" because not all women who have BOC genetic mutations—even high-risk ones—will develop breast cancer.

Neither women who have RRM nor their doctors can ever be certain whether they would

have developed breast cancer if they had not had prophylactic surgery. There is no counterfactual. Breast surgeons objectively know, based on current risk estimates, that a sizable proportion of women with BOC mutations—and a majority of women with MRMs—will never develop cancer in their lifetimes. Yet their surgical recommendations and practices, well-intentioned as they might be, often obscure that data and imply the opposite. By offering mastectomy to women with both high- and moderate-risk mutations out of a motivation to "save their lives" or a feeling that prevention is better than treatment, surgeons' practices in US genetic medicine both reflect and reinforce fatalistic notions about developing cancer and further entrench the medicalization of breast cancer risk.

Taken together, the stories from women in this section illustrate that the practices of BOC genetic medicine often frame mastectomy as the best medical choice for women with both high- and moderate-risk mutations. While several women's health care providers were cautious about being too directive regarding the decision to have mastectomy, the clinicians conveyed that it was the right choice and safest option for women in multiple ways: using "should" language about the procedure, not directly inquiring about women's feelings about surgery, initiating unprompted or decontextualized conversations about RRM with women who opted for ongoing surveillance, and informing them of other women's decisions to have the procedure. Health care providers sharing their thoughts with patients on the best course of action is not problematic; it is, in fact, an essential component of their work. However, when women's choices to have mastectomy are lauded while their decisions to avoid surgery are questioned, interrogated, and doubted, it communicates to patients that having surgery is the right, safest, and best choice, while avoiding it is misguided. In turn, these discourses and practices encourage women, regardless of the penetrance of their mutations, to seek out surgery.

## Co-Production of Genetic Testing and Mastectomy

While women's stories reveal that mastectomy is incentivized and framed as the "best" choice, they do not illuminate why and how the discourses and structures of US genetic medicine became, and continue to be, organized around surgery. In the final section of this chapter, I argue that the clinical value and social significance of the practices of genetic testing and risk-reducing mastectomy are co-constituted. BOC genetic testing produces the knowledge required to indisputably diagnose the "disease" of cancer risk, and positive results on genetic tests are now required to legitimize women's access to insurance-covered prophylactic breast surgery. At the same time, the availability of prophylactic surgery validates the utility of BOC genetic testing by providing a pathway for treating the "disease" of risk and transforming the molecular knowledge generated by genetic tests into action and power. The two practices mutually define, justify, and sustain one another.

### *Genetic Tests Legitimize Risk and Surgery*

One of the consequences of the geneticization and medicalization of cancer risk is that genetic tests have become the primary arbiters of access to surgical interventions, such as mastectomy and RRSO, which are currently the only highly effective means of *preventing* breast and ovarian cancers.[37] Risk-assessment tools and cancer pedigrees are still used to identify women at "elevated risk" who therefore qualify for genetic testing services and increased surveillance. But surgical eligibility is rarely based on family history alone or on the specific risk estimates or ranges of penetrance for particular mutations. Instead, clinicians and insurance companies now almost exclusively rely on the binary results of genetic tests (i.e., positive or

[37] While, as noted earlier in the chapter, surveillance and mastectomy are similarly effective at reducing mortality, surveillance only detects cancer early; it does not prevent cancer from occurring.

negative) to determine women's eligibility for risk-reducing surgeries. As Steve, an oncologist, stated, "The risk is continuous, and yet responses are dichotomous." When BOC genetic tests are negative, women are typically considered ineligible for mastectomy even if they have an extensive family history of cancer. Conversely, if tests are positive for any BOC mutation, even if those mutations have low or moderate penetrance and the patient has no family history of breast cancer, RRM is allowed and covered by insurance.

Eleanor's story provides an example of how genetic tests have molecularized risk and become the arbiter of whether women can "treat" their risk with surgery. When she was diagnosed with breast cancer at age 40, she initially opted to only test for BRCA mutations rather than to do a panel test. Because Eleanor had no known mutation when she was being treated for breast cancer, her providers and insurance company refused CPM. "They wouldn't take both [breasts]; they would only take one because I hadn't had the BRCA chain. The insurance company and oncologist wouldn't cover it, couldn't do a double because it was an elective surgery not indicated clinically." However, approximately a year after her treatment, Eleanor's gynecologist recommended a panel test because she was developing ovarian cysts, and through that test she discovered her ATM mutation. As soon as she had a positive result, mastectomy was presented as an insurance-covered option. She explained, "Now I have to decide if I'm going to have a second mastectomy because of the elevated risk of the ATM."

Naomi's experiences provide another example of how panel tests serve as the gatekeepers to surgery. Naomi had one of the most extensive family histories I encountered in my interviews. Her mother had two primary breast cancers, her maternal grandmother and one maternal aunt had breast cancer, and another maternal aunt had breast and ovarian cancer. Her paternal grandmother and one paternal aunt also had breast cancer, and her father passed away from

pancreatic cancer. Yet even in Naomi's case—one in which both sides of her family suggested a hereditary risk of cancer—family history on its own was not considered enough by her providers to justify surgical intervention, which she found extremely frustrating.

> You see the writing on the wall over and over again. It is like, "This is your genetic legacy." Then finding the genetic mutation was just almost a relief in that it was like, "Here is the evidence, or here is a *different kind* of evidence." And maybe that was coming from my first experience where the oncologist was like, "You don't have this [BRCA] mutation, so I don't know what to tell you." Use your knowledge of biology to understand genetics! … And that was, in part, frustrating because I was like, "How much cancer do I need to have in my family in order for you to step up my program or listen to me more or take seriously when I would say that I want to have this prophylactic mastectomy?" *(Naomi, Age 47, PALB2)*

Like in Eleanor's case, the reluctance among Naomi's doctors to consider mastectomy was, in part, because she was tested in 2007 for BRCA mutations and those results were negative. As a result, she felt somewhat relieved when she eventually discovered her PALB2 mutation because she knew that would enable her to have surgery.

Naomi's and Eleanor's initial BRCA results are what genetics providers refer to as an "uninformative negative." No one in their families had a known mutation at the time they were tested for BRCA mutations, so a negative result was not definitive and did not mean that they did not have significantly elevated risk.[38] The recommendations for managing people with uninformative negatives are very similar to the official recommendations for managing people with MRMs—to triangulate those results with the patients' family histories and information from risk estimation tools to determine their predicted degrees of lifetime risk and their eligibility for

[38] In contrast, when there is a known mutation in a family and an individual tests negative, that is referred to as a "true negative." When a woman receives a "true negative result," her cancer risk is considered similar to the risk of women in the general population because she did not inherit the mutation linked to the cancers in her family.

increased surveillance, medications, or surgery. Yet women with MRMs are routinely offered prophylactic surgery, while women with uninformative negatives are rarely offered mastectomy even when, like Naomi, they have an extensive family history of the disease.

Once Naomi was retested with a panel test and discovered her PALB2 mutation, everyone was not only willing to consider surgery, but also recommended it. The genetic test results gave her the "evidence" she needed to access surgery.

> I felt like there was then an '"Okay!" moment that we could move forward. I do not know, if for [the doctors] that is because working with insurance companies—maybe it is an easier process when you have a mutation or something? I am not quite sure. But there was some hesitation, and once I had that report, they were like, "Okay, when are we going to schedule you?" *(Naomi, Age 47, PALB2)*

Similar to Naomi's clinicians, some women said that despite their family histories, they personally felt hesitant about having mastectomy until their risk was confirmed by a test. For example, Marianne explained:

> I mean, I sort of felt like a ticking time bomb with the history, but it felt kind of crazy almost to go ahead and have the prophylactic mastectomy without finding out the mutation. It just sounded a little extreme. I was very comfortable with the idea of having a mastectomy if a genetic mutation was found. Like I said, it was a bit of a relief to almost have something concrete to point to to make that decision. *(Marianne, Age 59, CHEK2)*

Colette shared that her test results also made her risk feel more tangible and therefore actionable. "The genetic results made it absolutely more real because then it is on paper. There is a mathematical, quantifiable, thing that you can see on paper. Okay, here is the likelihood."

Eleanor's, Naomi's, Marianne's, and Colette's experiences illustrate how, without the confirmatory power of the genetic testing result, the subjective knowledge of family history is almost never enough to justify surgical intervention. To use epidemiological terms, family

history is not sufficient[39] for access to mastectomy. In fact, the only woman in this study who was advised to consider RRM *prior* to testing was Dana, who had her prophylactic mastectomy over a decade before the discovery of the BRCA genes in the early 1980s. Not one of the other 74 women, the vast majority of whom had family histories of cancer, were advised to consider mastectomy until they knew they had positive testing results.

Interestingly, while familial risk, on its own, does not qualify women for surgical interventions, the *NCCN Guidelines* encourage clinicians to strategically mobilize the subjective knowledge of family history when counseling women with MRMs about mastectomy. They state, "Evidence insufficient, manage based on family history" (National Comprehensive Cancer Network, 2018b, pp. GENE2-GENE3). Thus, in a circular move, family history, which is often required to qualify women for genetic testing in the first place, gets redeployed in combination with the "factual" genetic test result to justify a surgical response to risk-management. The subjective knowledge of family history, which on its own is insufficient, is mobilized to extend the reach of genetic (dis)embodied knowledge in order to transform the uncertainty surrounding the management of MRMs into a clear course of action. Notably, the power to define disease and justify intervention is still rooted in the molecularized, (dis)embodied knowledge. While the subjective knowledge of family history can amplify the technoscientifically produced knowledge of genetic testing, family history is still, on its own, insufficient.

Moreover, while the *NCCN Guidelines* formally require triangulation with family history to open the gates to prophylactic surgery for women with MRMs, a family history of breast

[39] The "Sufficient-Component Cause Model" is a heuristic that is often used in epidemiology to illustrate causal inference and the multi-factorial nature of disease. A sufficient cause is one that on its own will lead to the outcome of interest. A necessary cause is one that must be present in every combination of factors leading to the outcome (Aschengrau & Seage, 2008).

cancer is not necessary; positive results on a genetic test, even without a family history, are generally deemed sufficient for access to prophylactic surgery. There were five women in this study whose mutations or variants are what genetics experts refer to as incidental or surprise findings (Table 5). Four of the women were tested with cancer panels because they were in their 30s or 40s and had already had two cancer diagnoses. However, these women were suspected of having mutations on other genes associated with their types of cancer, and in the era of targeted testing, they would not have qualified for testing on BRCA2 or CHEK2, the genes of their mutations. Hannah's situation was unique. She managed a fairly large genetic testing program in an OB/GYN's office and tested herself to better understand the process and "see what [her] patients went through." She was shocked when her results came back positive.

| Name | Age | Mutation | Personal History of Cancers | Breast Surgery |
|---|---|---|---|---|
| Adele | 42 | BRCA2 | Endometrial and Kidney | Planning RRM |
| Deena | 45 | CHEK2* | Thyroid and Colon | RRM |
| Hannah | 23 | BRCA2 | None | RRM |
| Megan | 35 | CHEK2 | Endometrial and Thyroid | Planning RRM |
| Penelope | 32 | CHEK2* | Kidney and Ovarian | RRM |

*Variant had discordant classifications

**Table 5: Women with Incidental or Surprise Findings**

None of the five women had a family history of breast cancer or a known first degree relative with a mutation associated with breast cancer. Yet, because of their CHEK2 and BRCA2 mutations, all five women had been offered mastectomy—Deena, Hannah, and Penelope had already had the procedure, and Megan and Adele were both planning on breast surgery in the near future. Importantly, both Deena's and Penelope's CHEK2 variants are ones with discordant classifications; while consensus on both variants is converging and most labs now classify them as likely pathogenic, when Deena and Penelope were tested and had surgery there was less agreement on their pathogenicity. Hence, in the absence of a family history and even when the pathogenicity of variants was under question, positive results on genetic tests were sufficient for

women to gain access to prophylactic breast surgery.

The recommendation in the *NCCN Guidelines* to triangulate knowledge between genetic testing results and family cancer pedigrees to determine medical management options for women with MRMs reflects good clinical practice. However, based on the experiences of women in this study, those recommendations are only formally followed in the presence of a family history in order to bolster support for the decision to perform mastectomy. When there is an absence of family history, like in the cases of surprise findings, triangulating data would suggest taking a cautious approach and avoiding RRM, yet that did not occur with the women I interviewed. What this suggests is that, in practice, the risk management guidelines for MRMs in the *NCCN Guidelines* are largely disregarded. A positive genetic test result, regardless of the penetrance of the mutation, is deemed both necessary and sufficient for access to prophylactic surgery, while a family history of breast cancer is neither. Hence, while women's family histories of cancer are still assessed, those data are now primarily used to determine their eligibility for high-risk breast screening and access to genetic testing. In turn, the (dis)embodied knowledge produced by genetic testing then determines whether women are eligible for risk-reducing surgery.

***Surgery Validates the Utility of Genetic Testing***

Given the complexity of gene-environment interactions and the knowledge that, by definition, a majority of women with MRMs will not develop cancer, why, in practice, is a mutation alone sufficient for surgery while a family history, on its own, is not? The answer to this question is embedded in another question posed by Steve, an oncologist. When he discussed the debate over BRCA population screening, he rhetorically stated, “The genetic community to some extent participates in this because if using genetics to stratify people for risk by intervention isn’t going to work, then what is our goal? What is our purpose, you know?” While

Steve was not directly addressing how genetic tests became the gatekeepers to surgery, his question implied that there would be little value to genetic testing if women's risk could be managed based on family history alone. Hence, just as I illustrated in the previous section how genetic tests legitimize cancer risk and mastectomy, in this section I will reveal how prophylactic surgery validates the utility of genetic testing.

Earlier in the chapter I highlighted that after receiving genetic test results that confirm their risk for breast cancer, many women desire mastectomy because it will reduce their anxiety. While most women at genetic risk were cognitively aware that they were not 100% certain to develop breast cancer, they *felt* like it was lurking around the corner waiting to pounce. For example, Josephine stated, "I always felt like it was coming for me," and Naomi explained that genetic risk for cancer felt like a "predator that is stalking." Marianne, Hannah, Nora, and Katarina all said that they felt like they had "ticking time bombs" in their breasts. Breast screenings cannot alter this sense among women that they are under imminent attack by breast cancer. Surveillance through mammography and MRI can closely monitor women's bodies and hopefully detect cancer early if it develops. But screenings do not *prevent* breast cancer, nor do they remedy the anxiety of being at genetic risk.

Counterintuitively, treating the *risk* of breast cancer often involves a more invasive surgical procedure than treating actual breast cancer. Because nearly two-thirds of breast cancers are localized at diagnosis (National Cancer Institute, 2018d), breast cancer can often be treated by lumpectomy, which only removes the tumor and leaves the surrounding breast tissue intact. However, treating the *risk* of breast cancer requires removing both breasts in their entirety. Leah discovered her CHEK2 mutation after being diagnosed with high-grade ductal carcinoma in situ

(DCIS) (i.e., Stage 0 breast cancer),[40] and her reasoning for choosing treatment mastectomy and CPM[41] over lumpectomy highlights the distinction between treating cancer and treating the *risk* of cancer. "In talking with my husband and my adult kids we all decided—why not get rid of the risk for breast cancer entirely? Instead of always having to worry, 'Is it coming back?' We wanted to eliminate the worry." Because Leah was already going to have some form of surgery, the factors that she weighed in her decision to have RRM were somewhat different from those of women with BOC mutations without breast cancer. However, like many of the women in this study who chose BPM, Leah chose CPM and treatment mastectomy over lumpectomy in order to "get rid of the risk" and "eliminate the worry" of developing breast cancer in the future.

Women currently have one option for eliminating their worry and defusing the risk that feels like a "ticking time bomb" in their bodies: having their breasts removed. Steve, an oncologist, explained, "When they say, 'Well we have preventative interventions,' the truth is the only preventive intervention that has been proven to work is surgery. So yeah, we can talk about doing MRI screening, but the truth of the matter is, if you really want to make this a cost-effective intervention, everybody has to have surgery." While there are scientists and biotechnology companies researching and trying to develop highly-effective non-surgical approaches for preventing breast and ovarian cancer, those options do not yet exist. As one participant in a webinar about research into prevention of BRCA-related cancers poignantly

[40] There is debate in clinical practice and the scientific literature about whether or not DCIS should be labeled "cancer" or "pre-cancer" (Carlson, 2015; Tarkan, 2004). Currently, it is most often discussed and treated as cancer, so that is how I will refer to it in this analysis.

[41] Just as RRM and reconstruction are two decisions, not one, so are mastectomy of a cancer-affected breast and CPM. Mastectomy treats existing breast cancer, while CPM treats a future *risk* of breast cancer. However, the separateness of those decisions is often obscured, in part because the procedures are typically performed at the same time.

noted, “It’s amazing that in 2018 the only way we have to prevent breast cancer is to cut off our body parts.” But sadly, mastectomy is the only available “treatment” for the “disease” of cancer risk that is established through panel testing.

Throughout my fieldwork, the phrase “knowledge is power” was uttered by both patients and providers in reference to people doing genetic testing and learning about their genetic risk. However, as the literature on genetic testing for Huntington’s Disease reveals, when there is no possibility of changing the outcome of a disease, genetic knowledge can feel burdensome rather than liberating (Callon & Rabeharisoa, 2004; Lock, 2005; Novas & Rose, 2000). Many women in this study described feeling *both* frightened and relieved when their genetic tests came back positive. The indisputable confirmation of risk produced by genetic testing often initially heightened their anxiety and generated a feeling of being stalked by cancer. However, their positive test results also generated relief because those results were their tickets to mastectomy and the ability to take action to reduce their hereditary risk. Josephine explained:

> “It’s definitely brought with it a lot of anxiety, but also a kind of relief. It is like okay, we finally figured it out! We knew something was going on in our family but we just hadn’t discovered what it was yet or how to take any actions based on knowing that there was something there…. Now I have a little bit of knowledge that is going to give me a little bit of ability to take some actions and get insurance to cover some of those actions to try and prevent it.” *(Josephine, Age 41, CHEK2)*

Similarly, Amber, who learned about her BRCA1 mutation at the young age of 23, stated, “I always knew that we had a high risk of breast cancer because my grandmother and aunt both had it. Knowing that there was a risk of breast cancer was not something new to me, but knowing that it was that high was kind of shocking. Knowing that I now can take preventative measures was a real relief.”

Amber’s and Josephine’s statements illustrate how the power of genetic testing is rooted

in the permission positive results grant women to “treat” their risk of cancer through prophylactic surgery. The (dis)embodied knowledge of women’s genetic risk legitimizes the subjective knowledge reflected in their family histories of cancer and gives them access to surgeries that can transform their hereditary and genetic knowledge into power. “Knowledge is power” because it bestows the ability to act. But uncoupled from that potential for action, BOC genetic knowledge would likely leave many women with heightened anxiety and no relief.

By providing a means for transforming the abstract, (dis)embodied knowledge produced by genetic testing into "action and power", the availability of RRM both validates the utility of, and drives demand for, genetic testing. For genetic testing to be a valuable clinical tool, it needs to lead to changes in medical management. However, as I noted in the previous section, a strong family history of breast cancer is often sufficient for women to gain access to earlier and more frequent breast imaging. Since a family history is often a pre-condition of genetic testing in the first place, most women who undergo testing *already* have access to more intensive screenings. Hence, one of the primary ways in which the knowledge produced by genetic testing is valuable to women is that it determines whether they are eligible for mastectomy.

Multiple providers discussed how their patients believed that the primary purpose of genetic testing was to determine whether or not they could and should have a mastectomy. For example, Lisa, a genetic counselor, shared how a majority of her clients come into the genetic testing process with an eye toward surgery.

> You know, I ask them, "Tell me a little bit about why you're here to see me. What has been explained to you about your reason for seeing me today?" And I'd say 95 percent of the time their answer is "Well, this is going to tell me if I have to have both my breasts removed." And my response to that is, "No. That is your choice. This can give us information that might help you make the decision. But you do not have to have a mastectomy unless you want a mastectomy." But they very much come into it being told, “This is going to tell us if you have to have both your breasts removed or not." *(Lisa,*

*Genetic Counselor)*

Steve noted the fused relationship between mastectomy and genetic testing in a discussion about the pros and cons of population testing for BRCA mutations. He said, "I see this world where all 25 year old women go to their gynecologist to have their BRCA testing done to see whether or not they need to have a mastectomy, because that's the way things are getting framed right now."

Taken together, women's and providers' stories reveal how the practices of genetic testing and mastectomy are co-constituted and co-produced. The clinical utility and social significance of BOC genetic testing hinge on the availability of RRM; without prophylactic surgery, women could not seemingly transform their genetic knowledge into and "power," and that knowledge would instead contribute to anxiety. At the same time, the clinical value and social meaning of RRM are inextricably linked to BOC genetic testing; without the legitimization of cancer risk produced by positive results on genetic tests, mastectomy would be considered drastic *over*treatment rather than brave treatment. The practices of BOC genetic testing and prophylactic breast surgery mutually validate, grant meaning, and generate demand for one another.

**Conclusion: Which Choices?**

This chapter explored how and why RRM has become a normative practice for women at genetic risk in the United States. As cancer risk was medicalized and transformed from a liminal state into a disease, prophylactic surgery emerged as the treatment for the disease of risk. For many women, as their stories illustrated, having prophylactic breast surgery brought them tremendous relief, as they no longer felt stalked by cancer. In addition, mastectomy has undoubtedly spared some of the women in this study grueling chemotherapy treatments by preventing breast cancer. However, this chapter also revealed that surgical practices in US genetic medicine are not in alignment with the internal, evidence-based standards established by

experts in the field. Despite clinical guidelines that indicate that prophylactic mastectomy is not supported by evidence of effectiveness in women with MRMs, there was little variation in risk-management approaches between women with high- and moderate-risk mutations. Instead, women were typically lumped into two groups: positive for a mutation and therefore eligible for surgical interventions or negative/unknown for a mutation and therefore ineligible for them. Whereas a strong family history was once the primary determinant of whether a woman was considered at "high-risk" for breast cancer, family history is neither sufficient nor necessary for access to RRM. Instead, the power to define the "disease" of risk and therefore to grant or deny women access to the "treatment" of surgery is now almost exclusively located in positive genetic test results.

I further argued that the discourses and practices of genetic medicine continue to be organized around and to encourage women to have mastectomy because prophylactic breast surgery and genetic testing have a mutually constitutive relationship. The primary functional purpose of RRM is to treat the disease of cancer risk that is established and legitimized by panel genetic testing, and genetic tests have transformed mastectomy from a "drastic" action into a "powerful" and "brave" one. At the same time, the primary functional purpose of genetic testing is to determine eligibility for surgical management of breast cancer risk, and mastectomy transforms genetic knowledge, which on its own is anxiety-producing, into "action and power." Thus, the social significance and clinical value of genetic testing and RRM are simultaneously bound to and reconfigure one another—genetic tests legitimize the need for prophylactic breast surgery, while surgery validates the utility of genetic testing.

Because over half of the women in this study had MRMs with lifetime breast cancer risks below 50%, it is almost certain that some of the women who had prophylactic surgery never

would have developed breast cancer. In noting that, my intention is not to critique or interrogate any individual woman's choices; I respect the complex and deeply personal nature of women's decisions about their bodies. However, it is important to bring visibility to and put analytic pressure on how structures and systems constrain and enable those choices. For example, the "diagnostic loophole" is a critical but fixable failure of policy that incentivizes mastectomy and discourages surveillance by burdening women with the highest risk for breast cancer with the highest out of pocket costs for breast screenings. In addition, the social and clinical discourses that frame mastectomy as the "best" choice and associate it with bravery, strength, and empowerment can both encourage women to have the procedure and contribute to the marginalization of women who choose *not* to have surgery. Thus, this chapter revealed how US genetic medicine magnifies and facilitates certain choices. In the following chapter, through an analysis of breast reconstruction practices, I will explore how the structures of genetic medicine highlight certain risks while minimizing others.

## Chapter 3: "This Is How A Woman Is Supposed to Look": Breast Reconstruction in US Genetic Medicine

> "There's more to it than the way they look. It's how they're going to feel. It's the risk they pose. You know? I'm trying to reduce the risk." *(Marlene, Age 35, CHEK2)*

> "They're willing to rebuild my breasts because that's a sexual thing for men to look at. But I have no sensation in them. I need to be valued for who I am, not what I look like. None of the reconstruction is for me—it's so I look good to somebody else. They're giving me tits again." *(Nina, Age 35, BRCA1)*

> "They are always either living in pain or in surgery—they can't imagine an alternative. Because we live in a culture that doesn't allow that to be visible. There aren't images of being flat. Women aren't given all their choices, so then how do you know you can choose something different?" *(Eleanor, Age 42, ATM)*

### Introduction

The scientific literature on risk-reducing mastectomy (RRM), in both the biomedical and social sciences, tends to discuss and analyze mastectomy and reconstruction as a package deal that involves one choice rather than two. Despite mastectomy providing nearly all of the physical health benefits and reconstruction posing the vast majority of the risks, there is little research that disaggregates the procedures or examines the decision to not have reconstruction. Feminist breast cancer activists and advocacy groups have organized around some aspects of reconstructive surgeries, such as the invisibility of staying flat and the risks of specific types of breast implants. However, social scientists have not explored whether and how the structures of US genetic medicine normalize and encourage breast reconstruction.

This chapter examines how and why, in a medical field centered on minimizing and eliminating risks, the mainstream patient-pathways in breast and ovarian cancer (BOC) genetic medicine encourage women to undergo reconstructive surgeries that increase risks to their physical health. Drawing on fieldwork at cancer genetics conferences and interviews with women with BRCA1/2 mutations and moderate-risk mutations (MRMs), I explore women's

experiences with breast reconstruction. Paying special attention to the social and structural factors that shape women's decisions and outcomes, I illustrate how they are often un- or under-prepared for the severity and duration of the side effects of reconstructive surgeries.

I highlight three structural elements of breast reconstruction practices within US genetic medicine. First, the structures, architecture, and discourses of genetic medicine typically funnel women toward reconstructive surgeries, despite the added risks of the procedures. Second, while women value and identify with their breasts in multiple ways—as visible markers of femininity, for their ability to feed babies, and as sources of intimacy and pleasure—breast reconstruction practices tend to prioritize form over function and feeling. Third, many women are un- or under-prepared for the duration and severity of the side effects of their reconstructive surgeries. I argue that breast reconstruction practices in US genetic medicine both reflect and reconstitute normative, idealized constructions of desirable feminine bodies. Through a juxtaposition of the experiences of women who chose to stay flat against those of women who reconstructed, I identify pathways for disrupting and potentially reshaping these gendered expectations.

***Objectification and Fragmentation***

Feminist theorists and gender and sexuality scholars have long argued that women are socialized to be sexual objects, not subjects. In her feminist theory classic, *The Second Sex,* Simone de Beauvoir argues that women have been constructed as the "other" and are expected to define and see themselves as objects for men (de Beauvoir, 1949). Philosopher Sandra Bartky, in a feminist critique and advancement of Marx's theory of alienation, asserts that the objectification of women generates fragmentation between women's bodies and selves. "The sexual objectification of women produces a duality in feminine consciousness. The gaze of the Other is internalized so that I myself become at once seer and seen, appraiser and the thing

appraised" (Bartky, 1982, p. 134). Bartky argues that this fragmentation alienates women from their bodies and sexuality, as they often view or judge their bodies through the perspective of others rather than through their own embodied experiences.

Despite second wave feminist activism challenging these alienated constructions of women's bodies and roles, anthropologist Emily Martin argues that such "dismemberment is with us still" (Martin, 2001, p. 21). Through interviews with women about their experiences with menstruation, pregnancy, birth, and menopause, Martin illustrates how women consistently describe their reproductive bodies as separate from their selves, using language that suggests bodily fragmentation, alienation, and objectification. Similarly, in her interviews with adolescent girls, psychologist Deborah Tolman illustrates how the sexual alienation that Bartky described decades ago persists today and encourages girls to focus on being desirable to others rather than on understanding or exploring their own desire (Tolman, 2002).

This emphasis on women as objects, rather than their embodiment as agents and subjects, is both reflected and reified via the messages and practices surrounding prophylactic mastectomy and breast reconstruction. In her first op-ed in the *New York Times*, Angelina Jolie notes that the results of reconstruction can be "beautiful," that her children "see nothing that makes them uncomfortable," and that having a mastectomy and reconstruction has not made her "feel any less of a woman" or left her with a diminished sense of femininity (Jolie, 2013). Yet Jolie only describes how her breasts and body appear to *others* after her surgeries, not how they physically felt or looked to *her*. Similarly, as I will illustrate later in the chapter, my interviews with women reveal how the structures of genetic medicine place an emphasis on the appearance of women's bodies and breasts rather than on their embodied experiences. The practices of breast reconstruction prioritize form over function and embodied sensations, which leaves many

women unprepared for the side effects that accompany their reconstructive surgeries.

### *Reconstruction Options*

Mastectomy is a major surgery, but not a complex one, as there are few, if any, choices for women to make about having their breasts *removed*. In contrast, there is a dizzying array of breast reconstruction techniques, and most of the surgeries are lengthy, complicated, and increase the physical health risks that women face. There are two main types of breast reconstruction: implant reconstruction and autologous tissue reconstruction (i.e., flap surgery). In implant reconstruction, surgeons rebuild women's breasts by inserting pouches of synthetic material beneath the skin or muscle on women's chests (Table 6). With flap reconstruction, surgeons use tissue taken from other areas of women's own bodies to rebuild their breasts (Table 6). In some cases, surgeons need to perform a hybrid procedure in which they use both implants and women's own tissue to reconstruct their breasts (Nurudeen et al., 2017). For each type of reconstruction, there is a range of options to consider. For breast implants, there are decisions about the filling material (silicone or saline), shape (round or teardrop), and casing (textured or smooth). For flap surgeries, there are decisions about which part of the body the muscles and fat will come from (e.g., the abdomen, back, gluteals, or thighs) and how that tissue will be connected to a blood supply (Eisemann & Spiegel, 2018; Kulkarni et al., 2017; National Society of Genetic Counselors, 2017; M. M. Shah, Pederson, Djohan, Crowe, & Grobmyer, 2016). Table 6 lists the breast reconstruction types and options available to women.

| Options | Types of Reconstruction | | | |
|---|---|---|---|---|
| | None (Staying Flat) | Implants | Autologous Tissue (FLAP) | Combined |
| Timing | | Direct-to-Implant<br>Delayed w/Expanders | Immediate<br>Delayed | Immediate<br>Delayed<br>Delayed w/Expanders |
| Nipples | | Nipple-Sparing<br>Tattoos<br>No Nipple | Nipple-Sparing<br>Tattoos<br>No Nipple | Nipple-Sparing<br>Tattoos<br>No Nipple |
| Source | | | DIEP<br>Tram<br>Lat<br>SGAP | DIEP<br>Tram<br>Lat<br>SGAP |
| Filling | | Silicone<br>Saline | | Silicone<br>Saline |
| Shape | | Round<br>Teardrop | | Round<br>Teardrop |
| Casing | | Textured<br>Smooth | | Textured<br>Smooth |

**Table 6: Breast Reconstruction Types and Options**

For both implant and autologous tissue reconstruction, there are decisions about the timing of the surgery and whether and how to reconstruct nipples. Some women have immediate reconstruction that is performed directly after the mastectomy, while others need or choose to wait months between their surgeries. Implant reconstruction often requires the interim insertion of expanders to slowly stretch women's tissue on their chest wall to make room for the implants. Regarding nipples, some women leave their reconstructed breasts bare, some have 3-D nipples or other decorative designs tattooed on their reconstructed breasts, while others have nipple-sparing mastectomy and reconstruction. In nipple-sparing procedures, the breast surgeon retains a woman's nipples and areola from the tissue removed during the mastectomy, and then the plastic surgeon attempts to reconnect her nipples to the reconstructed breasts (Eisemann & Spiegel, 2018; Galimberti et al., 2017; National Society of Genetic Counselors, 2017; M. M. Shah et al., 2016).

No matter the type of reconstruction or the options selected (including delayed reconstruction), adding reconstructive surgery is always riskier than having mastectomy alone. Risks unique to implants include a rare form of lymphoma; a variety of health complications that can arise if silicone implants rupture and silicone leaks into women's body tissue; implant rejection; and the need for future surgeries (Grady, 2017a, 2017b; National Society of Genetic Counselors, 2017). Not only do expanders eventually have to be swapped for implants, but also implants have to be replaced approximately every 15 years because of their risk of leaking (National Society of Genetic Counselors, 2017; Nurudeen et al., 2017).

Flap surgeries are more complicated than implant surgeries. Flap procedures can take up to 14 hours, and the extended length of time in surgery compounds women's risks of infection, edema, and potential complications with anesthesia (National Society of Genetic Counselors, 2017; Nurudeen et al., 2017). However, it is not just the duration of tissue surgeries that makes them riskier—they also add other risks when compared to those of mastectomy alone or implant procedures. These risks include infection, swelling, wound-healing issues, and scarring at another incision site on the body; necrosis, or dying skin tissue; tissue rejection; muscle weaknesses and/or scar tissue and chronic pain in the "donor" area of the woman's body; and significantly extended healing time (Heidemann, Gunnarsson, Salzberg, Sorensen, & Thomsen, 2018; Kulkarni et al., 2017; Nurudeen et al., 2017; M. M. Shah et al., 2016; Sue & Lee, 2018).

With nipple-sparing mastectomy and reconstruction, the reconstructed breasts may have a more "natural" appearance and retain some sensation. However, recent studies indicate that rates of necrosis in nipple-sparing surgeries are as high as 10%, and overall complication rates are as high as 20% (Heidemann et al., 2018; Muller, Baratte, Bruant-Rodier, Bodin, & Mathelin, 2017). In addition, current research is mixed as to whether preserving nipple tissue slightly elevates

women's lifetime risk of developing breast cancer when compared to mastectomy without a nipple-sparing procedure (Galimberti et al., 2017; Jakub et al., 2018; Muller et al., 2017). Given that the goal with RRM is to reduce women's risk as much as possible, there is an inherent tension in electing a cosmetic reconstruction procedure that may add to that absolute risk, even if the percentage remains small.

One benefit to flap surgeries is that, unlike implants, they do not require replacement, and therefore they eliminate the need for repeat surgeries over the long-term. However, additional surgeries in the first year after autologous tissue reconstruction are quite common, with one study finding that over 57% (n=102) of women had an unexpected procedure and nearly 22% (=39) had a complication that required additional surgery (Nurudeen et al., 2017). Often those additional procedures are to remove dying or infected tissue, and even when women's bodies do not reject the transplanted tissue, they frequently have cosmetic revisions to remove "dog ears," the flaps of loose skin that can hang along the ribcage, or to enhance the shape of their reconstructed breasts through fat or skin grafting (National Society of Genetic Counselors, 2017; Nurudeen et al., 2017; Sue & Lee, 2018). Each surgical procedure, whether it occurs immediately or decades later, requires time off of work and a recovery period that includes notable physical limitations. Unfortunately, given that women in the United States often lack paid sick leave and disproportionately serve as the primary caregivers for children, many women cannot afford to be out of commission for several weeks or months.

### *A Swinging Pendulum*

Risk-reducing mastectomy is a medical procedure that provides both mental and physical health benefits by greatly reducing women's risk of developing breast cancer. Reconstruction, however, is a cosmetic procedure that does not provide physical health benefits. However,

several studies have shown that breast reconstruction has social and psychological benefits and positively affects women's mental and emotional well-being after having mastectomies (Fernandez-Delgado et al., 2008; Flitcroft et al., 2016; Matthews, Turner, Williamson, & Clyne, 2018). In addition, prior studies have confirmed that the availability of reconstruction has been critical to many women's decisions to undergo RRM (Nina Hallowell, 2000; Hesse-Biber, 2014; Sischo & Martin, 2014). For example, in her research on the surgical decisions of women in the United Kingdom (UK) at high-risk of breast cancer, health scholar Nina Hallowell found that women were hesitant about prophylactic mastectomy because they linked their feminine identities to a body with breasts. They viewed mastectomy as radical not because it was a surgery that would be performed on their healthy bodies, but rather because it would visibly remove a part of their bodies they viewed as inherently linked to their femininity. Hence, some women would only consider mastectomy in conjunction with breast reconstruction because they felt that without breasts they would no longer be 'natural' women (Nina Hallowell, 2000, pp. 166-167).

Women's right to insurance-covered breast reconstruction is relatively recent success of women's health activism. In the 1980s and 1990s, as breast cancer became a more visible disease, survivors shared stories about being denied insurance coverage for reconstruction procedures after mastectomy. In response, women's health advocates fought for federal legislation that required insurance coverage of breast reconstruction after a medically indicated mastectomy. In October 1998, the Women's Health and Cancer Rights Act (WHCRA) — bipartisan legislation, co-sponsored by US Senators Alfonse D'Amato of New York, Dianne Feinstein of California, and 21 others—was signed into law (US House of Representatives, 1998). WHCRA was a major women's health victory. It requires both individual and group health plans, regardless of whether they are insured or self-funded, to include coverage for

reconstruction if they cover mastectomy. It also requires plans to cover an out-of-network second opinion for all cancer patients, which provides individuals, many of whom previously lacked access, with the ability to consult with experts in academic medical centers or major cancer centers (US Department of Labor, 2018).

Like the women Hallowell interviewed, several women in this study expressed that their identities and self-image were linked to having breasts and were grateful for the option to have reconstruction. Collette, a CHEK2 mutation carrier in her thirties, explained: "Your breasts are so much of your womanhood. They are very intimate. There is the aspect of your womanhood and sexuality." Similarly, Bailey, another woman in her thirties with a CHEK2 mutation, stated, "You know, having your breasts, it defines part of who you are as a woman, it's part of your shape and it's part of how your clothes fit." Knowing that their pre- and post-mastectomy bodies could look similar provided women with a sense of normalcy. For example, Jill, who has a BRCA2 mutation, conveyed that she was glad she made the decision to reconstruct. "I'm happy I did something. Definitely it makes you feel more normal." Nora, who had recently discovered her BRCA2 mutation at age 32 and was waiting until she was older to have mastectomy and reconstruction, stated, "I want to look and feel as normal as I can when it's all done." Hence, reconstruction is important to many women, and because reconstructive surgeries are costly, mandating insurance coverage for reconstruction has, in practice, also enabled women to choose risk-reducing mastectomy. Without reconstruction as an accessible option, the decision to have risk-reducing breast surgery would be more difficult for some women.

However, some women in this study felt that the reconstruction pendulum has "gone too far to the other side." For example, Ingrid, who decided not to reconstruct, expressed frustration with what she perceived as slanted information-sharing practices:

> So, it's like, you know, if I hadn't done my homework, I would be on Tamoxifen right now. And I would be reconstructed. It's like, no. There was that time period when they wouldn't tell women what was available to them. And then the law came in that said that it's required to give you reconstruction, now they've gone totally the other way, that they don't even tell you about no reconstruction. You know, they do the opposite. And I don't think that that's right, either. I think that they need to give you all your options and help you decide, discern what's best for you as a person. *(Ingrid, Age 62, PALB2)*

Ingrid's point is not that the pendulum should swing back to where it was before WHCRA. The fact that women who have mastectomies are now routinely provided information about reconstruction and have their surgeries covered by insurance has been a positive development in women's health policy and practice. Rather, what Ingrid noted was that women also deserve to be provided with information about *not* having reconstruction. As she stated, doctors should "give you all your options and help you decide."

Yet the stories from women that I will share in the following sections reveal how they are often encouraged, and in some cases even expected, to have breast reconstruction. Even though reconstructive surgeries are complicated and involve additional risks, the option to not reconstruct and “stay flat” remains relatively invisible. Instead, clinicians often assume that women will want both mastectomy and reconstruction and treat them as a package deal, despite them being separate choices with distinct benefits and risks.

## Funneling Women Toward Reconstruction

### *Health Insurance Policies and Practices*

Multiple components of the structures of genetic medicine propel women like Ingrid toward reconstruction and away from staying flat. For example, health insurance regulations and policies in the United States privilege reconstruction over staying flat by covering cosmetic revisions for reconstructive surgeries but not for mastectomy alone. Several women I

interviewed who chose not to reconstruct shared stories of other women they knew whose breast surgeons disregarded their wishes and did not leave them with the "clean, tidy, flat look" that they had requested. For example, Eleanor, who was diagnosed with DCIS at age 41 before she discovered her ATM mutation, had a mastectomy of her affected breast with no reconstruction. She shared her frustration with the disrespectful treatment experienced by some women in "Amazing Flatties",[42] a private social media group for women who choose not to reconstruct. "I've seen countless surgeries that are just botched, they're horrible. And stories of women who said, 'My surgeon told me it wasn't a choice. I wanted to go flat but they said I would change my mind, they left me with all this extra skin.'" Naomi, who was awaiting her scheduled mastectomy and also did not plan to reconstruct, had seen and heard similar stories of doctors pressuring women to reconstruct and disregarding their wishes:

> The number one complaint is lack of counseling. Not lack of counseling in terms of support but in providing options or people saying that they were pressured into having reconstructive surgery. In some cases, I couldn't believe that it wasn't a lawsuit. Where they told them, straight up, "I want flat: nothing, nothing, nothing." And they woke up with the skin flaps because the doctor said, 'You will change your mind later.' Multiple times. *(Naomi, Age 47, PALB2)*

Yet, while health insurance plans are required to cover "touch-up" surgeries and procedures for women who are unhappy with the appearance of their reconstructed breasts, most plans do not cover revisions for women who stay flat. Emily, who was 50 when she discovered her CHEK2 mutation, shared a recent conversation she had about this inequity with other women on "Amazing Flatties":

> One of the things we were discussing was all the money that insurance companies put into multiple reconstructions, and even if everything goes right, after about ten years you

[42] Like all names in this study, this is a pseudonym.

> have to get it redone anyway. So, our thing was, "Well why won't the insurance pay for us to get our torsos to match our deleted breasts?" Like a lot of us have puckering and dog-ears and all this other kind of stuff. Why won't the insurance companies pay for that? And also, you know, we're grown women so we had rounded bellies to match, and it's normal. Once you take the breasts off and you actually take them down to the muscle, not only do you have dents in your chest and a pronounced sternum, even if you get clothes to fit, it looks bizarre, it looks strange. And you have this pronounced belly where before, it looked like a normal stomach. Why won't the insurance companies pay to get those divots filled in? Now, you're not trying to reconstruct breasts, you're just trying to make a more normal appearance. Pay to get the, you know, what is it called? Fat transfer?[43] Or whatever, just to fill in the divots, and also to remove the back fat or the stomach fat in order to give a more uniform torso. Because that would cost less than getting reconstruction. Why do women who choose not to get reconstruction and save the insurance companies all this money—why are they not given that option? *(Emily, Age 51, CHEK2)*

Like women who choose to have reconstruction, Emily expressed a desire to have a "more normal appearance" after her mastectomy. For her and other women on "Amazing Flatties," normal meant a smooth chest with minimal scarring and no indentations or loose, drooping skin along her chest and ribcage. Yet, as she notes, insurance companies rarely cover the costs of revisions and fat grafting for women who stay flat. Instead, they only cover these procedures when they help create a stereotypically feminine version of "normal"—a woman with breasts.

Emily voiced that some women who stayed flat desired surgery to remove belly fat that became much more visible once their breasts were removed. Marlene also discussed this issue. "Cause yeah, you don't have a chest, suddenly your belly seems bigger. That's the only complaint I've seen on Amazing Flatties, is their bellies are bigger than they thought. Take away your breasts, suddenly you're just staring at your belly." This was point was striking because, as I will illustrate later in the chapter, women and surgeons I spoke with often displayed gendered assumptions that other women would want flatter stomachs and bigger breasts when they had

[43] Emily is referring here to fat grafting, which plastic surgeons use to fill in and even out reconstructed breasts.

reconstruction. Several people touted the "benefit" of women getting a bonus "tummy tuck" along with their DIEP-flap reconstruction, which uses abdominal tissue to recreate breasts. Hence, Emily's story illustrates how the "tummy tuck benefit" is paradoxically available only to women who choose an additional surgery—reconstruction—that already works to conceal their normal bellies, while it is unavailable to women whose procedure—mastectomy alone—makes those normal bellies appear more pronounced.

Insurance plans are also required to cover the cost of prostheses for women who choose not to reconstruct and bras that will accommodate the prosthetic breast(s), but they do not typically cover the cost of special bras or clothing for women who stay flat and do not wear prosthetics. Eleanor, who referred to herself as a "uni-flat," was happy with her surgical results and body, but described difficulty finding a bra that would support her one breast and fit properly under clothing:

> The biggest frustration I had, really, was not being able to find a bra for the breast that's still here, that offers support but is also flat…. Bras are made for people who obviously, ideally, have two breasts. I hate sports bras and I've been stuck wearing sports bras since the surgery because that's what will stay flat. I don't have dog-ears to accommodate, I don't have problems with scarring and tightness around my chest, but wearing a sports bra means I have an elastic band around my chest that drives me nuts. *(Eleanor, 42, ATM)*

Eleanor's story illustrates how even when insurance companies provide services to women who stay flat, these services are structured around covering up women's flatness and giving them the appearance of breasts.

***Organizational and Referral Practices***

The typical organizational and referral practices in genetic medicine also funnel women toward reconstruction by fusing mastectomy and reconstruction and treating them as a singular decision. For example, breast surgeons, who perform mastectomies, and plastic surgeons, who

perform reconstruction, frequently work in teams. As a result, choosing a breast surgeon for RRM often involves being referred to work or consult with that team's plastic surgeon (or vice-versa). One participant expressed frustration with having to switch her breast surgeon in order to work with a plastic surgeon who would perform the reconstruction she desired:

> They often work in teams and have hospital privileges in different places. My first opinion, I just liked her. But the plastic surgeons that she would be working with kept saying, "You are a candidate for a lumpectomy, so why don't you go that route?" And they could only give me A cups,[44] if that. Because I wanted a different plastic surgeon, I couldn't then stay with that doctor. *(Leah, Age 55, CHEK2)*

Most genetic counselors (or other clinicians who order women's genetic tests) immediately refer women for consultations with one of these surgical teams after sharing their positive results with them. Alexandra, a genetic counselor in a regional hospital system, explained her process: "And then as far as prevention, I mention to them that I'm going to be referring them to a team of breast specialists and to a GYN-oncology surgeon."

Because breast surgeons partner with plastic surgeons, the architecture of the system funnels women along the pathway of care that Ingrid described in which providers rarely discuss the option to stay flat. Understandably, genetic counselors and primary care doctors or OB/GYNs who order genetic tests want to ensure that women at high risk for breast cancer consult with a breast surgeon so that they are fully-informed about their risk-reducing options. But then that breast surgeon passes the patient along to the plastic surgeon on their team. Eleanor explained that the standard message is: "You have to have a mastectomy, and we're going to do

[44] Leah is referring to the breast cup size that the first plastic surgeon said they could provide her. The possible size of reconstructed breasts is dependent on a number of factors, such as the amount of skin and fat along women's chests and, if they are having flap surgeries, from the "donor" area of their bodies. It is also dependent on the plastic surgeon's skill and training, and therefore it is common for different surgeons to quote different possible breast sizes to women.

reconstruction."

In fact, even women who expressed to their providers that they wanted to stay flat conveyed that they were still encouraged to see a plastic surgeon "just in case." Sylvia, an ATM mutation carrier in her 50s, described a conversation with her doctor: "I told her that I didn't want reconstruction. I just laid it down on the line. She encouraged me to still go see the plastic surgeon just to check that off of my list." Similarly, Ingrid shared her frustration with how her breast surgeon continued to bring up the possibility of reconstruction. "They really push the reconstruction. So, even yesterday when I was at the [breast] surgeon, and I have told her how many times I'm not interested? She said, 'And you can still have reconstruction if you decide.' They continually tell you."

The organization of breast and plastic surgeons into teams benefits women by ensuring clear communication and collaboration between their providers. Moreover, genetic counselors, oncologists, and breast surgeons who refer women to plastic surgeons usually do so with the intention of providing women with information about "all of their options" and empowering them to make informed choices. They encourage women to go talk to plastic surgeons so that they can find out what the reconstruction process entails. However, the women in this study were typically not provided with all of their options; while most were referred to both a breast and plastic surgeon, very few women's providers discussed staying flat with them as an option.

For example, Naomi, who is in her late forties and has a PALB2 mutation, described how her breast surgeon assumed that she would want reconstruction and repeatedly referred her to a plastic surgeon. "He always followed it up with, 'Okay, I can do the nipple sparing surgery and we will make a date with the plastic surgeon.' Always, always. The assumption is that you are going to see a plastic surgeon. That was it. There was no discussion of 'Here are all the

complications. Here are all the potential problems.' Never, ever." Naomi clarified that she deliberately avoided seeing a plastic surgeon because she did not want to feel pressured to reconstruct.

> [In the social media groups] it was a really common theme that women were saying a lot of pressure from plastic surgeons to get reconstruction. That worried me because I know that I am resolved, but I am also vulnerable. This is a vulnerable time and it is a hard thing to think about, and to look at pictures with women without their breasts because you are mentally trying to see your own body like that. I was like, "This is really hard." Part of my wanting to avoid seeing a plastic surgeon was that I didn't want to have to fight with the plastic surgeon about reconstruction. *(Naomi, Age 47, PALB2)*

Naomi felt she needed to remove herself from the typical patient pathway through genetic medicine in order to maintain her "resolve" to stay flat, which sharply highlights how the architecture of genetic medicine exerts pressure on women to reconstruct. Taken together, the stories from women in this section illustrate how that architecture is linked to assumptions that women will want to have reconstruction and that mastectomy and reconstruction are a package decision rather than separate choices.

***Highlighting Benefits, Obscuring Risks***

Naomi was frustrated that her breast surgeon did not discuss the risks of reconstruction with her before repeatedly referring her to a plastic surgeon because, like many women in this study, she wanted to weigh information on the risks and benefits of procedures as she was making her surgical decisions. She shared how she "began writing up a document" that helped her determine "the least sucky thing" she could do. Similarly, Maya conveyed, "You have to choose from unpleasant choices and decide which one you can live with," and Eleanor and Fiona explicitly mentioned "weighing the pros and cons" of their options.

Naomi's experience of having "no discussion" with her breast surgeon about the risks of reconstruction points to a communication pattern I repeatedly observed during fieldwork and

interviews in which the benefits of mastectomy were highlighted while the risks of reconstruction were obscured. As Chapter Two illustrated, there are both physical and mental health benefits of mastectomy for women with high-risk mutations that warrant being highlighted. The health benefits of RRM are available to women with or without reconstruction; however, patients and providers in genetic medicine often fused the benefits and risks of mastectomy and reconstruction and discussed them as if they were one procedure. That tendency skewed women's lists of "pros and cons" or "positives and negatives," making reconstruction appear less risky and more beneficial than it is in practice.

For example, when Marianne discussed the numbness and tingling she experiences in her reconstructed breasts, she said, "I guess it is a tradeoff that seems worth it, for me, to have less anxiety about 'Am I going to get breast cancer?'" Marianne's reduced anxiety about developing breast cancer is important to her quality of life, so it should not be disregarded. However, it is a result of her *mastectomy*, while the numbness and tingling she was experiencing were side effects of *reconstruction*; there is not an inherent tradeoff between the two. Similarly, Colette shared with me that she sometimes felt frightened by one of the social media groups for women having or considering RRM because other women posted pictures of what went wrong. However, what she described were pictures of complications with reconstructive surgeries, not pictures of complications with mastectomies. "There are a lot of women posting pictures of things that have gone wrong. It can tend to be kind of scary to think about with necrosis and extra fat grafting. That is just a place mentally that I am not wanting to go to yet."

This tendency to map the benefits of mastectomy onto reconstruction was also evident in other social science literature on BOC genetic risk. For example, in her study of women with BRCA1/2 mutations, Sharlene Hesse-Biber argues that breast surgeries are empowering for most

women despite the fact that "some women experience very difficult surgeries and reconstruction that leaves them with negative feelings about their bodies…. Why? By and large, women who have surgery have an unwavering belief in the power of preventive surgery to eradicate their risk and take away their fear of getting cancer" (Hesse-Biber, 2014, p. 125). Hesse-Bieber asserts that women who have difficult reconstruction experiences frequently still feel empowered by their surgeries because those surgeries eradicated their risk. Yet that cannot be the case for reconstruction, which is a cosmetic procedure; only mastectomy is a medical procedure that reduces women's risk of cancer.

While the benefits of mastectomy were often highlighted and mapped on to reconstruction, many women I interviewed conveyed that the converse was not true—their surgeons did not adequately convey the additional risks posed by reconstructive surgeries. For example, when Ingrid shared her experiences talking with plastic surgeons, she said, "They do not explain it to you. They just say whether you qualify and they'll do a nice job for you. But they do not tell you all of the negatives, no." Brenda noted that her genetic counselor explicitly told her that surgeons would not explain the potential side effects of reconstructive surgeries.

> How much information are women being given? That is one thing that I feel like I have heard from a lot of different people. My genetic counselor said that you need to advocate for yourself around these certain things because this surgeon is not going to talk to you about this or that issue. There are a lot of women who have had double mastectomies and reconstruction but no one ever told them about certain aspects about the healing or that they wouldn't have any feeling in their breast or nipples. Or that they didn't have the choice for nipple sparing surgery when at a time that would have been a choice for them. *(Brenda, Age 39, BRCA1)*

Emily explained how she initially considered flap surgery until she learned through her own research what the process actually entailed.

> And at first, the flap sounded like a reasonable thing, because it was using my own body

> parts. But then when we really looked into what was going into the surgery—as far as cutting the rib bones, removing blood vessels from the groin…. And this stuff is not really discussed with women. They tell women, "Oh, we can make you whole again." And it's like, "No, they can't." And there's lots of complications involved in that and they really need to be honest with women and I don't think they're being honest with them. *(Emily, Age 51, CHEK2)*

Like Emily, Naomi also had to do her own research to learn the potential side effects, issues, and complications involved in reconstruction:

> I didn't' know with the implants that they had to be replaced frequently; I didn't know that they recommend that every couple years you go in to have an MRI to make sure that they are not leaking. You know, there is all of this other stuff that is information that women are not provided with. It almost seems paternalistic in the fact that you just don't know. "We know what is best for you so don't worry yourself about it. We will take care of it." *(Naomi, Age 47, PALB2)*

The experiences of Brenda, Ingrid, Emily, and Naomi illustrate how practices in US genetic medicine tend to highlight the benefits of mastectomy but obscure the risks of reconstruction. To fully uncover those risks, women often had to do their own research and consult with resources and individuals beyond their medical providers.

Moreover, when the risks of reconstruction *are* acknowledged or discussed with women, they are often positioned against the benefits of mastectomy as a result of the tendency to fuse the procedures. Most people weighing 'not dying from cancer'[45] against 'experiencing chronic pain, infection, or edema' would understandably choose 'not dying from cancer.' However, if they could choose 'not dying from cancer' *without* those other additional side effects, they might prefer that pathway. Yet the structures of genetic medicine rarely disentangle mastectomy and reconstruction or explicitly highlight that the cancer risk-reducing benefits of RRM are available

[45] I am using this framing of the benefit of mastectomy because it is one that women often conveyed to me. I do not mean to imply that RRM eliminates women's risk of dying from breast cancer or that dying from cancer is an inevitable outcome without risk-reducing surgery.

to women without the additional risks and side effects that might be incurred from reconstructive surgeries.

***Finding Alternative Pathways***

Some women did uncouple mastectomy and reconstruction and deviated from the typical path through genetic medicine, but it was usually only after actively seeking out that information; women rarely conveyed that their decision not to reconstruct was rooted in guidance from health care providers. Instead, most of the women I spoke with who chose to stay flat had to conduct their own research and relied heavily on information and support from other women in Facebook groups like "Amazing Flatties." These are private groups devoted to women without breasts, either because they chose not to reconstruct or had implants removed (i.e., "explanted") after being unhappy with their reconstruction.

Women formed and participated in these separate support groups because they felt the other breast cancer-related Facebook groups and support forums were dominated by the voices and issues of women undergoing reconstruction. One participant shared how what she had learned about staying flat in one of these groups empowered her to change surgeons:

> There are two choices. And they don't really make that clear to you. And that's another reason why I'm seeing this surgeon. I saw a male surgeon here too. I saw a female and a male. The male was like—I told him I was thinking about not getting it [reconstruction]. When I had seen the female, I didn't think I wouldn't do it. But by the time I saw the male I'm like, "You know, I don't think I'm going to do that." And he basically said, "You'll lose a part of yourself. You'll lose a part of being a woman." And I thought, "Yeah, I don't want you as the surgeon." You know what I mean? There's more to me than my breasts. *(Marlene, Age 35, CHEK2)*

Another woman who was awaiting her scheduled mastectomy conveyed the breadth and specificity of the information she learned from other women in "Amazing Flatties," and how those women were a more valuable resource than her doctors:

> They post pictures. They provide me with support in terms of "This is what your outcome can be. This is what we suggest that we talk to your doctor about—questions to ask them because you don't want reconstruction—this is what your surgery will likely be like, what your recovery will be like. We suggest that you have these things in your home and organize your life in this particular way around this particular time." They are actually providing me with more information and knowledge about what is coming up than I have been provided thus far by my health care providers. Which you might expect in some way, but in another way, it is like "Wow, this is shocking!" Shouldn't my healthcare provider be providing this information? *(Naomi, age 47, PALB2)*

These digital support and information communities that help to make flatness visible were critical to many women's decisions to challenge normative ideas about their bodies and deviate from the mainstream pathway through genetic medicine.

Together, the stories shared by women in this chapter illustrate how the structures, architecture, and discourses of BOC genetic medicine in the United States guide patients along a standard path that moves from genetic counselor to breast surgeon to plastic surgeon and works to highlight the benefits and minimize the risks of the procedures. This pathway helps, in part, to explain why the United States has higher rates of RRM and reconstruction than our peer nations (Guth et al., 2012; Laitman et al., 2014; Mamtani & Morrow, 2017). Simply meeting with a surgeon and being placed along that pathway of care makes it more likely that women will choose both mastectomy and reconstruction. In combination with the tendency to fuse the benefits of mastectomy and reconstruction and provider silence around both staying flat and the risks of reconstructive surgeries, these practices normalize breast reconstruction and position staying flat as the unusual alternative.

## Prioritizing Form Over Function and Feeling

### *Breasts, Womanhood, and Identity*

When women choose to reconstruct, no matter how they arrive at that decision, they often

encounter gendered attitudes about their bodies that prioritize how they look over how they feel. As noted earlier in the chapter, women in previous studies and participants in this project expressed the importance of breasts to their identity (Nina Hallowell, 2000; Hesse-Biber, 2014; Sischo & Martin, 2014). For some women, this value was connected to the appearance of their breasts—to how their breasts and bodies looked, both in and out of clothes and to others and themselves. For example, Leah, a CHEK2 mutation carrier who had flap reconstruction but now regrets her decision because of the complications she has experienced, expressed that she initially was opposed to staying flat because she was very large-breasted. Having breasts had been a very important aspect of her identity.

> I was adamant that I did not. I did not want to stay flat. My girlfriend, my best friend, would tell me how she would choose to stay flat and she was upset that I was even thinking about lumpectomy at all. She said that I should just get rid of them. They are just breasts. I told her, "You've always had little ones, so it is probably not a big deal for you. But I have always had big honkers so it is kind of a big deal for me." I would not even entertain the idea of staying flat. *(Leah, Age 55, CHEK2)*

Similarly, Adele, a single woman with a BRCA2 mutation, said, "There's never really been any question for me about getting reconstruction." Having breasts was particularly important to Adele because she did not have a partner. "I'd like to have a sex life and I don't feel like I would be very comfortable having one without breasts…. You know, I'm single, I don't have a very active dating life, but I'd like to have the ability to date and I feel like that could really be a problem." Lily, who discovered her BRCA1 mutation at age 25, expressed how her concerns about her appearance made her more comfortable with the idea of risk-reducing salpingo-oophorectomy (RRSO) than mastectomy and reconstruction:

> I have thought about the surgeries, and I am like, "Well, at least an oophorectomy isn't how I look." And that's terrible because, actually, that does a lot more to you hormonally and all that, internally. But I am like, "Well, but I am only 27." Getting my breasts

> removed feels so crazy right now still. And I want to do it in the next ten years, but I want to get married, I want to have a kid, and I just want to be a regular 30-something person and not do that yet. *(Lily, Age 27, BRCA1)*

All of these women expressed that having the appearance of breasts was an important part of their identity and affected their considerations regarding risk-reducing surgeries.

In addition to valuing their breasts as visible markers of their femininity, many women I spoke with conveyed other important ways in which they felt connected to their breasts. Some cited their biological function, noting how their breasts had been successful at producing milk and feeding their babies. Wendy, who discovered her CHEK2 mutation in her early 60s and chose not to reconstruct, conveyed, "My breasts did a great job. They breastfed two kids, they were very good tits, and now they are gone and its fine." Other women cited lactation as one of the factors affecting either the timing of their mastectomy or their decision to not have risk-reducing surgery. Bailey, who had recently discovered her CHEK2 mutation and was not planning on having mastectomy, said, "I'd love to be able to breastfeed my own children." Anita was planning on having RRM, but wanted to wait until she was done with childbearing. "The thought of having children has made me delay because I wanted to breastfeed, and so I plan to have my family first and then to do that procedure afterwards."

Other women I spoke with appreciated their breasts as a source of intimacy and sexual pleasure and were concerned about losing that aspect of their sexuality. Eleanor, who opted for a single mastectomy with no reconstruction prior to learning about her ATM mutation, was considering removing her remaining breast prophylactically. "Making the decision about my other breast, that's tough, because there's an element of sexuality involved that would be lost if I don't have that breast there…. It gives you sexual pleasure so having it or not having it are two different things." Margaret, who had had recently learned about her CHEK2 mutation and

had scheduled mastectomy and implant reconstruction, told me, "I think the biggest thing is the loss of feeling that I will have in my breasts. That is probably bothering me the most, still. And the fact that my nipples and chest will be numb or not have any feeling or very little. And, you know, that is a very active erogenous zone so I hate to give that up." Ingrid, who had already had RRM for her PALB2 mutation, shared that losing sensation in her breasts was very difficult. "A big part of losing the breasts that was hard was losing the sensation. You know, I hadn't been in a relationship in ten years, and then I'm in this wonderful, loving, physical relationship, and then I lose my boobs."

***How You Look, Not How You Feel***

Yet women rarely described other people understanding that the link between their breasts and identity was multifaceted and not simply about appearance. Multiple participants shared stories about how their plastic surgeons focused almost exclusively on how their reconstructed breasts *looked* (or would look) rather than on how they *felt* (or would feel) from an embodied perspective. For example, Liza, who was 29 when she discovered her BRCA1 mutation and had implant reconstruction, was pleased with the appearance of her reconstructed breasts. "My boobs right now literally just look like boobs." However, she also conveyed that her plastic surgeon did not warn her about lack of sensation or potential numbness in her breasts. "He did such a great job, so I trust him. But feeling-wise and what to expect, he didn't go into any of that."

Luckily Liza had learned about issues with sensation and numbness from her sister and women in support groups, so she was prepared for those side effects even though her surgeon did not inform her of them. But other women expressed that they were unprepared for the complete lack of sensation in their breasts. Beatrice, a BRCA1 mutation carrier who had silicone implant

reconstruction, conveyed:

> I would say there were two things as I look back that I feel like I wasn't told about. I don't know if they would have completely changed my decisions, but I feel like I was completely unprepared. One was the complete lack of feeling in my breasts. They take out all the nerves, and the skin is cold. There's nothing there. It looks nice in clothes, but really, it can't move at all. *(Beatrice, Age 64, BRCA1)*

Talia, a BRCA2 mutation carrier who had flap reconstruction, stated, "I don't remember anyone talking about like how the breasts would feel *to me*, you know?" Adele, who was planning on mastectomy and flap reconstruction in the future, expressed wanting nipple-sparing surgeries in order to preserve sensation in her breasts. "I would like to keep my nipples in particular because they are erogenous zones." Unfortunately, Adele was unaware that the goal of nipple-sparing procedures is to produce a natural *appearance*, not to enhance sensitivity. Only a small proportion of women who have the procedure retain some sensation, and when they do, it tends to be limited (Eisemann & Spiegel, 2018; Galimberti et al., 2017).

Other women noted how awkward and uncomfortable their reconstructed breasts felt internally, and this was especially true for women with breast implants. Tara, a BRCA2 mutation carrier who discovered her mutation at age 27 and later had implant reconstruction, talked about her feelings about her breasts before and after her surgeries. "Prior to having this done they were part of our sex life and I enjoyed when he touched them. But after my surgery, I did not. They're so weird. You don't want anybody to touch them. So, then they just become not a part of it anymore. It's like I rarely take my shirt off when we're messing around. They became a non." Another woman I spoke with at a conference who had discovered her BRCA1 mutation in the late 1990s described how she used to avoid hugging her family members and friends because the pressure against her breast implants felt so awkward. When her implants needed to be replaced several years ago, that discomfort prompted her to have flap surgery rather than replacing the

implants. She was happy about that decision, as she felt much more comfortable with breasts that were reconstructed from her own body tissue.

However, some women who had had flap surgeries also described awkwardness and discomfort with their reconstructed breasts. Leah told me, “I feel like they are just lumps on my body.” Similarly, Scarlett, who had flap surgery, noted how different her reconstructed breasts felt, both internally and externally. “If I touch 'em it's like it's pressing—it's just like having a ball against your chest and you press against it and you can feel that ball pressing against you. It's nothing at all like, no comparison to real breasts. No comparison whatsoever.”

As I will discuss later in the chapter, several participants experienced complications as a result of their reconstructive surgeries. Some of these women had surgeons who dismissed their reports of pain or discomfort, and instead focused on how their breasts looked. For example, Talia, who struggled with abdominal weakness and back pain after her flap surgery, shared her surgeon’s response at their initial post-reconstruction visit:

> And I remember when I went to her office, and she saw the reconstruction for the first time, she said, "Cute! I did a good job." And I'm like, "I'm a 29-year-old woman, and I just had my breasts cut off. My body's cut up and sewn back together. It's not cute, and it's not about you doing a good job." It was so hurtful. I said to her afterwards that I didn't understand that this is what my abdomen would be like. And she just was really insensitive and defensive about it and told me I could go to the gym to firm up my abs if I wanted. *(Talia, Age 38, BRCA2)*

Not only was Talia unprepared for how her surgery would reduce her abdominal strength, but also her surgeon was dismissive toward her concerns about how her body felt and functioned. Rather than using Talia’s experiences of pain and muscle weakness to evaluate the outcome of the surgery and assess her performance, the surgeon concluded she had done a “good” job because Talia’s breasts looked “cute” to her.

Leah’s experience provides the most startling example of a woman’s appearance being

prioritized over her embodied experiences. While she desired reconstruction, she had explicitly requested *not* to have expanders put in because she had learned from other women that they could be extremely painful and uncomfortable. Yet when she awoke from her surgery, she discovered that her breast surgeon had inserted them. "I did expect to come out of the surgery flat until I had the DIEP[46] reconstruction done, so I was shocked when I had expanders in and had boobs. She didn't want me to see myself flat, but she made that decision without even asking me." This surgeon was so concerned with how Leah would feel seeing herself without any appearance of breasts that she disregarded Leah's concerns about pain and discomfort and chose to insert expanders, in direct violation of Leah's wishes.

The attitudes and behaviors of Leah's and Talia's surgeons are rooted in what sociologist Gayle Sulik calls an "aesthetic approach to coping" (Sulik, 2011, p. 35), which emphasizes restoring cosmetic femininity after treatment and concealing the emotional and physical impact of breast cancer. Initially promoted by the mainstream breast cancer movement in the 1980s and 1990s, it involves campaigns such as the American Cancer Society's *Reach to Recovery,* which supplied women with prostheses when they were not regularly covered by insurance, and *Look Good, Feel Better*, which provides women with hair and cosmetic products and services after chemotherapy. These campaigns that centered on improving women's appearance post-mastectomy highlight how "traditional feminine image and self-presentation became a touchstone for helping women to face breast cancer with greater confidence" (Sulik, 2011, p. 39). Providing women with services that focus on making them "look good," especially harmless ones such as wigs and makeup, is not problematic if those services actually help women "feel

[46] DIEP is a type of flap surgery in which skin, fat, and blood vessels are taken from women's lower abdomens to reconstruct their breasts.

better." However, when surgeons' aesthetics are prioritized over women's embodied experiences, a focus on women's appearance is problematic.

The tension between surgeons' aesthetic priorities and women's embodied priorities reflects a similar tension that medical sociologist Nina Hallowell found between women considering mastectomy and reconstruction and women who had already had the procedures. The women who had not yet had mastectomy or reconstruction embraced the aesthetic approach to coping and felt that "the materiality of the body, whether it is composed of flesh or silicon, was less important than having a body that looks feminine" (Nina Hallowell, 2000, p. 175). However, for the women who had already had RRM and reconstruction, how their body looked mattered much less than how it felt. In fact, many of these women reported *appearing* more feminine after their reconstructive surgeries, yet *feeling* less feminine as a result of the considerably diminished sensation in and sensitivity of their breasts (Nina Hallowell, 2000).

Collectively, women's stories in this section illustrate how the model of breast cancer survivorship that has long emphasized restoring "normal" feminine presentation has been imported into the dominant models of "previvorship." The practices of US genetic medicine often prioritize form over function or feeling and construct *real* breasts—breasts that produce milk and are women's embodied sources of pleasure—as disposable. Instead, the field embraces an aesthetic approach to coping that constructs the *appearance* of breasts as valuable, even when the process of creating that appearance poses additional risks to women's physical health. Hence, as Elianne Riska argues in her examination of gender and the processes of medicalization and biomedicalization, "the construction of the enhanced body recaptures normative, heterosexual notions of femininity and masculinity and gendered expressions of sex and sexuality" (Riska, 2010).

## Leaving Women Un- or Under-Prepared

### *Severe or Extended Side Effects*

The combination of the practices highlighted thus far in this chapter—funneling women toward reconstruction, mapping benefits and obscuring risks, and prioritizing form over function or feeling—results in many women being un- or under-prepared for the potential side effects of reconstructive surgeries. For some women, the duration of their side effects and recovery was much longer than they were initially told. Leah shared, "I knew that recovering from it was going to be at least two or three months long. That, I was prepared for. But you can never really prepare for it enough because it is a very difficult recovery. I thought that after two or three months all would be good. I did not think that it was going to be ongoing daily pain for the rest of my life."

Other women were unprepared for the muscle weakness and pain in the "donation" site on their bodies that is common with flap surgeries. For example, Beatrice, one of the women who felt unprepared for the lack of sensation in her reconstructed breasts, was also unprepared for the back problems she experienced after her reconstruction.

> I would say there were two things as I look back that I feel like I wasn't told about…. One was the complete lack of feeling in my breasts…. Second, because they removed a lot of muscle, I tend to have lots of upper back problems, which I am sure I make worse because I'm sitting around using an iPad all the time. But that is the main consequence of the surgery, is back problems. *(Beatrice, Age 64, BRCA1)*

Talia—the woman whose surgeon dismissed her concerns about abdominal weakness and instead focused on the "cuteness" of her breasts—was also unprepared for the muscle weakness she experienced.

> I didn't understand how much it would impact my abdomen, like the shape of it, the strength of it, primarily. And it totally--it changed shape fairly dramatically. It stuck out, and it was really firm, and it just didn't feel like my body at all. And the whole reason I

> had decided to have that type of reconstruction [flap surgery] was to keep my body as much like my body as I could…. So, I was thinking so much about my breasts, that I wasn't thinking about the abdomen. And I couldn't sit up. You know what I mean? I lost all strength in that part of my body. And you use the lower abdomen a lot, so it was like I just felt super-weak, and I thought I would never be able to be strong there again. I still feel really sensitive about that. *(Talia, Age 38, BRCA2)*

Talia's comment that she was so concerned about her breasts that she did not consider the impact on the other parts of her body involved in the flap surgery highlights the importance of providers emphasizing those risks and issues. It is not surprising that women would be more focused on what is happening to their breasts given that those breasts are the locus of the cancer risks they are attempting to manage. But surgeons perform these procedures regularly, are not making stressful personal decisions, and are aware of the range of issues women might experience. Therefore, it is incumbent on providers to highlight risks like these that patients may not yet know enough to inquire or think about.

Scarlett, one of the women in Chapter Two who decided to have mastectomy and reconstruction in part because it was less financially onerous than ongoing surveillance, was unprepared both for the range of complications that she experienced and their duration. First, she experienced necrosis while she had her expanders in:

> I had places that had turned black, that didn't heal on both sides. And he kept watching it and he kept saying, "I hope this is going to heal, but we don't know if it will or not." So finally, when I went in on my third week checkup he said, "We're going to have to go in and we're going to have to work on these places that didn't heal. I'll have to cut them out." Anyway, so the next week, which was almost exactly a month to the day that I had my surgery, I had to go back in and have some more surgery where they actually went on both sides and they cut all that black off and they restitched it. *(Scarlett, Age 61, CHEK2)*

After they removed all of the dying and infected tissue, Scarlett had wound healing issues, which limited her ability to do the physical therapy she needed to regain mobility in her arms:

> When they removed those stitches I immediately started bleeding in a few places. And

> within two days I had one place that had opened up probably a half an inch. I was sick. I was sick about it because that was the worst—that was one of the worst things that I went through because it took that place forever to heal. A long time to heal. And it prevented me from getting my physical therapy when I was supposed to because of the stress that it would put on that spot…. So, I couldn't like raise my arms up over my head. My arms were pretty much T-Rex. *(Scarlett, Age 61, CHEK2)*

Scarlett also developed surgical emphysema, which is air that gets trapped subcutaneously as a result of trauma to the tissue during a surgical procedure. "I noticed that my voice had changed. It sounded like I was talking out of my nose. I remember my grandkids were there. They were laughing at me because of the way I was talking. Anyway, then I noticed all this swelling that was taking place around my neck." Despite these symptoms, her plastic surgeon was dismissive. "My plastic surgeon, I e-mailed him the next morning and told him about it. But they were like, 'Oh well. You know, we've never seen that.' I thought, 'Oh well? Must not be that big a deal.'" Thankfully, Scarlett happened to hear from her breast surgeon soon after that, who conveyed to her, "This is not normal." He had her immediately return to the clinic for imaging and followed up with her over the coming days to ensure her breathing was unaffected.

***Reconstruction Regret***

Some women I spoke with who had not yet had mastectomy explained how witnessing their friends or relatives endure severe, ongoing side effects like Scarlett's had affected their feelings about having reconstruction in the future. They shared stories of women who—similar to Scarlett, Leah, and Talia—had unexpected, especially difficult, and/or extended side effects, and as a result experienced "reconstruction regret." For example, Maya, who had a lumpectomy to treat her breast cancer, was clear that if she had a recurrence, she would have a double mastectomy because of her PALB2 mutation. But she was still undecided about reconstruction. "You've got decisions and choices, but none of them are great." Maya's feelings about reconstruction were affected by friends who regretted their decisions. "I know, personally, at

least three women who've had their implants removed because of pain difficulties and just being fed up with it." Josephine, who is 41 years old and has a CHEK2 mutation, is currently undecided about whether or not she will have RRM. However, unlike Maya, Josephine is very clear that if she does decide to have her breasts removed, she will not do reconstruction because of the regrets she has heard from other women. "Almost everybody has some kind of regret about it. The couple people I have been DM-ing with on Twitter with were like, 'Let me tell you about the DIEP' or whatever one they did. 'I wouldn't do it again' is what at least two people have told me."

Leah's story was the most striking firsthand account of reconstruction regret that I encountered in my research. As I illustrated earlier in the chapter, Leah never considered staying flat before she had her surgeries, and even rebuffed her best friend who recommended not reconstructing. Leah originally had size DD breasts, and having breasts was important to her identity and sense of self. But after dealing with daily pain and discomfort under her arms and across her abdomen for over a year, she wishes she had heeded her friend's warning.

> Well, if I had to do it over again, I probably would have remained flat and not had the reconstruction done…. I have like a rope going across my abdomen because it's like a lot of cording that my body formed and there is nothing I can do about it. Still, I feel like I might have lymphedema going on, but I have not had the time to see my physical therapist for it. And there is always some kind of pain involved with it. I just wish I would have stayed flat…. It is awful. *(Leah, Age 55, CHEK2)*

Leah did not feel adequately prepared for the duration or severity of the side effects of her DIEP-flap surgery, and therefore, despite originally feeling certain that she desired reconstruction, she now strongly regrets her decision.

The stories shared in this section from Leah, Beatrice, Talia, and Scarlett are a selection of many I heard from women about being un- or under-prepared for the risks and side effects of

their surgeries and/or regretting their decisions to reconstruct. What is especially striking about the lack of preparation for reconstruction is that, unlike mastectomy and RRSO, reconstruction is a *cosmetic* procedure, not a *medical* procedure. In highlighting that distinction, I am not implying that reconstruction lacks value or is a frivolous decision. As I illustrated earlier in the chapter, several women also shared stories about how important reconstruction was to their social and emotional well-being, and it is critical that women having medically indicated mastectomies continue to have access to insurance-covered reconstructive surgeries.

However, it is also critical for women to be fully and accurately informed about the physical health risks of reconstruction so that they can make *truly* informed choices. Yet, as I have illustrated, women often are not provided with the full range of risk and benefit information. Instead, the structures, architecture, and discourses of genetic medicine propel women toward reconstruction and emphasize form over function and feeling, leaving many women un- or under-prepared for side effects and living with reconstruction regret. Being adequately informed about the risks of reconstruction might not alter women's decisions. For example, when discussing the two things she felt she was not told about, Beatrice said, "I don't know if they would have completely changed my decisions, but I feel like I was completely unprepared." But at minimum, additional information would likely make women feel more *prepared*—it could help them to calibrate their expectations and, as a result, cope better after their surgeries.

In addition, several women who had direct knowledge of the risks of reconstruction cited that awareness as a deterrent from having reconstructive surgery. For example, Tiffany opted to stay flat because she had witnessed her mother and sister both have severe complications with their reconstructive surgeries.

> It kind of started with my mom's first surgery. Like I said, all she really had was nipples, so they put expanders in and all this crap. And she had problems. It knotted up in there, and she had to go in and they had to release the pockets, and move things around and all of that. And my sister, she had—it starts with a D[47] now but it was called "tram flaps" back then—where they pull the stomach muscles and loop it and all that…. And my mom had to have hers redone now twice, and my sister still has an expander in from her second mastectomy. That hasn't been healthy enough to exchange it. *(Tiffany, Age 54, CHEK2)*

Similarly, Holly, a CHEK2 mutation carrier who happened to work for a breast surgeon, cited her knowledge of the risks and side effects as a major reason she had chosen not to have mastectomy or reconstruction. "Working in a breast care center, I take phone calls from people that are like, 'It's red, it's infected, my nipple's turning black.' Stuff like that that can happen, and I'm just like, 'I don't want that to be me.'" Hence, while there is no counterfactual, the perspectives of women who were more informed and understood the potential risks at a material level suggest that providing women with more precise knowledge of the risks and benefits of reconstruction might alter their decisions.

**Gendered Structures that Structure Gender**

By highlighting how the structures of genetic medicine funnel women toward reconstruction, prioritize form over function, and leave them under-prepared for the side effects of surgeries, I am not asserting that surgeons and other health professionals *intentionally* encourage women to take on more risks, objectify their bodies, conceal information from them, or disregard their feelings and embodied experiences. Just as I noted in Chapter Two that most breast surgeons want to help women reduce their risk of developing breast cancer, most plastic surgeons want to help women "return to normal" and feel good about their bodies. However,

[47] Tiffany is referring to DIEP-flap surgery.

intentionally or not, providers are participating in these macro-level processes, and drawing attention to them is important because they reveal how the practices that constitute genetic medicine are simultaneously *gender-structured* and work to *structure gender.*

Sociologist Raewyn Connell argues that gender is a process, or "linking concept," that is constituted by practices and organizes social life (Connell, 1987, p. 140). That is, gender is simultaneously something we *do* and something that *shapes what we do*. Returning to Connell's definition of structure as "the way practice (over time) constrains practice" (Connell, 1987, p. 95), one can see how the structures of genetic medicine can simultaneously reflect the existing gender order and reproduce the individual, social, economic, and political practices that constitute that order. The gender order is, to some extent, always in flux because patterns of social divisions and power relations between men and women are not static. However, in the prevailing gender order in the United States, women are still frequently objectified, they are disproportionately judged by and valued for their appearance, and they continue to perform a significant majority of the physical, social, and emotional labor of childrearing. As a result, practices in genetic medicine emerge from those gendered social realities and sometimes reinforce them.

However, as Connell illustrates, social reproduction is one possible outcome of practices, but not an inevitable one. She argues that the effects practices have on practices can be either "divergent or cyclical"—they can lead to new and different practices or reproduce existing ones—and that cyclical practices are what institutionalize gender regimes and stabilize the gender order. "[G]ender is institutionalized to the extent that the network of links to the reproduction system is formed by cyclical practices. It is stabilized to the extent that the groups constituted in the network have interests in the conditions for cyclical rather than divergent

practice" (Connell, 1987, p. 141). Earlier in the chapter I illustrated how the architecture of genetic medicine, which is its "network of links," funnels women toward reconstruction through regulatory, organizational, and referral practices. This is an example of cyclical practices institutionalizing gender. The pathways of care in genetic medicine emerge from gendered norms and assumptions about women's bodies, and then being on those pathways through genetic medicine makes it more likely that women will, in fact, conform to those norms. Hence, one can see how the architecture of genetic medicine is both gender-structured and structures gender.

Similarly, the focus on how women look over how they feel after breast reconstruction is an example of cyclical practices stabilizing gender. The surgeons I spoke with at conferences genuinely wanted to empower women making the difficult choice to have and to help them recover and return to "normal." However *normalized* bodies are *gendered* bodies. Moreover, plastic surgeons as a group have a strong professional interest in maintaining those norms and the high social value placed on women's appearance because their "success" is defined by aesthetic outcomes. Hence, their practices, like the architecture of genetic medicine, are simultaneously gender-structured and structure gender.

Surgeons are only one of many groups operating in the Risk Management field of practices that responds to genetic risk. Genetic counselors, gynecologic oncologists, clinical geneticists, policymakers, insurance providers, advocacy groups, and people with genetic mutations are other critical actors in this field. As I have illustrated thus far through women's decisions around reconstruction, many women with BOC genetic mutations engage in practices that reflect and reproduce the social value placed on women's appearance. Other women engage in divergent practices, like staying flat, that disrupt and challenge gender norms. In the next section, I will examine circumstances in which women with genetic mutations participate in cyclical practices

that reflect and reinforce gendered norms and ideals for women's bodies.

***Building Women's Bodies While "Cutting Them Down to Size"***

Breast reconstruction does not just "structure gender" in a figurative or conceptual sense. It is a cosmetic surgical process that quite literally reshapes and *constructs* female bodies. Because breast reconstruction practices are also gender-structured and shaped by social and cultural gender norms, they are not neutral. Rather, they often help to build *idealized* feminine bodies that are thin, toned, and have large or perky breasts. For example, during a webinar for genetics professionals about reconstruction options, one plastic surgeon referred to DIEP-flap surgery as "a great way to get a free tummy tuck *and* a new breast." This surgeon's quip illustrates how breast reconstruction not only involves building new breasts, but also what advertising critic Jean Kilbourne refers to as "cutting women down to size"—encouraging them to occupy less physical space in the world and to make their bodies smaller and thinner (Kilbourne, 1999).

Brenda, a BRCA1 mutation carrier who was planning RRSO but not mastectomy, shared her concerns about how breast reconstruction practices contributed to these gendered norms:

> I have been noticing how a lot of the culture-dominant things are reinforced through these processes. Automatically assuming that women want to get breast augmentation. Automatically assuming that women want to get some kind of liposuction in order to reconstruct their breasts…. They are all bound up in this really dominant society, which is white Western capitalistic patriarchal culture, view that women's bodies are this thing that need to appear a certain way to please other people, primarily men… and that there is this one body type that women want to achieve that is wrapped up in being approved on by the public, in general, and society or anybody who wants to chime in on it. *(Brenda, Age 39, BRCA1)*

I initially met Brenda at a patient advocacy conference and later spoke with her in two in-depth interviews. During one of her interviews, she noted how grateful she was for the advocacy group sponsoring the conference because they help women access current, accurate information about their medical options and provide safe spaces for women to share their stories and experiences.

However, as a self-described "gender nerd," Brenda was sensitive to how the discourses around reconstruction in previvor communities might reinforce stereotypically narrow conceptualizations of "ideal" feminine bodies.

Indeed, many women I spoke with participated in these discourses and felt positively about reconstruction precisely because it did or would help them achieve idealized feminine bodies. For example, at the patient advocacy conference where I met Brenda, there is an annual evening event, "Bare and Share,"[48] in which women who have had mastectomy or reconstruction volunteer to semi-privately display their surgical "results" (i.e., their flat chests or reconstructed breasts) and discuss their experiences with women considering the procedures. Women gather at signs posted throughout the room that correspond to different types of reconstruction, some of them with their tops off and others fully-clothed.

At the Gluteal and Thigh Flap station, I met Isabella, Bryna, and Jane. Isabella and Bryna were both "models" at the station, and Isabella was especially friendly—she smiled throughout the event and encouraged other women to come over and talk with her. Jane had not yet had mastectomy or reconstruction, and she was surveying the room to consider her options. When she approached Isabella, Jane, who was quite thin, said, "See these thighs? Would they get rid of these?" Jane then asked Isabella if she would mind showing her scars. Isabella turned around, pulled down her shorts, showed Jane the incisions along the bottom of her gluteals, and noted that she had gone down two clothing sizes after the surgery. Jane responded, "Are you kidding?! From a what to a what?" Bryna, who had also had gluteal-flap surgery, said, "They gave me a complimentary tummy tuck, too, to even me out. I got rid of my baby pooch." Jane turned sideways, pointed to her stomach, and said, "Oh, like this?" And when Bryna commented that

[48] Like other proper names used in this study, this is a pseudonym.

Jane didn't have a pooch, Jane replied, "Oh, that's me sucking it in."

Several women I interviewed also referred to these "side benefits" of their surgeries—the opportunity to have larger breasts and/or a "butt lift," "thigh lift," or "tummy tuck" that would make them appear thinner. For example, Liza who was only 30 when she had her mastectomy and reconstruction, said, "I knew that I wanted to try to get to my size and, if I could, get a little bit bigger. I figure since we have to go through it anyways." Adele, who has a BRCA2 mutation and is planning on having DIEP-flap reconstruction, said, "I kind of almost look at it as the, you know icing on the evil, I guess. Because it's not really cake. But that's the one upside—that I can finally have big boobs." Veronica, who has a BRCA1 mutation, also wanted her reconstructed breasts to be larger. "First of all, I asked the plastic surgeon to go up a size. I wanted bigger breasts. And I said, 'I'm gonna get some benefit out of this, and so I want bigger breasts and I want that tummy tuck, we'll just keep digging.' And, so I actually like my breasts better now than I did before, and I feel like, yeah, my stomach is flatter." Marianne, who has a CHEK2 mutation and was in her late 50s when she had mastectomy and reconstruction, referred to her surgeries as a "win-win": "I feel happy that I reduced my risk significantly. And I got some breasts that look better to me than they looked before." Together, these stories illustrate how the gendered the focus on form and appearance in genetic medicine also reflects many women's desires and priorities. Tiffany, a CHEK2 mutation carrier who chose not to reconstruct after her mastectomy, commented that "A lot of women are disillusioned into thinking 'This is the fix-all, and I get new boobs in the process.'"

In fact, some women were so convinced that surgeries were a "fix-all" that they felt disappointed that they could not have procedures that would provide them with these "benefits." For example, Colette, a CHEK2 mutation carrier who was in her mid-30s and had scheduled

implant reconstruction, shared how she initially had hoped for autologous tissue reconstruction. "So, at first, I thought that we could do the flap surgery, which means that they take fat from another part of your body. I thought, 'Oh cool! It is a tummy tuck at the same time! So, if I have to do this maybe I'll get the tummy tuck for what my son left me and get it off.' But the plastic surgeon didn't feel like I had enough." Alexis shared how her sister, who tested negative for the BRCA2 mutation in their family, had wanted the reconstructive surgeries to "improve" her post-baby body.

> My older sister, it's been very interesting because she had shared with me that she wants breast reconstruction 'cause she's had three children, breastfed all three, and is not happy with her appearance. And she alluded to me that she was actually, I think, disappointed that she wasn't [positive for a mutation]. *(Alexis, Age 34, BRCA2)*

In contrast to Adele, who framed the possibility of having larger breasts as a "silver lining" in an otherwise bad situation, Alexis's sister was *only* focused on the "benefits" of reconstruction. Her desire to improve the appearance of her body was so strong that she felt "disappointed" that she did not have a genetic mutation that confers risk for multiple cancers. As Alexis noted about her sister's response, "I don't think she's fully absorbing what it would all mean." Her sister's narrow focus serves as a powerful illustration of the pressure on women to have their bodies conform to idealized social expectations.

The framing of reconstruction as a benefit or silver lining is linked to discourses that refer to the surgery as a "boob job," which in turn can serve to obscure the risks of the surgeries. Amber, one of the two youngest participants in the study at age 23, was awaiting her scheduled mastectomy and flap reconstruction. She expressed how she framed reconstruction as a "boob job" in order to reassure herself about her decisions. "That is kind of how I look at it to make myself feel good about it. I just keep telling myself that it is a boob job. 'It is just a boob job.'"

Naomi, who eventually opted not to reconstruct, explained how she also had initially viewed reconstruction this way before she fully understood the complexity and risks of the procedures.

> My assumption, like many people, previously, was that it was just like having a boob job. In my mind, that was exactly how I built it up. Okay, no big deal. I will just get implants or something. When I thought it wasn't going to be so involved or complicated, I didn't actually mind. I knew it didn't meet my body expectations, but the reality is that it would probably be easier if the surgeries would be easier. That was before I really thought about what I was doing to my body afterwards. It was the fantasy of the breast reconstruction. *(Naomi, Age 47, PALB2)*

Naomi's story illustrates how a "boob job," which entails augmenting existing breast tissue with implants, is a very different—and far less complicated—procedure than constructing entirely new breasts. The "fantasy" of reconstruction as a "boob job" simultaneously reflects how the risks of reconstruction are often obscured and serves to perpetuate the relative invisibility of those risks. In fact, Amber clarified that she intentionally used the fantasy as a coping mechanism to help her not think about the potential complications. When I asked her, "Is it just a 'boob job?'" She replied:

> No, it is a mastectomy. It is a lot different than a boob job because they have to completely take everything out and you won't have sensation in your boobs anymore. I know that the scars are different. And I know it is different. I have really bad anxiety so if I think about having a major surgery like that it freaks me out and I won't be able to sleep. I just keep telling myself that it is just a boob job to kind of get through it. I just try not to think about all the other details that go along with it. *(Amber, Age 23, BRCA1)*

***Gendered Pressure to Reconstruct***

Brenda's unease about the discourses and practices of reconstruction were rooted in a larger concern "that women don't have the ultimate agency over their bodies." She described her feelings during *Bare and Share* when she observed other women participating in conversations that constructed "ideal" women's bodies as thin and/or large breasted:

> It just makes me really conscious of how are other women in the room reacting to this? How are other people feeling? Do they have an eating disorder? Is this talk about, 'Well of course there's this side benefit of a tummy tuck!' How is that making them feel? And how is that potentially going to impact their ability to get support from this group or get good treatment from their medical team? How much confidence did they feel to assert for what they wanted to happen for themselves, not only about their care, but their body overall? (Brenda, Age 39, BRCA1)

Jessie, a CHEK2 mutation carrier, shared Brenda's worry that some women's decisions would be constrained by social, relational, or cultural factors. She said, "I hope they don't get reconstruction just because they think they have to get reconstruction." Both Brenda and Jessie understood that some women might choose reconstruction not because it felt like the best choice for them, but rather because, as Tiffany expressed, "Society says 'this is how a woman's supposed to look,'" or, as Eleanor conveyed, "the only socially acceptable decision is for you to have two breasts after surgery."

Unfortunately, several women in the study did convey that they or other women they knew felt social expectations and pressure to reconstruct. Emily, who discovered her CHEK2 mutation after being diagnosed with DCIS, shared her experiences participating in an in-person support group for breast cancer survivors. "Almost everyone in my local breast cancer group has had reconstruction. But all they do is talk about how much pain they're in, how much numbness they have, how it doesn't look normal or natural, how they're disappointed with the results. But yet, they felt like they had to get 'em." Unlike the women in Emily's support group, Crystal, who was in her late 30s when she had implant reconstruction, expressed that staying flat sounded personally appealing. However, she also felt it was important to have the appearance of breasts given her relatively young age.

> And you know, staying flat sounded kind of nice, but I did feel like I was still young enough that I wanted breasts, the look of breasts, to balance me out. I thought to myself that if I were older then I probably would. You don't have to worry about—after a few

> years you have to get your implants redone. You don't have to worry about that [if you stay flat]. And you don't have to worry about bras, which I have always hated and much more now. It just seems a lot easier. It seems nice… But I guess for sanity reasons I got the reconstruction. *(Crystal, Age 39, BRCA1)*

Even though Crystal expressed multiple ways she would have felt more physically comfortable flat, she still perceived having the appearance of breasts as the best way to protect her "sanity."

Nina's story provides the sharpest illustration of the social pressure some women feel to reconstruct. When I interviewed her, she was 35 years old, but she had learned about her BRCA1 mutation nine years earlier, at age 26. At the time she chose to continue with surveillance rather than having RRM, and she formed an online support group for women at BOC genetic risk who chose surveillance because she felt there was little social visibility or support for that decision. At age 34, Nina was diagnosed with triple-negative breast cancer,[49] and subsequently underwent chemotherapy, a bilateral mastectomy, and reconstruction. When I asked about her decision to reconstruct, she said, "I would have chose to go flat, I mean that would have been my preference, but I felt a lot of societal pressure to have breasts as a woman." Nina chose implant reconstruction because she was concerned about the pain and extended recovery time involved in flap surgeries. Her expanders had been swapped with her implants only eight weeks before we spoke, so she was still experiencing discomfort and adjusting to life with her reconstructed breasts. "It hurts still. Things are sore and things are healing and things are itchy, and I can't scratch them, and things are numb so I can't relieve the pain, and there's pressure."

Nina later elaborated on social expectations she encountered about reconstruction. She

[49] As explained in Chapter Two, when a breast cancer is "triple negative," it lacks estrogen, progesterone, and HER2 receptors. Triple negative breast cancers are harder to treat than cancers with hormone receptors because they do not respond to hormone-blocking drugs. Women with BRCA1 mutations are disproportionately likely to develop triple negative breast cancer. While only 12-14% of breast cancers are triple negative, approximately 70% of BRCA1-associated cancers are (K. N. Maxwell, 2015).

remembered reading the critical comments people wrote about a Dove ad on Facebook in which shirtless breast cancer survivors were displaying their scars. "People are like, 'Well, their insurance would have paid for reconstruction!' And it was just so expected that they do that. There was so much negative comments." In addition, Nina felt concerned about how negative perceptions of a flat body might intersect with the discrimination she already faced as a younger, tattooed Asian woman.

> I had just been promoted in my career, and so it just felt—I already have tattoos from when I was young and wild, and was gonna live a short life, right? So, I already feel that I'm treated as 'less than' because of that, and also being a woman of color. So, I wanted to try to assimilate as much as possible and avoid any sort of implicit bias. And I thought moving forward or advancing my career would be challenging if I looked sick. *(Nina, Age 35, BRCA1)*

While Nina would have preferred to stay flat and understood reconstruction involved additional risks, she felt that a gender-non-conforming body might be perceived by others as looking "sick," and that this could impact her professionally. She also conveyed that her surgical team encouraged her to reconstruct. "Both the surgeon and the plastic surgeon said it's easier to do it now, and we'll do—do somewhat skin sparing, do reconstruction. If you don't like it and you don't want to keep it, or it's too challenging, we'll take it out."

Taken together, Nina's experiences powerfully illustrate how gender circumscribes women's choices in the risk management field of practices *and* how that field of practices works to reconstitute gender norms. Nina knew she would rather stay flat but felt she could not make that choice because of social expectations for how a feminine body should look and the gender and racial discrimination she faced in the workforce as an Asian woman. People and practices in genetic medicine are also shaped by those gendered expectations, leading Nina's surgeons to view and frame reconstruction as the "easier" choice, despite it being riskier and more

complicated than not reconstructing. In turn, by propelling many women toward reconstruction, these genetic risk management practices reify social expectations for "normal" feminine bodies, thus reconstituting the gendered norms from which they emerge.

**Resisting Gendered Structures**

Not all women who had or were planning reconstruction agreed with the discourses and practices that encouraged them to conform their bodies to gendered expectations. For example, Judy, who was in her mid-forties and had an ATM mutation, described how her surgeon had discussed DIEP-flap surgery with her. "Well, the plastic surgeon was like, 'You can kind of get a tummy tuck with it.' And I was like, 'I am already losing one thing, why would I want to tummy tuck too?'" She eventually chose to have implant reconstruction instead. Leah shared how removing that abdominal tissue for her DIEP-flap surgery had an unexpected psychosocial and emotional impact on her:

> Having the DIEP and going through it and thinking you are going to be skinnier because they are taking your abdominal fat from your kids that you have accumulated. This is going to sound weird, but having that taken off of me was a weird feeling. It was like I never carried babies in my body. That pouch was always there because I had birthed three kids. So, having that removed, it was nice because now I am going to fit into some things better, but not nice because, wow, all evidence of having been pregnant and birthing kids is gone. *(Leah, Age 55, CHEK2)*

Leah felt ambivalent about having a flatter stomach after her reconstruction. She welcomed it because she fit into smaller clothes, but mourned it because the extra weight on her abdomen was an embodied reminder of the physicality and materiality of motherhood. By noting that it was "going to sound weird" that she missed that weight, she simultaneously acknowledged and challenged the assumption that women should want to be thinner and have flatter stomachs.

Other women resisted the notion that larger breasts are always better. Hannah, a BRCA2

mutation carrier who, along with Amber, was one of the two youngest women in the study at age 23, shared how her experiences trying to "go bigger" with her implants left her dissatisfied.

> I tried going bigger for a bit with the expanders, but I hated it. So, I had her make me small when she did the reconstruction. It wasn't me. It really wasn't me. Everyone was like, "Go bigger you're getting your boobs done, you'll love it!" I tried it and I didn't like how my clothes looked. I didn't like how I looked. I was like, "I have been flat chested my whole life. It is one of my favorite traits about me." *(Hannah, Age 23, BRCA2)*

Colette also did not want to be bigger, and in fact was looking forward to reducing the size of her breasts. "I am going to have a reduction so I will be smaller than I am now, which is something that I wanted." Colette's experiences also highlight how women do not uniformly conform to or resist gendered expectations, as she was one of the women who felt disappointed about not being able to "benefit" from the "free tummy tuck" provided DIEP-flap surgery.

***Empowerment or Constrained Agency?***

In her study of women with BRCA mutations, Sharlene Hesse-Biber argues that women who have support for and feel "in control" of their risk management decisions are empowered by them, while women who are pressured to have preventive and reconstructive surgeries are more likely to experience regret. She asserts, "What have we learned? In the end, a woman can be empowered regardless of her treatment choice as long as she takes control of the decision-making process"(Hesse-Biber, 2014, p. 124). To illustrate this point, Hesse-Biber shares the experiences of Caroline and Liz. Caroline always knew "there was no question" she would have risk-reducing surgeries if she was BRCA-positive. Hesse-Biber claims, "Most important in making Caroline's experience an empowering one is her own confidence in preventive surgery being her own decision, and the right one" (Hesse-Biber, 2014, p. 120). In contrast, Liz initially opted for surveillance but eventually decided to have a mastectomy and a hysterectomy after one of her doctors told her that screening was "not enough." Hesse-Biber asserts, "Liz's experience is

disempowering, not only because of the circumstances leading up to the surgeries but also because she is uncertain about her decision when she reflects on it" (Hesse-Biber, 2014, p. 123).

However, as I have illustrated in this and the previous chapter, there are multiple ways in which the structures and architecture of BOC genetic medicine propel women toward RRM and reconstruction. That encouragement is rarely overt and explicit. Rather, the Risk Management field of practices funnels women toward reconstruction and encourages them to prioritize their appearance over their embodied experiences whether individual clinicians embrace and employ a rhetoric of choice (as many genetics professionals do) or are more directive and explicitly tell women to have surgery.

As individuals, we have agency and make choices, but our decisions are always filtered through and constrained and enabled by our social worlds. I have illustrated in both this chapter and the previous chapter that the structures and architecture of BOC genetic medicine in the United States funnel women toward RRM and reconstruction, making those choices appear natural and normal. Hence, when Caroline stated that she always knew she would have risk-reducing surgeries and reconstruction, her knowledge and decisions were not formed outside of the practices or influence of genetic medicine. We are never outside of structure or culture. However, it is often only when our decisions run counter to structures or culture, as Liz's decisions initially did, that the pressure they exert becomes visible. The practices in genetic medicine that funnel women toward RRM and reconstruction are like an ocean current: if you swim against the current, you feel its force, but if you float or swim with it, it is barely, if at all, noticeable. Hence, a key difference between Caroline's and Liz's surgical experiences was not whether those experiences were influenced by external factors or pressures; both women were swimming in the current. Because Caroline was swimming with the current, it was invisible to

both her and Hesse-Biber. Conversely, in trying to swim against the current, Liz rendered it visible.

***Side Effects Matter***

The fact that Caroline experienced no unexpected complications or extended side effects is also integral to the very feeling of being "in control" that Hesse-Biber argues is essential to women's "empowerment." Hesse-Biber conveys that Caroline described her surgeries as "'literally a breeze,'" and that she expressed bewilderment about why other women sometimes felt unhappy with their choices. "'I don't know why people have such bad experiences. I don't know if that's because they weren't ready, if their doctors maybe weren't right for them, I'm not sure. I knew what I was going to do was going to be good for me in the end'" (Hesse-Biber, 2014, p. 120). However, there is no way for any woman to know, in advance, that her decisions are "going to be good for [her]" because women do not have control over the physical outcomes of their surgeries.

Several women in this study—for example, Leah, Talia, and Scarlett—initially felt certain about and "in control" of their decisions to have RRM and reconstruction. However, they later expressed varying degrees of regret about those decisions because they felt out of control when they experienced severe or extended side effects that were not in line with their expectations. Hence, much like women's decisions are always in some way shaped by the structural systems that encourage them to reconstruct, women's subsequent feelings about their surgeries are always filtered through and influenced by their knowledge about the potential side effects of the surgeries and their actual surgical outcomes. When those outcomes are positive or align with women's expectations, the impact of side effects tends to be invisible, leaving women like Caroline happy and befuddled by other women's dissatisfaction. Conversely, negative or

unexpected outcomes like Leah's chronic pain and abdominal roping are often hard to ignore given the impact of those side effects on women's daily well-being and quality of life.

Understanding that negative side effects and a misalignment between expectations and outcomes are major factors in women's post-surgical satisfaction helps to explain why many women in this study who had reconstruction expressed regret about their decisions, but none of the women who stayed flat did. The range of potential side effects and complications for mastectomy alone is considerably narrower than the range for mastectomy with reconstruction. Hence, women who choose not to reconstruct may be more likely to be satisfied with their decisions because there is a reduced statistical likelihood that they will have a complication or side effect or experience misalignment between their expected and actual outcomes.

***Staying Flat, No Regrets***

Most of the women I spoke with who stayed flat vociferously conveyed their satisfaction with their choices. For example, Tiffany stated, "I have no regrets going flat. I wear stuff now I would have never worn before. I was raised very modest. My dad was a minister, and now I can wear tank tops and all kinds of stuff with no bra, no tan lines, no cleavage, no breast showing, and I actually really feel free. Free! That's the only way I can explain it. It's like, 'Finally!'" Wendy described feeling strong and empowered by her decision to stay flat, in part because she was actively resisting gendered norms. "It is like a warrior. I look in the mirror at my scars, and I'm delighted. Society tells you have to look a certain way, and it's sad." Jessie also expressed her happiness with her decision not to reconstruct, noting that if she felt differently in the future, she could still have it done.

> [I'm] incredibly grateful that I didn't do reconstruction…. My best friend from high school had reconstruction, she looks like she's been stabbed. She's had nothing but problems. So, I'm very, very happy and comfortable with my decision. Every day I am

> very happy and comfortable with my decision. That's not saying that sometimes breast cancer doesn't stare me back in the mirror like a vengeance, but at the end of the day I'm very, very happy with my decision. Or I'd have reconstruction tomorrow, and that's why I don't is, I'm very happy with my choice. *(Jessie, Age 48, CHEK2)*

In fact, the only woman who stayed flat who expressed any dissatisfaction was Ingrid, and she was not unhappy with her decision. Rather, the surgeon who performed her mastectomy was a general surgeon, and she left extra skin behind. Ingrid disliked how the loose skin on her chest looked, but more importantly she felt concerned that the skin contained breast tissue or cells that would elevate her risk:

> I'm fine with not having breasts, I really am. However, because of this genetic mutation and because I keep on getting the cancers, I needed to have all my breast tissue removed, and she did not do that completely. So. I just saw her yesterday, I just had a five-month follow-up with her yesterday. She left a lot of skin. I don't know if you've seen pictures of this, but she left a lot of skin on the prophylactic breast. So, I will need to go for a follow-up surgery…. If I didn't have the genetic component, I probably would be ok with the breasts the way that they are… but in the end, the bottom line is I want to do everything I can to not get the cancer again. *(Ingrid, Age 62, PALB2)*

Like Ingrid, other women who stayed flat expressed that they, in part, made the choice because they felt it conferred their best chances of survival. For example, Marlene referred to the iatrogenesis inherent in reconstructive surgeries when she posed the rhetorical question, "Why would I want to create another risk by reducing a risk?" Similarly, Wendy conveyed that her decision was affected by the recent finding that certain types of breast implants were associated with the development of a rare form of lymphoma. She explained, "I don't care if it's 1 in 5 million. I want to give myself the best chance of survival." For Wendy, any additional risk posed by a cosmetic surgery was too high for her to consider it a viable option. Emily was also concerned about added risks posed by reconstructive surgeries because, as a diabetic, she was disproportionately likely to have difficulties with wound healing. "Knowing that again, being diabetic, I was at high risk anyway, I thought to myself, 'Why do I want to chase after perfection,

when no matter how talented a plastic surgeon is, it can never give me back what I lost?'"

***Restructuring Gender***

Emily's concerns about risk intersected with her disinterest in "chasing after" an idealized feminine body—she saw staying flat as the best way to minimize risks to her physical health and as a means of resisting gendered norms. However, whether or not women explicitly conveyed a desire to do so, staying flat inherently involves challenging gendered expectations for women's bodies. One of the most striking examples of how linked breasts are to womanhood was illustrated by a thread Eleanor shared from "Amazing Flatties." I spoke with her after HB2 had passed in North Carolina. This anti-transgender state bill restricted people to using the bathroom for their sex assigned at birth. Eleanor conveyed that other people had attempted to stop several women in the group who lived in North Carolina from using a women's restroom because they were assumed to be transgender. The transphobia described in these stories was disturbing. In addition, these incidents revealed how breasts are such a powerful visible marker of womanhood that other people assumed that women without breasts must "really" be men. Hence, just by moving through the world in their flat bodies, women who choose not to reconstruct disrupt social and cultural constructions of idealized femininity.

Given the strong link between breasts and womanhood, it is not surprising that several of the women who chose to stay flat did explicitly challenge these normative, idealized constructions of women's bodies. Naomi, who is a biology professor, researched the peer-reviewed literature on her options before choosing not to reconstruct. She explained:

> I do know that breasts are not my body, they are not me, and they do not define me. All of the surgeries involved and all of the complications that I have learned about—not through my doctors, which really bothers me. In all the research that I had to do on my own, I started writing up a document that I could share with people at some point of these

> studies. Okay, what are the complication rates after the first year of surgery? There are meta-analysis studies. What are the complications after a couple years? What are the satisfaction rates of reconstruction and without reconstruction? Is there that much of a significant difference? I started reading all of these studies and looking at pictures of women with different reconstruction. I started reading "Amazing Flatties" and those different kinds of websites. I decided, look, none of these decisions are great for me. It all sucks. What for me is the least sucky thing that I can do? That is having the mastectomy and then stopping there in terms of continuing surgeries. I just do not want all of that to meet some kind of conception of what my body should look like in front of other people. I know that for a lot of women, that would help them, but I think for me it would not. It would feel like I am doing this thing to meet societal expectations and that is continuing to injure my body. That was why I made that decision. *(Naomi, Age 47, PALB2)*

Naomi's decision to stay flat was partially rooted in the knowledge she gained through her research on the literature on reconstruction and through connecting with other women who had faced decisions about breast surgeries. But her decision was also linked to her sense that reconstruction was about meeting "societal expectations" for women's bodies and appearing feminine to others. Because perpetuating those gendered expectations involved taking on additional physical health risks, she perceived it as "injury" to her body. Reconstruction would have left Naomi feeling less whole, not more.

Eleanor's decision to stay flat was also strongly shaped by her identity as a feminist and her dissatisfaction with social and cultural constructions of gender that value women and their bodies for how they look and as objects of desire.

> I have issues with cultural constructions of gender that matter on appearances. I felt like signing up for reconstruction surgery was only going to perpetuate that…. I don't feel like I need to hide behind some fake breasts to make other people feel more comfortable…. I'm sure you've figured it out, but I'm a feminist, and I've been a feminist for as long as I can remember. And I feel we should not be defined by our outward appearance, we shouldn't be defined by whether we conform to the cosmetic and beauty industry's definition, or the porn industry's definition of what a woman should look like. *(Eleanor, Age 42, ATM)*

Like Naomi, Eleanor felt that reconstruction was mostly about making "other people feel more

comfortable" and "conforming" to external, idealized standards of feminine beauty. She felt that choosing reconstruction would serve to "perpetuate" the gender order, and so instead she actively challenged and attempted to disrupt the reconstitution of that order by staying flat.

Women who stay flat actively challenge the gendered structures of genetic medicine and the ways risk management practices reinforce gendered expectations for women's bodies. Hence, they exhibit a high degree of agency, and may, in turn, also be more likely to feel and express satisfaction with their choices. On the surface, this might appear to support Hesse-Biber's argument that women with BRCA mutations are "empowered" by their surgical decisions when they feel in control of them. However, Hesse-Biber's argument is tautological—empowerment is, in part, defined by being in control. She conflates empowerment with satisfaction, and women being *empowered* in their surgical decisions is not the same as them being *satisfied* with those decisions. As this chapter has illustrated, when women are only or mostly given information on one set of options (reconstruction), and both the risks of that option and the alternative (staying flat) are obscured, they are neither empowered nor in control.

In addition, focusing on whether women are "empowered" by their surgical decisions perpetuates two common practices in research on BOC genetic medicine. First, it focuses attention on the individual or relational dimensions of women's decisions rather than on how structures constrain and enable those decisions. Second, examining whether women are "empowered" in their surgical *decisions* obscures the impact of surgical *outcomes* on women's lives. The absence of physical complications among women in this study who stayed flat was striking, particularly when compared to the severity and duration of side effects reported by women who had reconstruction. Focusing on women's decision-making diverts attention away from how the structures of genetic medicine frequently leave women ill-equipped to make those

decisions in the first place *and* un- or under-prepared for the outcomes of those decisions.

**Conclusion: Which Risks?**

This chapter shed light on the mutually constitutive relationships between gender and breast reconstruction practices in the United States. Drawing on the experiences of women with BRCA and moderate-risk BOC mutations, I illustrated three structural elements of breast reconstruction practices within US genetic medicine. First, women are propelled toward reconstruction through silence among providers about the option to stay flat, health insurance policies that privilege reconstruction, organizational and referral practices that fuse mastectomy with reconstruction, and practices that emphasize the benefits of mastectomy but minimize the risks of reconstruction. Second, reconstruction practices prioritize how women's breasts and bodies look over how they feel from an embodied perspective. Third, practices in BOC genetic medicine obscure and minimize the potential risks posed by reconstruction, leaving many women under-prepared for the side effects of the surgeries.

I argued that these practices reveal how BOC genetic medicine is both structured by the prevailing gender order in the United States and works to structure and reconstitute that order. That is, the field of practices that responds to BOC genetic risk simultaneously reflects and reifies constructions of "ideal" feminine bodies: bodies that appear thin and toned and have large or perky breasts. By encouraging RRM, the practices of BOC genetic medicine treat real breasts—ones with sensation or that feed babies—as disposable because of their risk of developing cancer. Yet, as this chapter has shown, the *appearance* of having breasts is constructed as essential, even when creating that appearance through reconstruction poses additional risks to women's health.

This chapter highlighted a tension in the Risk Management field of practices—it is

centered on reducing women's risks, but *which risks*? Current practices in genetic medicine serve to magnify certain risks while minimizing others. In the previous chapter, I highlighted how women's risk of developing breast cancer is emphasized and targeted for reduction through mastectomy. In this chapter, I illustrated how the psychosocial risks generated by mastectomy are emphasized and targeted for reduction via reconstruction, while the risks that are iatrogenically added through reconstruction, such as scarring, chronic pain, muscle weakness, necrosis, and infection, are often minimized or overlooked. Thus, the cosmetic procedure that makes risk-reducing mastectomy more socially acceptable also makes it more medically dangerous.

There is no question that the risk of developing, and potentially dying from, breast cancer is more severe than the risks of side effects and complications from reconstructive surgeries. *But mastectomy, not reconstruction, is what reduces women's breast cancer risk.* Hence, risk-reducing mastectomy is a medical procedure that increases women's social and cosmetic risks. In contrast, breast reconstruction is a social and cosmetic procedure that increases women's medical risks. Given that there is not parity in either the risks or benefits of the procedures, uncoupling mastectomy from reconstruction and making their unique risks and benefits visible seems critical in a field focused on risk-reduction and empowering women through knowledge. However, as I illustrated in this chapter, current practices in BOC genetic medicine in the United States tend to do the opposite. As a result, many women are un- or under-prepared for the risks and side effects of their reconstructive surgeries.

Women's lack of preparation for reconstruction is striking because it is a cosmetic procedure with numerous potential risks and limited benefits to women's physical health. However, women being unprepared for surgical side effects was not limited to breast reconstruction. In the next chapter, I will examine risk-reducing salpingo-oophorectomy (RRSO)

practices in the United States. In contrast to both mastectomy and breast reconstruction, RRSO has robustly-established, statistically-significant medical and physical health benefits for women at high risk of ovarian cancer. However, similar to the stories women shared about the side effects of breast reconstruction, women were also often un- or under-prepared for the impact of medically-induced menopause, which affects their cognitive, emotional, sexual, and physical health and daily quality of life.

## Chapter 4: "The Doctor Didn't Tell Me That": Under-Preparation for Medically-Induced Menopause

> "I'm on a roller coaster ride that's going so fast since my oophorectomy." *(Dorothy, Age 53, BRCA2)*

> "You're 40 and going into menopause. No sort of acknowledgment of what that means, the sexual repercussions. All the things that come with menopause were just not acknowledged at all." *(Marci, Age 39, BRCA2)*

> "As much as I complain about the implants and the fake breasts, the ovaries have definitely been more of an impact on my body overall, getting those removed. And again, I didn't really anticipate how much they were going to change me." *(Raina, Age 43, BRCA2)*

### Introduction

Several epidemiological and clinical studies have illustrated that risk-reducing salpingo-oophorectomy (RRSO) between the ages of 35 and 45[50] is the single most effective intervention for improving survival rates for women with BRCA mutations (S. M. Domchek et al., 2010; A. P. Finch et al., 2014; Ingham et al., 2013; A. W. Kurian et al., 2010; Parker et al., 2013). Yet, despite these findings, there is far less social science research on women's risk reducing salpingo-oophorectomy (RRSO) experiences than on their experiences with risk-reducing mastectomy (RRM) and/or reconstruction. Moreover, like with most mastectomy and reconstruction research, the limited social science research on RRSO tends to examine individual- or familial-level factors that shape women's decisions about and responses to prophylactic surgery (Borreani et al., 2014; Nina Hallowell, Mackay, Richards, Gore, & Jacobs, 2004; Mai et al., 2017).

Drawing on fieldwork at cancer genetics conferences and interviews with 33 women with

[50] The recommended age range for RRSO for women with BRCA1 mutations is ages 35 - 40. Onset of ovarian cancer tends to be later among BRCA2 mutation carriers, so they can usually safely delay RRSO until ages 40 - 45 (A. P. Finch et al., 2014; National Comprehensive Cancer Network, 2018b).

BRCA mutations,[51] this chapter examines how and why younger women who have RRSO are often under-prepared for the severity and duration of the side effects of medically-induced menopause. The first section of the chapter illustrates how tensions between patients' and providers' risk management priorities and contemporary social and medical discourses surrounding ovarian cancer, RRSO, and hormone replacement therapy (HRT) work together to encourage women to rush into RRSO without full knowledge of the surgery's side effects. I then explore biomedical discourses and broader social and cultural contexts that influence women's under-preparation and under-treatment for medically-induced menopause. The chapter reveals how RRSO practices prioritize protecting the reproductive functions and potential of women's ovaries over their non-reproductive functions and women's daily well-being and comfort. I argue that these practices emerge from and reflect gendered, racialized, and classed constructs of women's bodies and roles.

## Rushed in Blind and Undertreated

### *Reducing Cancer Incidence vs. Reducing Mortality*

Early in my fieldwork, I observed a tension between the priorities of providers and patients in cancer risk management: most health professionals prioritize reducing ovarian cancer risk, while most patients and the media are focused on reducing breast cancer risk. It is understandable that women are concerned about breast cancer given that it is the most common

[51] Because none of the moderate-risk mutations (MRMs) are associated with a statistically significant increased risk of ovarian cancer, I draw mostly on interviews with women with BRCA1/2 mutations in this chapter. However, some women with MRMs had salpingo-oophorectomies or hysterectomies because they were concerned about ovarian cancer. Therefore, when their experiences are relevant, I also draw on their stories. In addition, as I explain in Appendix B, all of the women with BRCA mutations who participated in the study learned about their mutations prior to natural menopause.

cancer in the United States, with 3,418,124 women living with the disease in 2015 (National Cancer Institute, 2018d; Noone et al., 2018). In comparison, ovarian cancer is relatively rare—in 2015, there were 224,940 women living with ovarian cancer, and it is the 17th most common cancer in the United States (National Cancer Institute, 2018e; Noone et al., 2018).

However, despite breast cancer's high prevalence, as one clinician said to me at a conference, "Ovarian cancer is what kills you." Current five year survival rates for ovarian cancer are only 47%, in part because there are no effective ovarian cancer screening tools (National Cancer Institute, 2018e; Noone et al., 2018). While many women at genetic risk for ovarian cancer continue to get annual pelvic ultrasounds and/or blood tests for CA-125,[52] these practices are not evidence-based or recommended (National Comprehensive Cancer Network, 2018b; U.S. Preventive Services Task Force et al., 2018). Neither of these tests are sensitive or specific[53] enough to be used for screening in either general or high-risk populations. In addition, randomized studies have shown no significant reduction in ovarian mortality among women who had pelvic ultrasounds and CA-125 tests (Jacobs et al., 2016; Pinsky et al., 2016). As a result of the lack of effective screening options, in nearly 60% of cases ovarian cancer is only caught after it has metastasized,[54] and the five-year survival rate for these women is an abysmal 29% (National Cancer Institute, 2018e; Noone et al., 2018).

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[52] The test for Cancer Antigen 125 (CA-125) is FDA approved for monitoring the effectiveness of ovarian cancer treatment. However, it is not recommended for screening because it has a high rate of false-positives and only detects approximately 50% of early stage ovarian cancers (U.S. Preventive Services Task Force et al., 2018).

[53] A test's sensitivity refers to its effectiveness at identifying positive cases; a high sensitivity results in few false-negatives or missed cases. A test's specificity refers to its effectiveness at identifying positive cases *only*; a high specificity results in few false-positives, or incorrectly identified cases.

[54] The epidemiological literature identifies three stages of cancer at diagnosis: localized (confined to the primary site), regional (spread to the regional lymph nodes), and distant (metastasized to other organs or parts of the body).

In contrast, there are excellent breast cancer surveillance tools, such as mammography, magnetic resonance imaging (MRI), and ultrasound, all of which are supported by decades of evidence of clinical effectiveness.[55] As a result, only 6% of breast cancer cases are identified after they have metastasized, while nearly two-thirds are found while the cancers are still localized (National Cancer Institute, 2018d; Noone et al., 2018). In turn, five-year survival rates for breast cancer are high: 90% overall, and 99% for the two-thirds of cases that are localized (National Cancer Institute, 2018d; Noone et al., 2018).

The effective early-detection tools and favorable survival rates for breast cancer help to explain why RRM is less commonly practiced in countries with national health systems. These tools and rates also illustrate why current clinical guidelines in the United States indicate that health professionals should *discuss*, not *recommend,* mastectomy for women at genetic risk (National Comprehensive Cancer Network, 2018b). RRM is a primary prevention tool, albeit a crude one. Because a majority of breast cancers are caught early, the vast majority of women diagnosed with breast cancer will survive, and most cases of breast cancer will not require chemotherapy. Hence, at the *population-level*, preventing breast cancer provides only marginal benefit over treating it. However, for ovarian cancer the opposite is true. A majority of ovarian cancers are discovered after they have metastasized, and a majority of women diagnosed with ovarian cancer will *not* survive. Therefore, preventing ovarian cancer provides significant benefit over treating it.

[55] The overall effectiveness of mammography at detecting breast cancers that are not palpable is well established. However, the age at which scientific evidence supports using mammography as a screening tool in the *general* population (not among high-risk women) has been debated by experts in recent years. These debates center on the age ranges in which the benefits of mammography outweigh its risks (Bleyer & Welch, 2012; Pitman et al., 2017).

### *Socio-Clinical Tension*

Because there are no effective surveillance tools for ovarian cancer and the prognosis for most patients is poor, health professionals working in cancer genetics, along with the clinical guidelines that inform their practices, place a high priority on managing ovarian cancer risk through RRSO. Linda, a genetic counselor, discussed how she introduces medical management options with her BRCA positive clients. "We talk about which ones are not really negotiable, meaning you really don't want to keep your ovaries. It's dangerous. We don't have a reliable way to detect that when it's curable." Similarly, Steve, an oncologist, explained how RRSO is different.

> Oophorectomy for BRCA has become so robustly established that, if you don't have a prophylactic oophorectomy at some point—I mean the issue is timing—but if you don't have one at some point, then you really are swimming against medical advice. Whereas for prophylactic mastectomy, it is a little bit more balanced in terms of the presentation, as long as it's not a breast surgeon.

Both Steve and Linda are experienced BOC genetics health professionals, and they illustrate how genetics providers place a high priority on reducing ovarian cancer risk through RRSO. In contrast to this approach, patients and the media often focus more heavily on managing breast cancer risk through mastectomy. These different emphases in BOC risk management practices are produced through what I refer to as *socio-clinical tension:* a tension between the concerns and issues magnified in social contexts and those amplified in clinical contexts.

Medical providers are trained to make recommendations based on standards of care and current evidence from scientific, clinical, and epidemiological research. However, laypeople are not generic rational actors who make personal decisions about their health based solely on statistics and population-level data. Even models of individual health behaviors that are rooted in rational choice theory, such as the Health Belief Model, account for how people's decisions and

actions are based on their *perceptions* of risks, benefits, and barriers, not the numeric estimates of their risks (Glanz, Rimer, & Viswanath, 2008). In addition, people's perceptions are not formed in a vacuum—they are filtered through their emotional, relational, social, and cultural contexts. As more complex interpersonal and community-based theories of health behavior illustrate, individuals are influenced by the stories they see in the media, the issues they encounter in their communities and workplaces, their own life experiences, and those of their colleagues, friends, and family members.

Given breast cancer's high prevalence, nearly everyone knows someone who has been affected by the disease. Moreover, even though five-year survival rates for breast cancer are nearly double those for ovarian cancer, because over 3 million women are affected by breast cancer, the absolute number of deaths from breast cancer is almost three times greater than the number for ovarian cancer. In 2018, the estimated number of female breast cancer deaths is 40,920, while the estimated number of ovarian cancer deaths is 14,070 (Noone et al., 2018). Hence, somewhat counterintuitively, even though ovarian cancer is proportionally far deadlier, people are more likely to know someone who died of breast cancer.

Breast cancer also dominates media coverage, and as a result, the social imagination. As sociologist Gayle Sulik illustrates, "[B]reast cancer has become one of the most mass-mediated illnesses of our time" (Sulik, 2011, p. 113). Features on breast cancer are regularly printed in newspapers and women's magazines and aired on local TV news and national morning programs like *The Today Show* and *Good Morning America*. One study that tracked coverage of cancer in major newspapers over a two-year period found that breast cancer was mentioned at least four times as frequently as any other cancer in headlines and at least twice as frequently in article text (Saywell, Henderson, & Beattie, 2000). Pink ribbons have become so ubiquitous that it would be

difficult to *not* know that they are the symbol for breast cancer. From Band-Aid, to the NFL, to Boeing, countless companies have commercially branded products that they sell or display in October during Breast Cancer Awareness Month (S. King, 2006; Sulik, 2011).[56] There are also numerous breast cancer advocacy organizations that are household names and sponsor huge events in cities across the country, such as Susan G. Komen's *Race for the Cure* and the Avon Foundation for Women's *Walk to End Breast Cancer* (S. King, 2006).

Yet there is no comparable movement for ovarian cancer. As Sulik states, "October is now so closely identified with the cause of breast cancer that it is commonly referred to as 'Pinktober'" (Sulik, 2011, p. 48). However, outside of individuals in families affected by ovarian cancer, most people could likely not report that September is Ovarian Cancer Awareness Month or that its ribbon color is teal. While there are a handful of ovarian cancer advocacy organizations who sponsor local fundraising events, such as The Ovarian Cancer Research Fund Alliance and The National Ovarian Cancer Coalition, these groups—in visibility, size, participation, funding, and donations—are shadowed by those for breast cancer. The differential impact of Angelina Jolie's two Op-Eds also highlights how public and media attention on ovarian cancer is scant when compared to the focus on breast cancer. While Jolie's initial Op-Ed was extensively covered by media outlets, I only observed her Op-Ed on RRSO discussed in social media groups for BOC mutation carriers.

The tremendous visibility of breast cancer activism in the media combined with breast cancer's high prevalence magnifies its risks and is reflected in women's priorities around risk-reducing surgeries. Over two-thirds of the 33 women with BRCA mutations who participated in

[56] Several feminist advocacy organizations and social scientists have critically examined these practices of "pinkwashing" and the neoliberal consumer culture of breast cancer activism (Breast Cancer Action, 2018; S. King, 2006; Klawiter, 2008; Sulik, 2011).

this study either had or were planning to have *both* RRSO and mastectomy. At the outset of this study, given my knowledge about clinical guidelines, ovarian cancer mortality rates, and the effectiveness of breast cancer surveillance tools, I expected many women with BRCA mutations to have had or be planning on RRSO but not mastectomy. Yet only three women in this study had (or intended to have) RRSO but were not planning on having a mastectomy. However, an even more surprising finding was that three other women in the study had undergone mastectomy but were "swimming against medical advice" and were not planning on having RRSO.

As Angelina Jolie illustrates, even when a woman's family history involves ovarian cancer, she might still prioritize managing her breast cancer risk. Her mother died from ovarian cancer, not breast cancer, yet Jolie chose to undergo mastectomy first. In "My Medical Choice," she invoked her "risk" as an explanation for this decision: "I started with the breasts, as my risk of breast cancer is higher than my risk of ovarian cancer, and the surgery is more complex" (Jolie, 2013). However, the standard medical recommendation to a 37-year-old woman with a BRCA1 mutation whose mother had died of ovarian cancer would be to have RRSO as soon as possible, not mastectomy. Hence, while Jolie's statement is technically accurate, it depends on which risks you focus on. While Jolie's lifetime risk of *developing* breast cancer was greater than her risk of developing ovarian cancer, her risk of *dying* from ovarian cancer was greater. In addition, removing women's ovaries may also reduce their risk of developing and/or dying from breast cancer(Jacobson & Narod, 2018),[57] but removing their breasts has absolutely no effect on their ovarian cancer risk or odds of overall survival. Yet like Angelina Jolie, despite these clinical

[57] Recent research suggests the reduction in breast cancer *risk* may only be significant among BRCA2 mutation carriers (Heemskerk-Gerritsen et al., 2015; Kotsopoulos et al., 2017), but the reduction in breast cancer *mortality* may only be significant among BRCA1 mutation carriers (Huzarski et al., 2013; K. Metcalfe et al., 2015). These differences in findings highlight the importance of disentangling cancer incidence and mortality outcomes in research.

guidelines and/or their personal family histories, many women in this study conveyed that they were initially more concerned about the prospect of breast cancer and the effects of mastectomy than the possibility of ovarian cancer or effects of RRSO.

***RRSO Is Quick and Easy***

One of the reasons women tended to be more concerned with mastectomy and reconstruction than RRSO is that, as Jolie stated, with RRSO "the surgery is less complex" (Jolie, 2013). RRSO is almost always performed laparoscopically, and as a result is a relatively short and minimally-risky surgery. It is frequently performed as an outpatient procedure, on average lasts under two hours, and typically involves a brief recovery period of one or two weeks (Dawood, 1999; De Felice et al., 2017; Kenkhuis et al., 2010; Piszczek, Ma, Gould, & Tseng, 2017; Shushan, Mohamed, & Magos, 1999). Most women in this study reported that their gynecologic oncologists (GYN/ONCs) or OB/GYNs appropriately informed them that RRSO was, as surgeries go, a short procedure that rarely involved complications.

Providers' emphasis on the safety and simplicity of the surgery itself and recovery from the surgery led many women to believe that the overall impact of RRSO on their bodies would also be easy and manageable. Several women conveyed that prior to their surgeries they were much more concerned about the effects of their mastectomies and reconstruction than they were about the effects of their salpingo-oophorectomies. For example, Raina, who had RRSO and mastectomy in her early 40s, told me about RRSO, "It just didn't seem as big of a deal to me as getting the breasts taken off." Similarly, Alicia also had RRSO in her early 40s, and she told me that she didn't think she "approached it with the right amount of respect." One of the factors that shaped her initial attitudes toward RRSO was her understanding that the procedure itself was simple. "I was probably a little cavalier about that surgery. I kind of was so worried about the

mastectomy because it seemed like such a big surgery that, you know, '[RRSO] is gonna be a walk in the park!' You just go in, it's going to be laparoscopic, da-da-da-da…. I think I was looking at it from the physical standpoint of the surgery, how it was an outpatient surgery."

Even women who were not at increased ovarian cancer risk thought RRSO would be "a walk in the park" compared to mastectomy. Maya, who has a PALB2 mutation and therefore was at increased risk for breast cancer but not ovarian cancer, was not interested in mastectomy. But she conveyed that she would have considered RRSO because it seemed like an easier surgery. "Now, if it were something like an increased risk for ovarian cancer. I'd probably very happily have my ovaries removed. That's a pretty minor change and surgery compared to a bilateral mastectomy."

The examples from Raina, Alicia, and Maya illustrate how the discourses and practices in BOC genetic medicine correctly convey that RRSO is a less complicated procedure than mastectomy or reconstruction and involves a shorter recovery period than either type of breast surgery. Yet this factual information about RRSO compounds the effects of socio-clinical tension in BOC risk management practices and leaves many women un- or under-prepared for the enduring and sometimes severe effects of medically-induced menopause. As I illustrated earlier, most women are disproportionately worried about breast cancer and RRM, while most clinicians in BOC genetic medicine are more concerned about ovarian cancer and RRSO. When women hear from their providers that RRSO is a relatively quick and easy procedure but mastectomy and reconstruction are complicated, they understandably focus even more intensely on learning about and planning mastectomy and reconstruction.

Conversely, because most providers know RRSO is a comparatively simple and safe procedure that confers a significant survival benefit, some doctors encourage women to have the

procedure as soon as possible. For example, Veronica, who had two adopted daughters and was not planning on having biological children, shared her doctor's RRSO recommendations:

> It was a more minor surgery. You know, it was outpatient, laparoscopic. And I was kind of nervous about it, because it puts you into menopause. But the doctor, my oncologist, he said, "If you're not having biological children and you were my wife, I would tell you, 'Get them out now,' because ovarian cancer is so bad and if you get the surgery, your risk will be, like, you know, lower than the general population, you know, which is already pretty low." So, I said, "Fine, let's do it." *(Veronica, Age 32, BRCA1)*

Hearing that her oncologist would recommend to his wife to "get them out now" encouraged Veronica to jump in and have RRSO right away. Marci explicitly stated that she felt pressured by her clinicians to have surgery as soon as possible, despite the fact that she had not yet completed her desired childbearing.

> What I heard was, "Cut off your breasts and cut out your ovaries," was what I heard. That's not exactly what she said. She did say that they recommended an oophorectomy, and—this was the part I laughed about—that research suggests that women who have the oophorectomy closer to 36 end up faring better. And at the time I was already 38, so I was just like, "Well, shit, you know, guess I'm screwed!" You know, it was just one of those—it made it feel like, "You should really do this as soon as possible, like people closer to 35 have better results." But then I also recognize that they don't know and it's individual. And so, it was this sort of—things were couched in certain ways. But I definitely felt the pressure to have these surgeries quickly. *(Marci, Age 39, BRCA2)*

Importantly, both Veronica and Marci were below the recommended age ranges for RRSO, which are ages 35 - 40 for BRCA1 mutation carriers but can be safely delayed to ages 40 - 45 for women with BRCA2 mutations (A. P. Finch et al., 2014; National Comprehensive Cancer Network, 2018b). Hence, while Marci noted that the pressure she experienced was "couched" in data on RRSO outcomes, the data her clinician cited was relevant to BRCA1 mutation carriers, but not to Marci, who has a BRCA2 mutation. At age 38, she did not need to immediately rush into surgery to protect her health. The same was true for Veronica—at age 32,

she was several years younger than even the lower end of the clinically recommended age range for BRCA1 mutation carriers.

Having RRSO earlier than the recommended age ranges is not necessarily better for women's health, and may in fact be worse because of the potentially severe health risks and effects of medically-induced menopause. Linda, who has been a cancer genetic counselor for over 25 years, explained, "So right now the guidelines say you need to do [RRSO] ideally by 35 or 40. But it's also important for people to know it's not a healthier thing to do it at 25. Right? You're not getting a bunch more protection by putting yourself in menopause in your 20s." While neither Veronica nor Marci were in their twenties, they were still encouraged to have RRSO earlier than necessary without fully being presented with how the surgery might have an ongoing impact on their bodies. And as the stories in the following section illustrate, while RRSO may be a relatively short and easy surgery, the effects of the procedure on women's health and lives are far from simple.

***Menopause Is Enduring and Difficult***

Medically-induced menopause is associated with a wide range of risks, some of which are also life-threatening. These effects include an increased risk of cardiovascular disease, Parkinson's disease, osteoporosis, fractures, vaginal dryness, hot flashes, diminished sexual response, cognitive impairment, and mood and sleep disturbances (Faubion, Kuhle, Shuster, & Rocca, 2015; A. Finch & Narod, 2011; C. Garcia, Lyon, Conell, Littell, & Powell, 2015; W. A. Rocca et al., 2016; Shuster, Gostout, Grossardt, & Rocca, 2008; Tucker et al., 2016). Despite these risks, the overall clinical benefit of RRSO among BRCA mutation carriers has been robustly established. While research has shown that among women in the general population, salpingo-oophorectomy prior to the age of 45 significantly *increases* all-cause mortality (E. C.

Evans et al., 2016; Parker et al., 2013; Walter A. Rocca, Grossardt, de Andrade, Malkasian, & Melton, 2006), several recent studies have demonstrated that among women who are BRCA-positive, salpingo-oophorectomy prior to age 45 significantly *reduces* all-cause mortality (S. M. Domchek et al., 2010; A. P. Finch et al., 2014; Ingham et al., 2013; A. W. Kurian et al., 2010).

As I argued in Chapter Three, the practices surrounding breast reconstruction—a cosmetic procedure that contributes additional physical health risks—can be in tension with one of the central goals in BOC genetic medicine: reducing women's risks. In contrast, RRSO is medically-indicated among women with BRCA mutations and confers the health benefit that most people looking to reduce their risk of cancer ultimately desire—to increase their overall chances of survival. Thus, unlike with reconstruction, RRSO practices do not funnel women toward a relatively risky procedure with limited health benefits that they might later regret. Rather, with RRSO, BOC genetic medicine practices propel women toward a surgery that has some physical health risks, but also very significant benefits that, on balance, usually outweigh those risks.

The favorable risk-benefit profile for RRSO was reflected in women's feelings about the surgery. Many women expressed certainty and relief about having RRSO even if they struggled with, or felt unprepared for, medically-induced menopause. For example, Alicia, the woman who didn't feel she treated RRSO "with the right amount of respect," conveyed, "I had a harder time, I think, emotionally with that surgery just because of the hormone levels and everything going out of whack. But that was, for me, just a no-brainer for that surgery, just knowing how unreliable the surveillance is for ovarian cancer." Beatrice used similar language to describe her certainty about having RRSO. "It was a no-brainer. I don't know what the numbers in terms of risk would have had to have been for me to say 'we should wait and think about this.' It was

presented as an extremely high risk." In fact, Dorothy was the only woman who expressed some regret about her decision to have RRSO. She was still experiencing severe menopausal side effects five years after her surgery, but even she felt that it was the "right" choice. "I had a friend who had ovarian cancer and it was horrible, and she died. And I learned that it is really hard to test for that. By the time you know you have it, you're half dead. So, for that reason, it felt like the right thing to do."

However, even though most women who had RRSO expressed that they felt they made the "right" decision, many of them were notably un- or under-prepared for the side effects of the surgery and struggled with quality of life issues. Some women were surprised by the severity of their menopausal symptoms. For example, Alicia shared, "I just, I was a little cavalier about how that surgical menopause was going to hit me…. And I pretty much went insane. I lost the ability to cope. The hot flashes were just crazy. I was having heart palpitations—it was just insane." Dorothy, who had RRSO in her late 40s, was similarly unprepared for the severity of the menopausal side effects she experienced. Her doctors had told her she would "go into menopause," but they not describe the specific side effects that might occur, nor did they explain how the abruptness of medically-induced menopause was different than natural menopause. Because she was fairly close to menopausal age and her mother had managed natural menopause smoothly, she expected to have a similar experience and was shocked when she did not. "I was catapulted into menopause, and it was such a surprise…. the hot flashes were so frequent I couldn't believe it…. it's been harder than I ever expected it would be.*"* The duration and severity of Dorothy's menopausal side effects is what led her to feel some regret about her decision to have surgery.

There's some days when I would say, 'Oh my gosh, I would take this back, just give me

> my ovaries again'…. I think that the effect of that oophorectomy has been more defining in my life than my breast cancer risk. It is a thing that I deal with every single day. I feel well taken care of with my [breast cancer] screening, and so I don't really have anything to complain about in terms of my risk. What I have to complain about is menopause." *(Dorothy, Age 53, BRCA2)*

Like Dorothy, many women who had RRSO reported that they were cursorily warned that the surgery would cause them to "go into menopause," but their clinicians provided them very little detail on the severity or duration of menopausal symptoms or the ongoing impact RRSO could have on their quality of life. Talia explained, "I think the conversations were like, were really rushed and sort of just factual, like, 'You may experience some vaginal dryness. You may experience hot flashes.' You know, like that kind of thing. And then, it wasn't like, 'Let's really delve into this topic, you know?" However, some women's providers did not mention any of the consequences of RRSO in conversations with them. Marci, who was in her late 30s, was still undecided about both RRSO and mastectomy. As I illustrated earlier, she felt very pressured to have RRSO by an oncologist and was frustrated that neither that doctor nor her other providers had conveyed the health risks associated with the procedure. "Actually, there's been zero mention by any of the doctors that if I get my ovaries removed it's going to put me straight into menopause, which has risks of heart disease and emotional stuff and all these other things. Zero mention."

The experiences of Alicia, Talia, Dorothy, and Marci illustrate how the practices of BOC genetic medicine encourage women to rush into RRSO without fully informing them about the severity and duration of the menopausal symptoms they might experience. It is understandable that providers would want to encourage BRCA-positive women to have RRSO as soon as possible. Not only does RRSO reduce all-cause mortality in BRCA mutation carriers, but also several studies have shown that unsuspected ovarian cancers are discovered in 4% - 8% of

women with BRCA mutations who have RRSO (Conner et al., 2014; Powell, 2014; Zakhour et al., 2016). Yet, even for a procedure that, on balance, may have stronger benefits than drawbacks, it is still critical that providers give women a comprehensive picture of the risks and side effects they may face. One of the axioms I heard throughout my fieldwork was "knowledge is power." And while women were almost universally glad to know about their mutation and to have the opportunity to manage their risk, few women in this study felt adequately prepared with knowledge about how RRSO and medically-induced menopause might negatively impact their quality of life. Instead, women often rushed into the procedure unknowingly blind, and as a result, several of them struggled to manage and cope with their menopausal symptoms.

***HRT or No HRT?***

Another important finding in this study is that women were not only uninformed about or under-prepared for their menopausal symptoms—they also were often *untreated* for those symptoms. Studies have shown that for women who have RRSO, supplementing with short term hormone replacement therapy (HRT) that does not extend beyond the average age of natural menopause reduces many of the risks and side effects of medically-induced menopause. Premenopausal HRT use among women who do not have ovaries reverses their increased risk of all-cause mortality, protects against bone loss and heart disease, and reduces hot flashes and sexual side effects, all without significantly increasing BOC risk (De Felice et al., 2017; Faubion et al., 2015; Amy Finch, Evans, & Narod, 2012; Johansen et al., 2016; Kenkhuis et al., 2010; Rebbeck et al., 2005; W. A. Rocca et al., 2016; Vermeulen et al., 2017). Given the demonstrated health benefits of HRT in premenopausal women who have salpingo-oophorectomy, offering HRT to BRCA-positive women who have RRSO and have not had breast cancer has become standard practice at the top cancer-genetics clinics in the United States. Yet, provision of HRT to

women at BOC genetic risk remains uneven because many women do not receive care at the nation's top academic medical centers.

There were eleven women in this study who had their ovaries removed premenopausally (through salpingo-oophorectomy or total hysterectomy), had not had cancer of any kind, and had no other contraindications (e.g., a history of blood clots) to taking hormones. All eleven of these women should have been eligible for HRT, yet six of them were not taking hormones. Three of the women who were not on hormones had doctors who had erroneously told them that their BRCA mutations made them ineligible for HRT because it might increase their breast cancer risk. For example, when Dorothy complained about the severity of her hot flashes and menopausal symptoms, her doctor said to her, “Oh, gosh, you know, it’s bad, I know. A lot of women go through it. Because of your mutation, we don’t recommend hormone replacement therapy. We’re trying to reduce the estrogen in your body.” Dorothy was the only woman who expressed some regret about having RRSO, and those feelings were connected to the severity of her symptoms. She noted that, unlike her risk for cancer, menopause is something she deals with “every single day,” so she, in particular, could have benefited from taking the HRT that she should have been offered. In addition, four of the six women not taking hormones had already had mastectomy, and of the other two, one was planning her breast surgery in the near future. Hence, even if those women’s doctors were not aware of studies showing that HRT has protective effects for premenopausal women without ovaries, concerns about an increase in breast cancer risk among women whose breast tissue had already been removed (or soon would be) should have been minimal.

The other three women who were not on hormones had been prescribed HRT by their doctors, but they either never started taking the drugs or went off them because they were

personally concerned about them increasing their breast cancer risk. While these women were at least offered HRT, they were not appropriately counseled about the *protective* health effects of hormone use, and this was also true for several women in the study who were taking HRT. Instead, women's doctors often suggested that taking hormones was either neutral or still posed some risk, but that it was "their choice" or "up to them" because HRT could improve their quality of life. For example, Jill, one of the women who elected not to take hormones, explained what her doctor told her about HRT:

> He said that it didn't show that it really hurt you and you know it was really a choice. I wasn't willing to do it, because I felt like if I'm doing this surgery to get rid of all of these hormones and take everything out and decrease my risk for everything. And I also thought, "Well, it'll just prolong the whole menopausal thing." Might as well just rip the band aid off and just be done with it. *(Jill, Age 45, BRCA2)*

Brooke, who has a BRCA1 mutation, was another woman who stopped taking hormones because of concerns about the cancer risks. "I just went off them myself. I knew that the estrogen would feed the potential to feed the cancer if there was one that was going to develop, and I just said, 'I don't need these.'" After Brooke went off HRT, she had a very hard time with her menopausal symptoms, and she approached her doctor about going back on hormones. She reported that her doctor said, "It's up to you. You know the risk. If you want to go back on and improve your quality of life and take the estrogen, let's take it." When patients are being asked to weigh risks and benefits and make a choice about their health, they need accurate information, yet this is not what women reported receiving. There is a notable difference between hearing from a doctor that hormones "don't hurt you" or "you know the risk" and hearing that taking HRT prior to the natural age of menopause reduces all-cause mortality and protects your cardiovascular and bone health.

Hence, women with BRCA mutations are often denied or not given accurate information

about HRT, a treatment that could mitigate many of the side effects of medically-induced menopause and increase their quality of life without significantly increasing their risks of developing breast cancer. Withholding HRT from BRCA-positive women who have RRSO is especially problematic in light of research showing that medically-induced menopause often produces more severe side effects than natural menopause. A recent study in the Netherlands of women with BRCA1/2 mutations who underwent RRSO prior to menopause found that the severity and duration of menopausal symptoms was significantly greater for women who had RRSO than for women who experienced menopause naturally (Stuursma, van Driel, Wessels, de Bock, & Mourits, 2018). Over two-thirds of the women in the study experienced moderate to severe menopausal symptoms, and for a majority of women, those symptoms persisted for 10 or more years after the surgery. Notably, unlike in the United States, premenopausal Dutch women who have RRSO are routinely prescribed HRT to reduce menopausal symptoms. Given the unevenness of the provision and use of HRT among women in the United States who have RRSO, the severity and duration of medically-induced menopausal symptoms in US women may be, on average, even greater.

## Ovaries: Egg Factories or Endocrine Glands?

### *Obscuring Non-Reproductive Functions*

A majority of the doctors and genetic counselors I interviewed and met during my fieldwork were concerned about the side effects of RRSO and recommended HRT to previvors. However, the health professionals with whom I spoke were are all cancer genetics specialists who either work at nationally renowned cancer genetics clinics or regularly attend cancer genetics conferences. It is not surprising that the health care providers who are most knowledgeable about current research and best practices in the field are also more likely to

comprehensively inform their patients about the wide range of risks of RRSO and to appropriately manage those risks. But unfortunately, as I noted in Chapter Two, most women are not seeing those clinicians.

Regardless of their training or where they practice, GYN/ONCs and OB/GYNs do not intentionally withhold information from their patients or actively attempt to obscure the lived realities of medically-induced menopause. As I argued in Chapter Three in relation to breast and plastic surgeons, most clinicians want to help their patients. But because many GYN/ONCs and OB/GYNs have witnessed the gravity of ovarian cancer with previous patients, they are also likely to want to spare their current patients from that experience. Given the robustness of the research on RRSO, GYN/ONCs and OB/GYNs are likely to know that the procedure dramatically reduces ovarian cancer risk, significantly reduces all-cause mortality, and is a fairly safe and simple procedure. Hence, for most clinicians, RRSO is, like Alicia and Beatrice said, a "no-brainer." From doctors' perspectives, the benefits of RRSO heavily outweigh the potential side effects, so it is understandable that they might quickly run through a list of potential side effects without delving into them in depth, as Talia described earlier.

However, the under-preparation for medically-induced menopause that many women in this study experienced is not solely rooted in the injurious benevolence of some doctors. RRSO practices in the United States both reflect and reinforce other social, cultural, and medical discourses about women's bodies. There is an established history in US biomedicine of ignoring the non-reproductive functions of steroid hormones and treating ovaries as if they are egg factories that are only important for making babies (Fausto-Sterling, 2000; Oudshoorn, 1994; C. Roberts, 2007). In common discourse, ovaries make eggs and "sex hormones", and those "sex hormones" affect mood, desire, and reproduction. Yet in reality, ovaries are important endocrine

glands that store, grow, and release eggs and make steroid hormones, which regulate numerous critical functions in the body beyond reproduction and the development of secondary sex characteristics. As feminist biologist Anne Fausto-Sterling has written, hormones are “multi-site chemical growth regulators” (Fausto-Sterling, 2000) that affect bone mass, blood clotting, blood lipids, vasoconstriction and vasodilation, body temperature, immunoregulation, metabolism, fat deposition, muscle mass, and sexual response, (Manolagas & Kousteni, 2001; Muñoz-Cruz, Togno-Pierce, & Morales-Montor, 2011; S. I. A. Shah, 2018; Sloane, 2002, pp. 77-81).

Science studies scholar Nelly Oudshoorn argues that "sex hormones" are not preexisting natural substances that scientists discovered, but rather have been constructed through biomedical discourses and practices. Oudshoorn describes how in the early twentieth century, laboratory scientists and gynecologists measured and defined hormones in a variety of ways. In 1932, they convened the Conference on the Standardization of Sex Hormones, where they settled on the vaginal smear test as the standard test for “female sex hormones,” thereafter labeled “oestrus-producing hormones” (Oudshoorn, 1994, pp. 46-47). The vaginal smear test measured changes in the vaginal cells of rodents characteristic of estrus. In 1935, at the Second Conference on the Standardization of Sex Hormones, scientists and clinicians accepted the comb test, which measured comb growth in castrated roosters, as the standard test for “male sex hormones” (Oudshoorn, 1994, p. 49). Oudshoorn highlights how these standardized measures were not preordained, but rather were decisions with consequences:

> [I]n this process of sorting out the specific tests for sex hormones, all functions and processes that were unrelated to sexual characteristics and reproduction were dropped. The testing methods that became accepted as standard tests for sex hormones were based not on muscular activity or body weight, but on internal sexual organs (vagina and seminal vesicles) and on a so-called secondary sexual characteristic (the comb of the rooster). In this way, scientists attributed to the substances they had just isolated, and which they had named sex hormones, the properties predicted by the biological paradigm

> in which sex hormones were defined as the chemical messengers of masculinity and femininity. (Oudshoorn, 1994, p. 53)

Oudshoorn argues that these active choices by scientists illustrate how medical and scientific "facts" and discourses about bodies are not neutral or natural, but rather reflect and reconstitute the social and cultural contexts from which they emerge.

Building on Oudshoorn's argument, Fausto-Sterling argues that these standardized tests and measures for hormones transformed steroid hormones—substances that have systemic effects in bodies and regulate multiple functions and processes—into "sex hormones."

> From the moment the process of measuring male or female hormones was standardized, a set of molecules of a known chemical composition and structure officially became sex hormones. From that time on, any physiological activity those hormones had were, by definition, sexual, even though the "male" or "female" hormones affected tissues such as bones, nerves, blood, liver, kidneys, and heart (all of which was known at the time). (Fausto-Sterling, 2000, p. 187)

By settling on standardized tests and definitions for hormones that were linked to sexual and reproductive systems, clinicians and scientists "shaped the sexing of the sex hormones" (Fausto-Sterling, 2000, p. 187). They focused attention almost exclusively on how hormones regulate sex and reproduction, thus obscuring the numerous other physiological functions that are regulated by hormones.

Contemporary RRSO practices emerge from, and then further contribute to, this history of rendering the non-reproductive functions of hormones invisible. Clinicians in BOC genetic medicine are sensitive to the reproductive impact of oophorectomy. The NCCN guidelines specify that "RRSO should only be considered upon the completion of childbearing" (National Comprehensive Cancer Network, 2018b, pp. MS-27), and as I will illustrate in the next section, clinicians almost always talk to women about completing childbearing prior to the surgery. However, many women's doctors failed to address the non-reproductive risks and side effects of

RRSO, even for some of the most well-known effects. For example, Jessie is one of the women I discussed in Chapter Two who has a CHEK2 mutation and had a hysterectomy due to her concerns about potential links between ovarian cancer and CHEK2. Jessie conveyed that her doctors did not address the risk of bone loss from medically-induced menopause. "And the biggest thing that I wish there would be more talk about is the osteoporosis side. I know from what I have read on the osteoporosis side, but nothing has been talked about." Marci's doctor did not discuss the cardiovascular effects of RRSO with her despite her strong family history. "As I mentioned, heart disease is really rampant in my family. So, if going into menopause early increases an already-increased risk, nobody has asked me about that…. There was just no mention of osteoporosis or heart disease." Bone loss and cardiovascular risks have long been established as harmful side effects of medically-induced menopause, but Jessie's and Marci's doctors did not discuss these risks with them.

Other women reported getting little to no information about the potential effects of medically-induced menopause on sleep, weight, and cognition, all of which are dimensions of health that can have a major impact on quality of life. Raina shared, "Actually one of the biggest side effects of not having my ovaries, which I had no idea it was even a side effect, was disturbing my sleep." Dorothy explained that she had other side effects in addition to her severe, unrelenting hot flashes. "Like weight gain, that whole middle. I'm exercising, I was always very thin. And so now I have really had to reduce my food intake and exercise a lot more. And yet I'm still kind of getting that middle…. And my memory, and I don't know how much of this is just aging, but my memory, my short-term memory especially, is just noticeably worse. And that bothers me a lot." Dorothy stressed that being unprepared for all of these symptoms made it harder to cope with them. She wished that her providers had taken more time to prepare her for

the range of possibilities. “The surgeon that removed my ovaries, she said, ‘Now, you probably will go through menopause.’ But she didn’t talk to me anymore. You know, her job was surgical, I guess. The genetic counselors didn’t either. I wish that I’d had a chance to talk that through. Not that I would have made a different decision, but my expectations might have been managed.”

***Silence about Sexuality***

Several women also noted that their providers were silent about the impact of RRSO on sexual response. For example, Liza explained that she had to learn about the sexuality-related effects of preventative surgeries from her sister and a family friend who had had the procedures.

> The doctors would talk about everything except for sex. It was so weird to both of us [Liza and her sister] how bright red and shut down they all get when it came to that. It is such a huge part of it. I don’t know. I think it is silly that people aren’t willing to talk about it and help out patients with regaining a part of their sex life. It is a big part of everybody’s life. *(Liza, Age 30, BRCA1)*

Similar to Liza, Raina shared that she only learned about the sexual side effects of RRSO from other women in online support groups. Her doctors had not given her any information about risks of decreased libido or vaginal dryness, and as she noted, “I mean, that’s not really something I would talk about with my mom, and I don’t really have any friends who had it done.” Without other people to inform her in the way Liza’s sister did, Raina was unprepared for the sexual side effects she experienced.

Brenda’s genetic counselor explicitly told her to ask her surgeons about the impact of RRSO on quality of life issues like libido and sexual response because they would not bring those topics up on their own. Brenda said her counselor stated, “Here are some questions to ask around that. And know that you should ask questions but that is not something that surgeons are going to want to talk to you about, so you have to find your own information about it.” Jackie, a

genetic counselor who ran the cancer genetics program at a regional hospital, mentioned her own reluctance to discuss the sexual side effects of medically induced menopause. "Even I don't talk about it that much. I often mention heart health, bone health, but not libido."

In addition to providers' silence around the sexual side effects of RRSO, some women were not told by clinicians that having a total hysterectomy instead of RRSO could compound the impact on their sexual response. Involuntary uterine contractions are involved in orgasm, and for some women, removing their uterus leads to decreased sexual response and pleasure (Sloane, 2002, pp. 172-177). For example, Elaine, the nurse with a BRCA2 mutation who had to fight with her doctors to get HRT, was not informed of the potential sexual side effects of total hysterectomy and regretted choosing the procedure over partial hysterectomy or RRSO. She said, "If I had to do it over again, I would keep my cervix because of sexual orgasm." The first GYN/ONC Brenda spoke with—the same man who discouraged HRT—also urged her to have a full hysterectomy.

> He was very focused on small percentages of remaining risks, and the most risk-reducing thing I could do was a full hysterectomy. He said that the bonus is that if you don't have a cervix, you don't ever have to get another pap smear…. he was assuming that I would be so glad to jettison my cervix. Yeah, he was very surgically minded. *(Brenda, Age 39, BRCA1)*

While Brenda's doctor highlighted the "benefit" of not needing pap smears when you don't have a uterus, he did not inform her that one potential drawback of "jettisoning" her cervix might also be less pleasurable sex. Luckily Brenda's genetic counselor had encouraged her to educate herself about the relationship between gynecologic surgeries and sexuality, so Brenda knew that she wanted to keep her uterus going into that meeting with the gynecologic surgeon.

The silence in US genetic medicine about how medically-induced menopause affects a wide range of bodily systems and functions, including sexual response, is both rooted in and

reconstitutes broader social and cultural discourses that portray women's ovaries and uteruses as primarily valuable through their work in reproduction. As I argued in Chapter Three, breast reconstruction practices that prioritize women's attractiveness over their internal sensations and pleasure reflect a higher regard for women as sexual objects than as sexual subjects. Similarly, RRSO practices prioritize women's procreative capacities over their daily well-being and comfort, which reflects a higher regard for women as reproducers than as embodied agents. In the following sections, I will highlight how these practices are filtered through and reflect not only gendered constructs of women's bodies and roles, but also racialized and classed ones. A majority of BOC genetic medicine patients are white, middle-class women (Armstrong et al., 2015; Cragun et al., 2017; McCarthy et al., 2016; Underhill, Jones, & Habin, 2016), individuals whose reproductive futures are most valued in the prevailing social order in the United States (Bridges, 2011; D. Roberts, 1997; Silliman, Fried, Ross, & Gutiérrez, 2004; Vandenberg-Daves, 2014). It is perhaps not surprising, then, that while the structures of US genetic medicine often gloss over the effects of RRSO on women's sexual response and other critical bodily functions, they frequently emphasize the impact of the procedure on women's reproductive capacity.

***Hurry Up and Have Kids***

Women in this study were well-informed that if they desired biological children, they would need to have those children or freeze their eggs prior to having RRSO. In fact, nearly all of the women who had or were planning on having their ovaries removed conveyed that their doctors had discussed, often in detail, the reproductive impact of the surgery with them. But many women also reported that when their clinicians talked to them about RRSO and childbearing, the conversation frequently included encouragement to have kids soon or at a younger age than the women might have otherwise planned. Several women conveyed hearing

from their doctors what Lily heard from other women with mutations in her in-person support group: “I gotta get married and have a kid, so I can have the surgery.” For example, Alicia expressed that one factor that had shaped both her mother’s and her decision to get genetic testing was that her mother’s oncologist had said, “Well, you really need to get tested. If you have the mutation, then your daughter needs to hurry up and have kids.” One of Talia’s doctors communicated a similar message about having kids without first asking her about her childbearing preferences or if she was partnered. “He didn't ask me anything. I felt scared. And that was part of the thing, that he was so surgeon-like. He was just totally detached and basically was like, ‘If you're going to do it, do it now.’ And I was thinking like, ‘I’m not even with somebody.’ You know what I mean?” Even though Talia was only 30 at the time, which is well before the recommended window for RRSO for BRCA2 mutation carriers, her doctor encouraged her to have children right away.

Becky described hearing constant reminders from her providers about having children, despite being fairly young. She was only 27 when she discovered her BRCA1 mutation and 31 years old when I interviewed her. She conveyed, “Most of my gynecological appointments are talking to me about the age of which I should be thinking about having children…. that it’s the sooner the better, and that I’m not getting any younger.” Becky had a particularly difficult time dealing with the pressure surrounding reproductive decision-making; she teared up as we discussed childbearing. She felt ambivalent about having children, both in general and with her current partner, and the constant reminders added to her stress:

> I don’t have any children, but every doctor reminds me that I should think about that. So, it’s definitely forced me to do that planning a lot earlier. I still don’t have immediate plans to have kids, but it’s definitely something on the back of my mind as I need to make that decision pretty quickly. So, it’s affected my relationship in that sense, my relationship with my partner, just deciding if that’s something that I want to do and it should happen

as soon as possible. *(Becky, Age 31, BRCA1)*

Becky's doctors likely had good intentions in checking in with her regularly about childbearing. Many clinicians in BOC genetic medicine have also had patients like Marci, who wants to be a mother and discovered her BRCA2 mutation as a single woman without children in her late 30s. Marci grappled with difficult decisions about if and when to have preventative surgery and using reproductive technologies. Hence, it is understandable that providers would want to help other patients who learn about their mutations at younger ages avoid choosing between having biological children or delaying RRSO and increasing their risk of developing cancer.

Indeed, some women I spoke with experienced reminders from or discussions with their health care providers about the reproductive impact of being BRCA-positive as opportunities to make different choices. For example, Audra conveyed, "Definitely at a younger age, it's like the pressure is on to have kids. But in my mind, it's like it's better to know that. Because I would really hate to not know these results and, not knowing my risks, waiting and waiting and waiting for the right time to have kids, and waiting too long to the point where I can't." Audra, who was 28 years old and had very recently discovered her BRCA2 mutation, preferred being encouraged by providers to have children sooner over waiting and later being unable to have them. There examples illustrate that initiating discussions with BRCA-positive patients about reproduction can be helpful, especially given that women are increasingly delaying childbearing and there is a significant medical benefit to having RRSO in those later childbearing years. Thus, the problematic aspect of the communications between Becky and her doctors was not that they repeatedly addressed childbearing; rather, it was that in those conversations, her doctors made assumptions and did not inquire about her personal fertility desires or life context.

The assumption that women would want to be or should be mothers was also illustrated by Alexis's experiences. Alexis was in her mid-thirties, and unlike the other women in her age range with BRCA mutations, her doctors did not explicitly discuss childbearing plans with her. Instead, Alexis said they would not talk to her in detail about RRSO, which was highly unusual. She felt that their reluctance to discuss RRSO with her was because she was single and childless:

> Because I was single and I don't have kids, they didn't want to do much talking about, like, surgery or egg freezing. They're like, "You have plenty of time. You have until you're 40. Just keep doing screenings." So, I didn't feel like they were being flippant, but they just didn't seem—I obviously did, well, I did and I do have a lot of anxiety about it, and I don't think that they like took that into account. And they definitely were like, "We're not doing surgery. You still need to have kids if you want them." But for me, I'm like, "Well, I don't know if that's going to happen." And I, I am really nervous about this. So, I think they had an idea in their minds of like what I should do. And I don't feel like I got all of the options…. I feel like I need to have a child. Then they'll discuss stuff with me." *(Alexis, Age 34, BRCA2)*

As a BRCA2 mutation carrier, Alexis had up to age 45 to have RRSO within the recommended age range, so her providers were accurate that she had "plenty of time" to make decisions. But making decisions requires information about "all of the options," which Alexis did not feel she received. Alexis's doctors could have asked her about her personal priorities or how she felt about the tradeoff between RRSO at an earlier age and having biological children. Such a conversation would have enabled her to make her own informed decisions. Instead, similar to Becky's doctors, they "had an idea in their minds" about what would or should be most important to Alexis, which they thought was preserving her ability to have a naturally-conceived child.

***HRT vs. PGD***

For women who have not yet had their desired number of biological children but are approaching or within the recommended age-range for RRSO, egg or embryo freezing allows

them to preserve the possibility of having a biological child while still doing RRSO within the recommended timeframe. Later, when they are ready to have children, women can undergo in-vitro fertilization (IVF) cycles using their frozen eggs or embryos. Preimplantation genetic diagnosis (PGD) is another fertility procedure available to women with genetic mutations that allows them to avoid passing their mutation on to their children. Whether women are doing immediate IVF or using frozen eggs or embryos, if they choose to add PGD to the process, all of their embryos are tested for their genetic mutation, and only embryos without the mutation are implanted (Derks-Smeets et al., 2014; H. J. Stern, 2014).

Many of the women in this study mentioned egg freezing and/or PGD in our conversations and, unlike Alexis, said their genetic medicine providers had either discussed reproductive technologies with them or had referred them to fertility specialists. For example, Liza, the woman who noted that doctors were reluctant to discuss sexuality, told me, "My ovarian doctor already mentioned freezing eggs and how they can test for BRCA-positive and negative even down to that level to make sure that they fertilize BRCA-negative babies. She has talked to me about all of that." Hannah's clinicians informed her that some women with BRCA mutations have diminished fertility and mentioned egg freezing in that context. "I have to have my AMH[58] tested every six months to make sure my egg reserves are still okay. If they ever do start to decrease they talked about my need to freeze my eggs to make sure that when I do want to have kids I will be able to." Alexandra, one of the genetic counselors I interviewed, shared that she makes referrals to reproductive specialists for women of childbearing age. "When you talk about younger women, fertility preservation is something else that comes up. So, I talk about

[58] Anti-Mullerian Hormone (AMH) is secreted by cells in ovarian follicles and is sometimes used to measure women's ovarian reserve.

finding reproductive endocrinologists that will work with them, partly because they may be interested in having an oophorectomy, and partly because they may be interested in some reproductive technology to avoid having an affected child."

Making referrals to reproductive specialists and informing women with BOC mutations about their fertility options are important practices that expand women's knowledge and respect their reproductive desires and autonomy. For example, Marci, who was 37 when she discovered her BRCA2 mutation, benefited from being referred to a fertility specialist. She chose to freeze her eggs because she wanted children but was not partnered and did not want to rush into becoming a parent. "And then she referred me to—I don't know if it was a reproductive endocrinologist or a reproductive cancer doctor. I don't know which was my next visit. I had two different things that I was looking at. One was to explore egg freezing, so I started that process of looking and ended up doing that." Because Marci was informed about egg freezing and able to afford and access the procedure, her desire to have biological children is not a barrier to her having RRSO. Joan, who discovered her BRCA2 mutation at age 24, also had benefited from referrals to reproductive specialists. She and her husband had embryos frozen soon after they got married, both because of fertility issues that she was told were related to her BRCA mutation and in order to give her flexibility in her risk management decision-making. When I interviewed her, they had two healthy children as a result of those fertility procedures.

Several women expressed anxiety about the possibility of passing on their mutation, and they were reassured by the availability of PGD, even if they were not certain they would use the procedure. For example, Anna explained that she and her husband, who were exploring adoption, had never considered having biological children prior to the availability of PGD. "We started just recently talking about biologically having kids, before that wasn't even really on the table.

Especially now with the introduction of tests being able to test the embryos for specific genes, that got him really interested. And that was the only reason why we're now introducing the actual genetic kids, biological kids, into the discussion." Nora wished that she had known about her BRCA2 mutation and had had the option to consider PGD prior to having children. Worrying about her daughters having inherited her mutation made Nora feel "sick to [her] stomach."

> I think about it a lot. The guilt. And I think about my girls, that they're going to have this fear, and I think about when is the right time to tell them? Because when I found out, automatically I was just convinced in my head that I had cancer. I was a ticking time bomb. So, when do you tell these young girls? At 18, when they could get tested and be proactive? I don't want them at 18 years old thinking that they're going to get cancer and going through what I went through. I wish I would have—it probably wouldn't have stopped me from having kids, but I wish I would have known. I don't feel that it's a life or death sentence, but I maybe would have chosen different avenues to have children had I known. Maybe had my eggs tested. *(Nora, Age 32, BRCA2)*

Nora expressed that she could not say, with certainty, that she would have gone through the PGD process, but she was very clear that she wished she had had the option.

Egg and embryo freezing, PGD, and IVF are all procedures that require women to use hormones that stimulate ovarian follicle growth and, in turn, estrogen production (Brinton, Sahasrabuddhe, & Scoccia, 2012; Lederman, 2017; H. J. Stern, 2014). Recent studies and meta-analyses indicate that, in the general population, fertility treatments do not significantly increase women's risk of developing ovarian cancer (Brinton et al., 2012; Diergaarde & Kurta, 2014; Rizzuto, Behrens, & Smith, 2013; Siristatidis et al., 2013). Research also suggests that fertility drugs are not associated with a significantly increased risk of breast cancer, but findings on that relationship are not as strong (Brinton et al., 2012; Derks-Smeets et al., 2014; Kotsopoulos et al., 2008; Lederman, 2017). However, studies have been mixed on whether fertility treatments increase women's risk of endometrial cancer (Brinton et al., 2012; Lederman, 2017; Reigstad et al., 2017). In addition, research on the cancer risks of fertility treatments in BRCA mutation

carriers has been limited, in terms of both the size and number of studies. However, the studies that have been done suggest that it is relatively safe for women with BRCA mutations to use fertility treatments, particularly given that women with mutations are often pursuing egg/embryo freezing because they are planning on having risk-reducing surgeries (Gronwald et al., 2016; Kotsopoulos et al., 2008; Lederman, 2017; Perri et al., 2015; Rodriguez-Wallberg & Oktay, 2012). Hence, fertility drugs and HRT share a number of similarities. Both treatments expose women to hormones, have the potential to improve women's quality of life, and appear to be safe for previvors with BRCA mutations. Yet, interestingly, people's perceptions of the safety of HRT and fertility drugs differed.

In contrast to several women's concerns about the potential for HRT to increase their risk of breast cancer, only two women expressed worries about the potential risks of hormone exposure from fertility treatments. One of those women was Joan, the BRCA2 carrier who had two healthy children through embryo freezing and IVF. Joan explained that she stopped doing additional IVF cycles due to her concerns about the effects of continued hormonal stimulation. "[C]hoosing not to just keep going through IVF cycles, was also, you know, kind of because of the BRCA diagnosis. I didn't want to keep exposing myself to a bunch of estrogen and progesterone." Similarly, Veronica and her husband were "on a break" from doing fertility treatments when she unexpectedly learned about her BRCA mutation from a direct-to-consumer ancestry test. She explained how concerns about additional hormone exposure made them decide not to continue and to pursue adoption instead. "I didn't want to keep stimulating my ovaries. I mean, I don't ovulate on my own, so I didn't wanna keep stimulating my ovaries with the hormones, because I was at risk for ovarian cancer."

Women with BOC mutations who are considering RRSO often learn that one of the ways

RRSO is believed to reduce women's breast cancer risk is because it reduces women's circulating estrogen and progesterone. Hence, it makes sense that, without additional information on safety, Veronica and Joan might feel concerned about taking drugs that could increase their hormone exposure. In fact, I was somewhat surprised that only these two women expressed concerns about the risks of fertility drugs. As I illustrated earlier, several women remained worried about using HRT to treat their menopausal symptoms despite studies showing that the drugs improve survival and outcomes for premenopausal previvors. Given that the safety data on HRT use by BRCA mutation carriers is more robust than the safety data on their use of fertility treatments, I expected *more* women to be concerned about the latter, not fewer.

Even more surprisingly, *none* of the women in the study reported that their health care providers had mentioned concerns about potential cancer risks associated with fertility procedures. As I noted earlier in the chapter, even some of the providers who prescribed HRT to women had indicated to their patients that they would incur some risk by using HRT to manage their menopausal symptoms. However, those doctors told women that the decision to take HRT was "up to them" because the slight increase in breast cancer risk could feel worth the tradeoff in quality of life improvements. Given that there is robust data on the safety of HRT use by premenopausal women with BRCA mutations who have RRSO but very little data on the safety of fertility treatments among BRCA mutation carriers, I expected more women to share stories of primary care providers' misconceptions about fertility drugs and cancer risks. Yet none did.

What can explain this contrast between perceptions of the risks of HRT and those of the hormones used in association with IVF, egg freezing, and/or PGD? One possible explanation is that clinicians who are not cancer genetics experts are not aware of current data on HRT safety for premenopausal women who have RRSO, and as a result their patients are not aware either. In

my fieldwork and interviews, I frequently heard stories about primary care and other medical generalists who had misconceptions about BOC genetic testing and/or risk management. Many women and most doctors would likely have heard that HRT use is associated with an increased risk of breast cancer, which is accurate for postmenopausal women in the general population. The link between HRT and breast cancer has been widely publicized since July 2002, when the combined estrogen and progestin trial in the Women's Health Initiative (WHI) was halted mid-study due to a significantly increased risk of breast cancer in the treatment arm (Fred Hutchinson Cancer Research Center, 2018). Lacking current data on outcomes in premenopausal women and/or in BRCA carriers, women and their doctors might assume HRT use is unsafe for women of any age who are at high risk for breast cancer.

Differences between the duration of women's hormone exposure with HRT and fertility drugs may also affect people's perceptions of the safety and risk of the drugs. When women take HRT, they usually do so daily over several months or even years, whereas the hormones in fertility treatments are most commonly used intermittently for a few months. Hence, it is possible that because women and their doctors understand that fertility drugs will be used for less time, they feel less concerned about them, regardless of what the scientific literature indicates in relation to health risks and benefits.

Another interpretation of why patients and providers are wary of HRT use but open to fertility treatments is that these attitudes reflect the gendered tendency in BOC genetic medicine to overlook sexuality and quality of life issues and focus on reproduction. As women's stories in this chapter have illustrated, genetic medicine practices often encourage women to rush into RRSO and leave them un- or under-prepared for the effects of medically-induced menopause. Not offering women HRT or framing the drugs as potentially risky emerges from and reinforces

larger practices that de-prioritize women's sexuality, embodied experiences, and quality of life. At the same time, the practices of genetic medicine encourage women to hurry up and have kids and emphasize how RRSO will affect reproduction. Informing women about the availability of fertility treatments and referring them to reproductive endocrinologists while refraining from raising concerns about their use of fertility drugs are practices that further reflect and reproduce the high value placed on childbearing and motherhood. Of course, women *should* receive medically accurate information about their options and appropriate referrals to specialists. But the high priority placed on reproduction in BOC genetic medicine illuminates the relative low priority placed on non-reproductive issues that affect women's quality of life. Thus, the problem is not that motherhood and childbearing *are* valued, but rather that women's sexuality and daily embodied experiences *are not*.

## Valuing Reproductive Bodies

### *Ovaries Are Disposable*

The contrast between attitudes toward fertility drugs and HRT illustrates how practices in BOC genetic medicine signal both what is and what is not valued about women's bodies. Encouraging women to "hurry up" and have children so that they can have their ovaries removed conveys that ovaries are important until women have completed childbearing, but afterward are expendable. Veronica's oncologist who encouraged her to have an oophorectomy before the recommended age range is a prime example of these practices. He explicitly told Veronica that if she wasn't "having biological children," that she should "get them out now." Discourses that construct ovaries as disposable after childbearing both reflect and reinforce the invisibility of the non-reproductive functions of hormones.

Several women I interviewed had internalized these discourses and the belief that ovaries

were only important for reproduction. They made references to how they no longer "needed" their ovaries or uteruses anymore because they were done having children. For example, Rose is a CHEK2 mutation carrier who was relieved that there was not a confirmed link between CHEK2 mutations and ovarian cancer. She said, "With the CHEK2 gene they give you a list of other things you can have—brain cancer, thyroid cancer. But not ovarian!" When I asked Rose how she felt about ovarian cancer not being on that "list," she conveyed that she was glad not to need another surgery. "Because I would have just had a hysterectomy. I don't need my ovaries anymore, so I would have just taken it all out." Similarly, Adele talked about her mother's experiences managing her BRCA2 mutation, and noted, "They did a full hysterectomy with her as well because she's not having any more kids either."

Talia's story sharply illustrates how women's bodies are valued for their reproductive capacity and how, in turn, their internal organs are treated as disposable when they are no longer "needed" for reproduction. Unlike with breasts, very few women explicitly connected their femininity, identity, or womanhood to their ovaries or their uterus. However, Talia was an exception. She shared how she grieved the loss of her ovaries because she had always envisioned being a mother. Giving up the ability to conceive and bear children felt like losing a major part of her womanhood. "It was much more emotional for me to have the ovaries removed. I felt like I was not a woman…. I think the recovery from the mastectomy and reconstruction was much more about the physical, and the recovery from the ovarian was more emotional for me."

Talia was one of three lesbian women I interviewed, and she was also the only woman who shared a story about a doctor openly dismissing her grief or concerns about giving up the ability to conceive and bear children through RRSO. Talia described a conversation with the first gynecologic oncologist she saw:

> I was really crushed about not having a baby, and I said that to her. And she was like, "Well, you're lucky you're with a woman. She can carry the baby." And that's just like, that's not how it works, you know? We're not all interchangeable. Women are not like—we don't all want to carry a baby, and it's my experience, not her experience, you know? It's my body. She can't be my body for me. (Talia, BRCA2, Age 38)

This GYN/ONC did not ask Talia about her fertility desires, listen to her grief, provide her with resources on egg freezing, or discuss delaying RRSO with her, despite the fact that Talia was only in her early 30s at the time. Instead, the doctor dismissed Talia's emotional and embodied experiences, and treated her ovaries as disposable even before she began childbearing. Whereas most clinicians only constructed women's ovaries as disposable after they had babies, Talia's doctor saw her ovaries as immediately expendable because there was another woman in Talia's partnership who had eggs and ovaries that could be used for babymaking. As Talia said, this clinician treated women's bodies as "interchangeable" rather than addressing Talia as an individual embodied agent.

Moreover, constructing ovaries as expendable organs that lack usefulness after women have completed childbearing contributes to women's under-preparation for medically-induced menopause. For example, Raina conveyed how she initially thought RRSO would be "no big deal" because she was done having children, and then was surprised by how her body was affected once they were gone. "It just didn't seem as big of a deal to me as getting the breasts taken off. Like, 'Oh they're just my ovaries. I've already had my kids, no big deal, you don't need them anyway' kind of thing. I don't think anybody really prepared me for how different I would feel without them." Raina's account illustrates how discourses that frame ovaries as only relevant for making babies can lead to shock when women experience other side effects after their oophorectomies.

Perhaps if women had better understandings of the significant systemic effects of steroid

hormones and how they impact heart and bone health, cognition, mood, sleep, and sexuality, some women at genetic risk might be more cautious about "jettisoning" their ovaries. That is not to say that they would not have them removed—the data on RRSO reducing all-cause mortality among BRCA mutation carriers are strong. However, if ovaries were regarded as important and functional at all life stages and people better understood how ovarian function changes over the lifespan, women would be better prepared for the range of risks they might face with RRSO and could advocate more effectively for their menopausal side effects to be treated.

### *The Pancreas Is Essential*

Examining the practices in BOC genetic medicine for managing women's increased risk of pancreatic cancer, which is the third most common cancer associated with BRCA mutations, sheds further light on how ovaries are constructed as disposable. The pancreas and ovaries are both endocrine glands, and there are several similarities between pancreatic cancer and ovarian cancer. The prevalence of the two cancers in women is nearly identical, with 11.2 out of every 100,000 women per year being diagnosed with pancreatic cancer, and 11.6 out of every 100,000 women per year being diagnosed with ovarian cancer (National Cancer Institute, 2018e, 2018f; Noone et al., 2018). Both cancers lack effective screening tools and therefore are extremely difficult to detect. Similar to ovarian cancer, at diagnosis over 80% of pancreatic cancers have spread regionally or to distant organs, with 52% having metastasized and only 10% being localized (National Cancer Institute, 2018f; Noone et al., 2018).

Recent risk estimates indicate that BRCA mutation carriers' lifetime risk of developing pancreatic cancer is, on average, 5%, but ranges from 2-10 times the risk in the general population (Iqbal et al., 2012; Mersch et al., 2015). These estimates are lower than current estimates of BRCA carriers' lifetime risk of developing ovarian cancer, which are approximately

17% for women with BRCA2 mutations and 44% for women with BRCA1 mutations (Kuchenbaecker et al., 2017). Hence, among BRCA mutation carriers, women's overall risk of developing pancreatic cancer is lower than their risk of developing ovarian cancer.

However, five-year survival rates for pancreatic cancer are less than 9%, by far the worst of any cancer (National Cancer Institute, 2018f; Noone et al., 2018). With 44,330 people estimated to die of pancreatic cancer in 2018, it is the third leading cause of cancer death in the United States, trailing only lung cancer and colorectal cancer, both of which are far more prevalent (National Cancer Institute, 2018f; Noone et al., 2018). Moreover, while both pancreatic and ovarian cancer tend to be caught after they have spread, even in the 10% of cases when pancreatic cancer is localized at diagnosis, the five-year survival rate is only 34% (National Cancer Institute, 2018f; Noone et al., 2018). In contrast, in the 15% of ovarian cancers that are localized at diagnosis, the five-year survival rate is 92%(National Cancer Institute, 2018e; Noone et al., 2018). Because of its terrible prognosis, more women in the United States die each year from pancreatic cancer than ovarian cancer. From 2011-2015, the annual death rate per 100,000 women from pancreatic cancer was 9.5, whereas for ovarian cancer it was 7.2 (National Cancer Institute, 2018e, 2018f; Noone et al., 2018).

Given the extremely low survival rates from pancreatic cancer, any significantly elevated risk is of concern. One might think that concerns about pancreatic cancer risk would be particularly high for women with BRCA2 mutations, who, compared to BRCA1 mutation carriers, have almost twice the lifetime risk of developing pancreatic cancer but less than half the risk of developing ovarian cancer (Cavanagh & Rogers, 2015; Kuchenbaecker et al., 2017; A. W. Kurian et al., 2010; Salo-Mullen et al., 2015). In fact, for a woman with a BRCA2 mutation who has no family history of ovarian cancer but two or more relatives who have had pancreatic

cancer, estimates of her lifetime risk of developing *both* cancers might be close to 10%. Yet risk-reducing pancreatectomy (RRP) is never considered in the absence of clinical symptoms of pancreatitis, even for BRCA2 mutation carriers who have strong family histories of pancreatic cancer. RRP is only considered in individuals who have pre-cancerous lesions or chronic pancreatitis, and even then, it is rarely performed (Canto et al., 2013; Del Chiaro, Segersvärd, Lohr, & Verbeke, 2014; Lucas, 2014). At the ten multi-day scientific meetings and two dozen webinars on cancer genetics that I attended between 2013 and 2017, I never once heard anyone even mention RRP in a session or discussion.

In highlighting patients' and providers' reluctance to consider or speak about RRP, I am not suggesting that BOC genetic medicine should move toward the procedure as a mass practice. When people have their pancreas removed, they instantly develop insulin-dependent, or Type 1, diabetes, which is associated with an increased risk of heart disease, stroke, kidney disease, blindness, and nerve damage (Imperatore, Mayer-Davis, Orchard, & Zhong, 2016). Given the low prevalence of pancreatic cancer, every death averted by RRP might also result in many more individuals experiencing harms, even when accounting for pancreatic cancer's extremely high mortality rate. But because of that high mortality rate, in targeted populations at very high risk of pancreatic cancer, all-cause mortality might go down with RRP, similar to outcomes of RRSO in populations at high risk for ovarian cancer. Yet scientists cannot test either hypothesis because the data on RRP are too thin—providers only consider and offer the procedure in extreme circumstances.

One might suspect that RRP is an almost unthinkable practice *because* data are lacking on the morbidity and mortality associated with the procedure. Being launched into insulin-dependent diabetes in mid-adulthood might result in different health outcomes than becoming a

Type 1 diabetic in childhood or young adulthood, when the disease typically develops (Imperatore et al., 2016; Menke et al., 2013). But RRSO was recommended to BRCA mutation carriers long before 2010, when the first studies were published showing that RRSO reduced all-cause mortality (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010). Prior to that, there were only data on oophorectomy in the general population, and those findings suggested that premenopausal salpingo-oophorectomy in BRCA carriers might increase all-cause mortality. The hesitation to even discuss RRP is also not because people are unable to live without their pancreas or endogenous insulin. Type 1 diabetes is a serious disorder, but with access to quality medical care, it is also a treatable and livable one; current estimates indicate that over one million children and adults in the United States currently live with the disease (Imperatore et al., 2016; Menke et al., 2013). Hence, we know that with careful medical management, people can, and do, live otherwise healthy lives with a non-functional pancreas by taking injectable insulin. Living without a pancreas or with one that does not produce insulin is by no means optimal, but it is manageable. So why is RRP viewed as unfathomable, even in individuals with a high risk of pancreatic cancer, but RRSO is regarded as an "easy" procedure that women at high risk of ovarian cancer should hurry up and get?

The discrepancies in the discursive and clinical practices surrounding pancreatic cancer risk and ovarian cancer risk are, in part, linked to differences in how ovaries, the pancreas, and the hormones they produce are constructed. The pancreas is an endocrine organ that produces a hormone, insulin, that is widely presented and understood as critical to healthy bodily functioning. But, as I have illustrated through women's stories in this chapter, ovaries are endocrine organs that are commonly constructed as disposable after childbearing, and the systemic, non-reproductive effects of the steroid hormones they produce are largely rendered

invisible. In other words, the different ways in which we view and talk about parts of our bodies have material effects and consequences. When body parts are framed as essential, like the pancreas is, doctors are cautious and reluctant to even discuss the possibility of removing them. But when bodies are fragmented and organs are constructed as disposable, like ovaries are, individuals are more likely to be willing to remove them or to be rushed into surgery under-prepared. Perhaps if the systemic effects of hormones were more widely understood and ovaries were regarded as valuable organs throughout women's lives, clinicians would more consistently inform BRCA mutation carriers about the sometimes severe side effects of RRSO and manage those effects with HRT. As I have emphasized, there are solid data on the health benefits of RRSO in high-risk women. But some of those benefits are offset by the casual practices surrounding the surgery, and the seriousness with which medical professionals regard RRP brings the "cavalier" discourses and practices surrounding RRSO into sharp focus.

***Intersectional Bodies***

The discursive and clinical practices in BOC genetic medicine that construct women's ovaries and uteruses as disposable after childbearing are highly gendered. Jackie, the genetic counselor who shared that she often does not address with her clients how RRSO might affect their sexuality, noted about that practice, "I think it's an incredibly sexist thing that we don't talk about it more. If this were men, we wouldn't be telling them to take their reproductive organs out at the same rate." Indeed, there are no stages in the life course or circumstances in which men's sexual and reproductive organs are portrayed as unimportant or disposable. Instead, it is widely assumed that men will want to retain their testes and prostate throughout their lives and not have their organs removed after they have had their desired number of children. Prostate cancer is the most prevalent cancer among men in the United States and is the second leading cause of male

cancer deaths (National Cancer Institute, 2018g). Yet prophylactic prostatectomy is not a phenomenon, even among BRCA2 mutation carriers and other men at high genetic risk (National Cancer Institute, 2018g; PDQ® Cancer Genetics Editorial Board, 2018; Pesmen, 2015).

Even more than the prostate, testicles are constructed as essential to maleness. Approximately 50% of testicular cancers are genetically linked, which is a much higher proportion than the 10% - 15% of breast and ovarian cancers that are heritable (Litchfield et al., 2015; Wang et al., 2017). However, no one suggests that men consider prophylactically having their testes removed if they have mutations or clusters of genetic markers associated with high testicular cancer risk. It is also nearly impossible to imagine a man who is done having children saying, like many women did about their ovaries, "I don't need my testicles anymore." In fact, when a nationally-regarded gynecologic oncologist referred to RRSO as "castration" in a plenary talk at a cancer genetics meeting, there were visible looks of shock on the faces of several audience members, and one of the genetic counselors sitting near me uttered "Wow."

The GYN/ONC's usage of the word castration was medically accurate, as the scientific definition of the verb "castrate" means to remove the testes or ovaries. But that instance was the only time in my three years of research on this topic that I ever encountered a person referring to oophorectomy as castration, either in speech or writing. In common parlance, "castration" is understood as the process of cutting off a man's testicles, and it is perceived as a severe intervention that has negative associations; "castrate" also means "to render impotent or deprive of vitality" (Merriam-Webster, 2018). By referring to oophorectomy as castration, the GYN/ONC drew attention to the severity of the procedure, which elicited surprise among some members of the audience. Those reactions, in turn, highlighted the gendered discursive and clinical practices in genetic medicine. Removing a woman's ovaries is often constructed as

routine and easy, but invoking the parallel procedure in men made it seem shocking and extreme.

Moreover, the discourses and practices in BOC genetic medicine that embrace reproductive technologies and frame women's ovaries and uteruses as disposable after childbearing are not just gendered—they are intersectionally gendered, racialized, and classed. Gender, race, and class—as constructs, social structures, and axes of identity—are interactive; they do not operate separately or additively, nor can they be neatly disentangled. This is reflected in reproduction, which is stratified, both in the United States and globally (Colen, 1995; Ginsburg & Rapp, 1995). That is, the ways in which reproduction is and is not socially valued is markedly uneven by race and class. Anthropologist and science studies scholar Rayna Rapp explains, "Reproductive futures are embedded inside other forms of hierarchy: Access to respectful, competent prenatal care, eugenic attitudes toward 'excessive' or 'wasteful' pregnancies, and financial and social resources for differently abled children are socially stratified in familiar patterns" (Rapp, 2000, p. 311). In the United States, motherhood among middle- and upper-class white women has mostly been valued, while, comparatively, motherhood has often been devalued among poor women, immigrant women, and women of color (Bridges, 2011; D. Roberts, 1997; Silliman et al., 2004; Vandenberg-Daves, 2014). Moreover, economically advantaged white women's reproductive concerns have often been prioritized within major women's health advocacy organizations, whether those priorities have been to *not have* children through access to contraception and abortion services or to *have* genetic or biological children through access to reproductive technologies (Gordon, 2002; McFarlane, 2001; D. Roberts, 1997; Silliman et al., 2004; Staggenborg, 1991).

The patient population in BOC genetic medicine in the United States is disproportionately female, white, highly-educated, and middle-class (Armstrong et al., 2015; Cragun et al., 2017;

McCarthy et al., 2016; Underhill et al., 2016), and thus it reflects the groups of women among whom reproduction and motherhood tend to be more valued. Science studies scholars have illustrated how the skewed demographics of patients in genetic medicine are, in part, a reflection of the field's early engagement with Ashkenazi Jewish and other European populations (Mozersky & Joseph, 2010; Wailoo & Pemberton, 2006). Scientists created databases of genetic samples from these populations that were used for early genetic research, which concentrated knowledge on variants more commonly seen among Ashkenazi Jews and other people of European ancestry. In turn, greater knowledge about cancer genetic risk in those populations has sedimented racialized ideas, among both lay people and health professionals, about who is and is not at risk and therefore who tends to use genetic testing services (Montoya, 2011; Mozersky & Joseph, 2010; Wailoo & Pemberton, 2006). The demographic distribution of the women who participated in this study is similar to the typical patient population in BOC genetic medicine--they were overwhelmingly white and over 80% of them had at least a college degree.[59]

The effort made by clinicians in genetic medicine to inform women about, and provide them with referrals to, reproductive technologies is an example of how practices in the field are not only gendered, but also racialized and classed. Like BOC genetic medicine, reproductive technology services, such as egg/embryo freezing, PGD, and IVF, are disproportionately used by white women (Dieke, Zhang, Kissin, Barfield, & Boulet, 2017; Ethics Committee of the American Society for Reproductive, 2015; Smith et al., 2011). In addition, these services also are extremely expensive and are rarely covered by insurance. Prices for reproductive technologies are variable, but estimates for the average cost of medications and treatment for one cycle of egg

[59] Appendix B contains tables of the demographic characteristics of the women who participated in interviews.

freezing range from $10,000 - $15,000, and then storing those eggs costs approximately $500 annually. When women are ready to use their frozen eggs, the average cost of IVF (which is always required with egg/embryo freezing) and PGD (which is optional) are an additional $5,000 and $3,500 per cycle, respectively (Advanced Fertility Center of Chicago, 2018a, 2018b; Beltsos, 2018; Neighmond, 2014; Shady Grove Fertility, 2017). As Marci, who froze her eggs, stated, "Egg freezing is a car. It's its own thing. There is nothing cheap about that process at all." Given the high costs of using reproductive technologies, they are likely to be difficult to access for many women. For example, Lily was exploring the possibility of PGD, but she was doubtful she could afford it. "I am interested about the genetic testing—like, the pre-genetic testing with the children. I have looked at that, and it's very expensive, as you may know. It's really expensive and I'm just like—I don't know if that's really an option for me."

As I have illustrated throughout these chapters, scientific and medical practices are filtered through larger historical, social, and cultural contexts. Thus, women's experiences shared in this chapter, such as referrals to reproductive technologies, should be understood within a broader landscape of contemporary gender politics that disproportionately values motherhood among middle-class, white women. The lens of distributed reproduction focuses attention on how RRSO practices that prioritize and emphasize women's reproductive capacities are not reflective of how all women's bodies in the United States are valued. Rather, these practices in genetic medicine align with social and cultural values about women's bodies and roles that are specific to the intersectional racial and class locations of the women who tend to access BOC genetic medicine.

**Conclusion: How Much Knowledge?**

This chapter examined the discursive and clinical practices involved in constructing and managing genetic risk for ovarian cancer in the United States. Drawing on fieldwork at cancer

genetics conferences and interviews with clinicians and BRCA mutation carriers, I illustrated multiple axes of competing priorities in BOC genetic medicine. First, there is a foundational socio-clinical tension in the field: concerns about breast cancer risk and pressure to have mastectomy are magnified in social contexts, while concerns about ovarian cancer risk and encouragement to have RRSO are amplified in clinical contexts. Second, there is a disparity between how RRSO is framed, which is as a quick and easy surgery, and women's embodied experiences after the procedure, which are enduring and difficult. Third, the structures of genetic medicine reflect longstanding biomedical practices that emphasize the reproductive functions of ovaries and steroid hormones while obscuring their systemic non-reproductive effects. I argued that there are material, embodied consequences of the social, clinical, and discursive practices that prioritize the reproductive capacities and functions of women's ovaries and uteruses over their non-reproductive functions. These discourses and practices often result in women rushing into RRSO without having without adequate information about the severe and enduring side effects of medically-induced menopause.

When viewed in isolation, several of the RRSO practices highlighted in this chapter are positive, and even optimal. Most clinicians are accurately conveying the health and survival benefits of RRSO to BRCA carriers, which helps women make informed decisions. In addition, the structures and architecture of BOC genetic medicine in the United States largely respect women's reproductive autonomy. The field tends to provide appropriate information about the impact of RRSO on fertility and often issues referrals to reproductive medicine specialists when women are nearing the recommended age ranges for RRSO and want more children. Hence, the tension evident in RRSO practices is most often not around the information women *do* receive, but rather around the information they *do not.*

BOC genetic medicine patients need to be better informed about the systemic impact of steroid hormones on multiple systems in the body, the full range of potential health risks and side effects of medically-induced menopause, and current research on the health *benefits* of HRT use for premenopausal previvors. While most women stated that with this information they still would have chosen RRSO, not having that knowledge prior to their surgeries caused them added stress and, in the case of information about HRT, led to their symptoms being under-managed. I cannot count the number of times I heard women in this study repeat the phrase "Knowledge is power." BOC genetic medicine is centered on helping women "take control" of their lives and make "strong choices." But the stories in this chapter illustrate that when women are not provided with accurate, current risk and benefit information—when they only have a *slice* of the knowledge they need rather than the full picture—their choices are circumscribed, and it can lead to their experiences feeling out of control.

Women's under-preparation for medically-induced menopause is also especially striking because participants in this study, like most patients in BOC genetic medicine, were disproportionately privileged. Almost 95% of the women I interviewed were white, 43% had a graduate degree, another 40% had graduated from a four-year college, and 100% of them had health insurance. In addition, the vast majority of the women were active in a patient advocacy group, whether that was an in-person support group, a local chapter of a national organization, or a virtual group on Facebook. In other words, these are the very women whom one would expect to have the *best* access to resources, information, and services, and yet even their care and knowledge were falling short. How can we improve the quality and evenness of the information and clinical care women receive in BOC genetic medicine? I will address this question and other policy and practice recommendations in the final chapter that follows.

## Conclusion: "A Higher Level of Communication, a Basic Standard of Care": Policy and Practice Recommendations for the Panel Testing Era

> "I think if there was some sort of generalized plan for people with mutations. I don't know if that could happen, it's so relatively new. But if there could be a plan..." *(Marlene, Age 35, CHEK2)*

> "We really do have to update the way that we think about delivering our services if we want to accomplish our mission of making sure people have the genetic information that they need." *(Alyssa, Genetic Counselor)*

> "We also have to have some sense of what the right answer is. And it can't just be, 'We're going to do all of this testing so people can make up their own minds about what the heck it is that they should be doing.'" *(Steve, Oncologist)*

This project examined practices in breast and ovarian cancer (BOC) genetic medicine in the United States in the new era of multi-gene panel testing. Departing from frameworks in clinical research on BOC genetic risk, I explored the active construction of risk, and I extended social science scholarship on cancer genetics by studying the recently emerged groups of women identified as having "moderate" or "uncertain" BOC risk via panel testing. Going beyond an individual- or familial-level analysis of women's risk management decisions, the study explored how social and structural aspects of BOC genetic medicine limit or expand women's options and actions.

Over a three-year period, I collected data at cancer genetics conferences, analyzed reports and documents from genetic testing laboratories, and conducted interviews with women with BOC mutations and health care providers working in BOC genetic medicine. I examined the technologies, practices, tools, and documents used to interpret and classify cancer genetic risk, generate risk estimates, and explain BOC genetic risk information. I then explored women's risk management experiences—the guidance they received, their insurance coverage for testing and surveillance, the surgical and medical management options they were provided, and

their participation in support groups and health activism.

One major finding of this study is that the shift to panel genetic testing has contributed to the blurring boundary between risk and disease. Women with high-risk BOC mutations like those on the BRCA1/2 genes are now rarely viewed or treated, by health professionals or themselves, as occupying a liminal state between health and illness. Rather, women with BRCA mutations are now typically viewed and counseled as if they have a disease that should be managed according to clearly defined protocols. Instead, it is women with variants of uncertain significance (VUSs) or moderate-risk mutations (MRMs), such as those on the CHEK2, PALB2, or ATM genes, who now face confusion and uncertainty in their medical management.

This study also finds that the organization and practices of US genetic medicine point women with BOC mutations toward risk-reducing mastectomy (RRM) and breast reconstruction and encourage choosing those surgical responses over breast surveillance or staying flat. The experiences of women in this study revealed how mastectomy is both viewed and used in practice as the "treatment" that cures the "disease" of genetic risk for breast cancer, regardless of whether women's mutations are high- or moderate-risk. Even though mastectomy is a medical procedure that reduces women's risk of developing breast cancer and reconstruction is a cosmetic procedure that confers additional risks to women's physical health, the two surgeries are often presented to women as a package deal. I argue that the practices in genetic medicine that structurally encourage breast reconstruction both reflect and reinforce gendered norms and expectations for women's bodies.

Beyond this encouragement to undergo mastectomy and reconstruction, this project illustrates that women—particularly those with moderate risk mutations—experience tremendous unevenness in the care they are provided. Broadly, the US healthcare landscape is marred by

variability in providers' knowledge and training and the cost and coverage of health care services. However, genetic medicine, in particular, lacks uniform protocols for interpreting and reporting variants and managing women's risk through surgeries. These inconsistencies in provider knowledge and practices left many of the women in this study un- or under-prepared for the risks and consequences of breast reconstruction and risk-reducing salpingo-oophorectomy (RRSO).

This project also revealed that the high social value placed on conventional femininity implicitly and explicitly encourages women to take on additional risks in order to have breasts that lack sensation or biological function. I illustrated how having the visible appearance of breasts is framed as essential, while real breasts are treated as disposable. However, while breasts are marked by their visibility, ovaries are both literally and figuratively marked by their invisibility. Because they are internal organs, you can cannot physically see their presence or absence, and at the same time social and medical discourses obscure the systemic bodily effects of the steroid hormones produced by ovaries. Hence, ovaries, which are endocrine organs with critical biological functions beyond reproduction, are constructed as disposable, while breasts are considered so indispensable that women are encouraged to replace them despite the additional risks to their health reconstructive surgeries pose. Together, breast reconstruction and RRSO practices reflect and reinforce gendered, racialized, and classed social and cultural values that prioritize women's appearance and their reproductive capacity over their embodied experiences and daily quality of life.

Women's stories illustrated that their involvement in cancer genetics communities and advocacy networks sometimes improved their knowledge and helped them to more effectively navigate the complex maze of genetic medicine. As institutions, social and support networks for

women at BOC genetic risk have become valuable education and advocacy blocs that help to buffer the unevenness of the US healthcare system. However, while these groups make efforts to collectively reshape clinical care, in the fragmented, private insurance-based US system, those opportunities are limited and stymied. Hence, the knowledge shared through advocacy and support groups may result in individual-level improvements for the women who find them, but the information-sharing in these groups is a patchwork stopgap that leaves the larger structures of genetic medicine unchanged.

One of the themes explored throughout this study is how the practices of genetic medicine are framed by rhetorics of "choice" and "empowerment" but are often marked by constraint and inequality. Focusing on women's testing and surgical choices instead of the structures that circumscribe and facilitate those choices puts the onus on women to be informed and manage their care rather than asking the system to better serve their needs. But women at BOC genetic risk should not have to bootstrap themselves into quality, informed care. As Steve, an oncologist, said, "I'm all in favor of shared decision making, I think it's important. But we also have to have some sense of what the right answer is. And it can't just be, 'We're going to do all of this testing so people can make up their own minds about what the heck it is that they should be doing.'" Indeed, several women in this study indicated that they wished they had clearer guidance, information, and recommendations so that they could make truly *informed* choices. What follows in this final chapter are suggestions for system- and structural-level changes to the policies and practices of BOC genetic medicine that could improve women's experiences and options.

**Develop a Uniform Risk Classification System**

Susan Domchek, the director of the Basser Center, one of only two BRCA research

centers in the United States, succinctly summarized the conundrum at the heart of breast cancer risk management for women with BOC mutations: "Although the risk of breast cancer is high among women with BRCA1 and BRCA2 mutations, it is not absolute; some women will not develop cancer; thus, mastectomy would have been unnecessary. Conversely, despite screening and early detection, not all breast cancers will be curable but may have been prevented with risk-reducing mastectomy" (S. M. Domchek, 2019, p. 27). Several women who participated in this study understandably felt that developing an incurable cancer that might have been preventable was a worse fate than having a mastectomy that was unnecessary, and therefore they chose to have RRM. However, women's stories also illustrated that many of them were not accurately informed about the ranges of penetrance for their mutations or the consequences of reconstruction and RRSO, all of which are critical to women's personal risk/benefit calculations about surgeries.

Moreover, the probabilities of having unnecessary RRM or opting to wait and subsequently developing an incurable cancer are not equal to one another or evenly distributed across women. Rather, both probabilities are modified by the type and location of women's particular mutations, their family histories, and their personal lifestyle factors (such as whether they smoke or drink). Women with higher-risk mutations that tend to develop aggressive cancer subtypes, such as BRCA1 mutations, are more likely than women with mutations on moderate-penetrance genes like CHEK2 to develop an incurable cancer if they avoid mastectomy. Conversely, RRM is more likely to be unnecessary among women with CHEK2 mutations than among women with BRCA1 mutations given that the highest lifetime risk estimates for CHEK2 mutation carriers are approximately half those of BRCA1 mutation carriers (Couch et al., 2017; Kuchenbaecker et al., 2017; Tung et al., 2016). Yet current approaches to reporting genetic test

results group these two very different mutations together as "positive" results, which frames them as similarly risky.

The current approaches to communicating BOC genetic risk derive from the targeted-gene testing era, when women who had genetic testing were typically screened for mutations on only the BRCA1 and BRCA2 genes. The lifetime risk estimates and risk profiles of mutations on these two genes, while different, are similar enough that they were initially grouped together. In addition, standardized reporting practices were not essential in this era, given the general consensus on the risk profiles of the BRCA genes and the limited volume of genetic information being communicated to patients and other providers. However, now that panels screen for variants on dozens of genes that confer a much wider range of risks, the volume and complexity of information provided by genetic testing has dramatically increased, but reporting and counseling practices have not kept pace with these changes. In combination with the fact that BOC genetic risk is increasingly viewed and managed like a "disease," the binary division of genetic testing results into "positive" and "negative" is no longer sufficient and, I have argued, contributes to the over-management of risk.

Chapter One highlighted that while clinicians and scientists have devoted resources to assessing and improving VUS knowledge and management, there is practically no discussion in genetic medicine about the over-management of MRMs. Most genetics *experts* understand that prophylactic surgeries are only recommended for high-risk and not moderate-risk mutations, but those distinctions are not clearly communicated to patients or providers without expertise in genetics. Rather, the current unstandardized reporting system is both highly variable and overly simplistic, as labs provide patients with different risk information but then classify all variants deemed likely pathogenic or pathogenic as "positive," regardless of whether the variant poses a

25% or 75% lifetime risk of developing cancer. This binary positive/negative approach to reporting genetic testing results encourages patients to view and manage all BOC mutations as similarly risky when they are not.

Genetic medicine would benefit from a simple, uniform system for classifying and reporting on mutations that 1) groups them according to their varying ranges of risk, and 2) indicates the appropriate interventions for managing each range of risk. Such tiered classification systems, like the ones currently used in oncology for staging and grading tumors, clearly communicate complex information about tumor biology and disease progression to patients and their other providers. If, for example, genetic experts developed a similar scale for classifying mutations into four risk groups (e.g., Risk Levels 1 - 4) and laboratories uniformly used that system, then patients and their primary care providers or surgeons who do not have training in genetics might more clearly understand the *spectrum* of risk and calibrate their responses accordingly. Most cancer patients understand that while all cancers are bad, Stage III tumors are worse than Stage I tumors and require more intensive and invasive treatments. Thus, it follows that if women and providers were given the appropriate conceptual frameworks and tools, they could grasp similar distinctions about *risk* for cancer and would understand that having a "Level 4 Risk" might warrant RRM but a "Level 1 Risk" would not. Such an approach would also help to distinguish between the risks of having BRCA1 and BRCA2 mutations, which Domchek emphasizes are "related but distinct cancer susceptibility syndromes" (S. M. Domchek, 2019) that require different responses.

Of course, even with a uniform risk classification system, there will always be individual cases that are difficult to categorize, and multiple factors would have to be considered to determine patients' risk classifications. Just as breast tumors are classified as Stage II when

either there is lymph node involvement or tumors exceed two centimeters in size, individual women with CHEK2 mutations might be upgraded in their risk level if they also had multiple relatives with breast cancer. But similarly, the criteria for each risk level and the interventions considered appropriate at each level would not vary across genetics laboratories or clinics, just as hospitals and pathology labs do not each develop their own tumor grading and staging criteria. A standardized risk classification system for BOC genetic medicine would make notable strides in improving clarity and consensus about the health and clinical implications of different BOC mutations, something many of the women with MRMs in this study said they desired.

**Provide Patient-Centered Reports that Minimize VUSs**

Genetic testing results reports are enduring documents that communicate risk information. While many of the women in this study who met with genetics experts before or after being tested remembered their interactions during these pre- and post-test counseling sessions, for some women, their recollections of the detailed specifics of those conversations, such as numeric risk estimates they were provided, had faded over time. However, their test reports were firm sources of information that they could (and did) refer back to to remind themselves of their risks and locate additional resources. Hence, the organization, content, and framing of panel test reports is critical, and modifying those factors could alter patients' understandings of, and responses to, being at risk.

Chapter One highlighted the tremendous variability in the reports of the five major cancer genetics laboratories in the United States. The labs differed in how they conveyed information about VUSs, who their target audience was, the different associations they identified between specific genes and cancers, and the types of risk estimates they provided. The variability in the information provided in panel test reports contributed to women's confusion about what cancers

they were at risk for, how serious those risks were, and the most effective ways to manage those risks. Developing a uniform risk classification system would help to rectify some of the inconsistencies and variability in information that women encountered. In addition, modifying genetic test results reports so that they are directed to patients rather than providers could improve women's experiences navigating BOC genetic medicine. Color's current reporting practices can serve as a model for other laboratories. As was illustrated in Chapter One, Color's reports are patient-oriented in their language and presentation, minimize VUS results, and list only robustly established cancer associations.

In the debates within genetic medicine over whether and how to report VUSs, advocates for providing information on uncertain variants typically argue that VUS findings are owed to patients, both because it is their genetic data and because variants might be upgraded and later reclassified as harmful. However, as Chapter One illustrated, all variant classifications are active interpretations by genetic scientists, and therefore all variant classifications can change. Yet laboratories do not currently report on benign or likely benign variants that they identify during sequencing, despite that information also being patients' personal genetic data and the possibility of those variants being upgraded in the future. Moreover, recent studies have shown that even after 10 - 20 years, at most only 25% of VUSs are reclassified, and over 90% of the VUSs that are reclassified are downgraded to benign or likely benign (Macklin, Durand, Atwal, & Hines, 2018; Mersch et al., 2018; M. L. Murray et al., 2011; T. P. Slavin et al., 2018). Hence, only approximately 3% of the people given VUS results are likely to eventually have a reclassification to pathogenic or likely pathogenic that would warrant additional medical management. Yet, according to studies on responses to receiving VUS information, as many as 10% - 20% of individuals who were told they had a VUS had prophylactic surgeries (Miller-Samuel et al.,

2011; M. L. Murray et al., 2011; Vos et al., 2008). These results suggest that the current approach to reporting taken by most laboratories, which is to prominently identify all VUS results from BOC panel tests, is associated with a greater proportion of women being overtreated with surgery than the proportion of women who would be under-screened if those VUSs were never reported. If more laboratories utilized Color's approach of noting that a VUS was found but not highlighting that information or indicating the location of the variant unless the patient or provider requested additional information, it is likely that fewer women with VUSs would end up having mastectomy or RRSO.

Either in addition or as an alternative to adopting Color's reporting practices, laboratories also could follow the recommendations from scientists and clinicians at the Transforming Genetic Medicine Initiative (TGMI). In a 2017 blog post, TGMI proposed that only the specific VUSs that scientists were suspicious might be harmful, which they referred to as "variants under surveillance/suspicion," be reported as VUSs.[60] They stated:

> The variants the current system doesn't handle well are the tiny group of VUS that we are already suspicious are pathogenic. They don't quite meet the formal evidence requirements to be called likely pathogenic, but we would willingly stake a decent wager that they will. Much of the over-management of VUS occurs because people think all VUS are variants we are suspicious are pathogenic. But these suspicious VUS form a tiny minority of the variants we include within the VUS category…. A simple fix might be to change VUS to be the Variants Under Suspicion or Variants Under Surveillance. We have ample evidence that people assume this is what a VUS is. If we put the variants that are appropriate to be considered in this way into that category we will have less of a mismatch between what we mean and what others think we mean. (Nazneen Rahman, 2017)

[60] Both Color's approach to reporting and TGMI's re-definition of VUSs would benefit women who are in active cancer treatment. As noted earlier in the study, genetic findings are increasingly being used to determine eligibility for certain drugs and clinical trials. Therefore, access to information about the specific location of VUSs and knowing whether they are under suspicion of being pathogenic can be even more important for cancer patients than for unaffected individuals.

Rather than asking patients to understand the nuances of geneticists' complicated terminology and classifications, the TGMI team argues that genetic scientists and clinicians should alter their language and definitions of VUSs to align with the mass public's understandings of the term.

**Eliminate the Diagnostic Loophole**

Eliminating the diagnostic loophole, which is a failure of women's health policy and practice, is another system-level change that could greatly improve women's experiences navigating US genetic medicine. Annual mammograms and breast MRIs spaced six months apart are the *routine screening procedures* that are recommended for women with BOC mutations. Thus, like annual mammograms for women 40 and older in the general population, annual mammograms and breast MRIs should be coded and treated as screening services and covered by insurance with no cost-sharing. Instead, mammograms and MRIs are currently coded as diagnostic for asymptomatic women with BOC mutations in the United States, which erects sizable financial barriers to breast screening services only for women with higher-than-average risk. As the stories from women in this study revealed, the diagnostic loophole discourages the women who most need breast screening services from seeking them, and, in some cases, encourages them to seek surgery instead. Hence, coding these important breast screening services as diagnostic is both fiscally nonsensical and threatens women's health. But, in addition, the diagnostic loophole discursively contributes to the conflation of genetic risk with disease and the sense among women with BOC mutations that developing breast cancer is inevitable. A symptom is a physical manifestation of illness. Thus, if women's BOC mutations are considered "symptoms" that warrant their screening services to be coded as diagnostic, then either their "disease" is risk or their mutation is being treated as a sign of an impending cancer.

Recent activism around the US Preventative Services Task Force (USPSTF) breast

screening guidelines for women at average risk not only highlights that it is possible to eliminate the diagnostic loophole, but also brings its injustice into sharp focus. The Affordable Care Act requires that insurance companies cover the costs of screening services graded B or better by the USPSTF with no patient cost-sharing (111th Congress, 2010; Johns & Bayer, 2016). In 2016, the USPSTF finalized revisions to their breast screening guidelines that included changing the recommended frequency of mammography screening from annual to biannual and downgrading mammography from a B to a C among women ages 40 - 49 (US Preventative Services Task Force, 2016). The breast screening recommendations were revised after a thorough, multi-year review of the scientific evidence illustrated that, among women at average risk, the optimal screening interval was biannual and prior to age 50 the risks of breast surveillance outweighed the benefits (Gotzsche & Jorgensen, 2013). However, there was swift backlash among women, health care providers, and advocates who expressed concerns about how the revised guidelines would reduce women's insurance-covered access to mammography, which many women had become accustomed to and perceived as "lifesaving" (Pitman et al., 2017; Squiers et al., 2011; Witten & Parker, 2018). In response, Congress mandated that the Department of Health and Human Services (HHS) continue to use the USPSTF's 2002 breast screening guidelines, which issued a B grade to annual mammography for women 40 and older (US Preventative Services Task Force, 2018). This new legislation that required HHS to rely on the 2002 guidelines rather than the more recent 2016 guidelines ensured that women at average risk could continue to affordably access breast screening services.

The public and legislative response to the USPSTF guidelines suggests that widespread support would exist for eliminating the diagnostic loophole if it were brought to light. In contrast to women in the general population, there is robust scientific evidence of the benefits of annual

mammography screenings and breast MRIs in women at higher-than-average risk of breast cancer. Yet current medical coding practices that wrongly classify these critical screening services as diagnostic exempt insurance companies from covering them without cost-sharing. In turn, women with BOC mutations who have high co-pays, co-insurances, or deductibles have to pay hundreds or thousands of dollars every year to receive their necessary routine screenings, leading some of them to skip those services or choose surgery instead.

Throughout this analysis, I have highlighted the fact that while RRM dramatically reduces women's risk of developing breast cancer, it has not been shown to significantly reduce mortality *when compared to the high-risk breast screening protocol.* But mastectomy unquestionably confers a survival benefit to women with BOC mutations when it is compared to doing nothing (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010), which is precisely what women might receive in the current context that financially penalizes them for seeking their recommended screenings. As the USPSTF guidelines saga illustrates, legislators mandated adherence to old breast screening guidelines *not* supported by current medical evidence in response to public outcry over mammograms becoming costlier for women at *average* risk. Hence, surely advocates could spur Congress to issue legislation requiring similar coverage of mammograms and breast MRIs for the women *most* at risk and for whom screenings provide significant medical benefits. Given the considerable resources devoted to breast cancer advocacy in the United States and bipartisan support for breast cancer research and funding, eliminating the diagnostic loophole is both a worthy and feasible goal.

**Provide Risk and Benefit Information on All Choices**

The current structures and architecture of BOC genetic medicine are geared toward supporting women through their "choice" to have mastectomy and reconstruction. But this

project has highlighted the importance of also supporting women who choose not to reconstruct and those who choose surveillance. We need to make sure that the full spectrum of women's options are being supported and that women truly have choices, not just veneers of choice. If women were provided with a full spectrum of options, those options would not only include having insurance-covered access to surgeries, but also choosing *not* to have surgery and still receiving full insurance coverage for their necessary screenings and tests. Similarly, there should be education and social support provided to help guide women through both surveillance and surgery. Eliminating the diagnostic loophole is a critical component of making breast surveillance services more patient-friendly. But in addition, providing online information and sessions at patient advocacy conferences on managing scanxiety and creating support groups or buddy systems at breast imaging centers for high-risk women could also help women navigate the stresses of screening.

In addition, clearly separating mastectomy from reconstruction in initial discussions about RRM, and presenting the risks and benefits of each procedure separately, would be a small discursive shift that could make large strides in providing women with more patient-centered information and care. As I highlighted in Chapter Three, mastectomy is a risk-reducing procedure while reconstruction is a cosmetic procedure, and the two surgeries have very different profiles in terms of what risks the procedures, themselves, pose. Disentangling the risks and benefits of mastectomy and reconstruction and providing women with honest, comprehensive information about each procedure separately is critical.

Separating mastectomy from reconstruction is one component of a much broader shift that is needed in BOC genetic medicine in the United States: ensuring that comprehensive risk and benefit information about the full range of risk-management options is provided to women.

Providing women with honest, comprehensive information and patient-centered care requires neither dismissing their social and emotional needs nor deferring to their desires or choices. For example, clinicians should discuss the potential mental health benefits of mastectomy with women at high genetic risk of breast cancer. Eliminating the constant daily stress of "waiting for cancer to come" and the intense episodic anxiety generated by yearly MRIs and mammograms could improve women's daily quality of life. At the same time, women also deserve to know that mastectomy has not been shown to significantly reduce mortality, and women with MRMs should be clearly informed that the physical health risks of breast surgeries likely outweigh their benefits. Clinicians and counselors have an obligation to provide women with current, evidence-based information about all of their care options; anything short of that means women are not making fully informed choices.

Health care professionals also should critically examine what "informing and educating" patients looks like in practice. For example, it is not enough to say to women about RRSO, "You will go through menopause," because that does not convey the daily impact the procedure could have on their lives. Instead, women should be informed about the specific consequences of medically-induced menopause—which can include sudden and intense hot flashes, vaginal dryness, disruptions in sleep, decreased libido, challenges with cognition, and bone loss— and told how they can mitigate some of those side effects. Similarly, women considering reconstruction deserve to know the high rates of complications and revisions associated with those surgeries and what those complications include, such as necrosis, scar tissue, muscle weakness, numbness, and pain at incision sites. If women were fully informed about the risks and benefits of surgeries prior to their procedures, perhaps they could avoid being blindsided and overwhelmed by the side effects.

Linda, one of the genetic counselors who also ran a support group for women with BOC mutations, shared how she discussed mastectomy with her patients, and what she described was a more patient-centered approach that did not funnel women toward RRM but instead encouraged them to weigh risks and benefits. She explained:

> And so, we talk about some benefits and some limitations. And the other thing that I'd like people to know up front is having a positive result opens up the conversation and it doesn't mean a person has to make immediate decisions, you know? The positive result is not an emergency, it's showing us which direction to go. Because sometimes people come in and think, especially with the Angelina Jolie, "If I have this that means I'm having a mastectomy." And I try and make sure people understand, "No, that's not true. What it means is we get a breast MRI and then we start thinking about, 'Is that something I want to explore, is that something I want to learn more about?' It puts it on the table as a conversation piece. It makes it fair game for doctors to talk to you about it or you to talk to your doctors about. *(Linda, Genetic Counselor)*

Marci also shared a story about an oncologist who provided her with comprehensive information and had a sensitive, patient-centered approach. This doctor did not make assumptions about Marci's preferences, and instead listened to her and asked her questions. However, Marci only found this supportive clinician after first seeing a "very pressuring" oncologist who had encouraged her to hurry up and have RRSO without inquiring about her personal reproductive desires or broader life context. Marci contrasted her new oncologist's approach to the first doctor she had seen: "[The new oncologist] was a lot more open. She started with an, 'Ok, where are you in your life? What do you want? Do you want children? How do you feel?'" If more providers considered the social and emotional context of women's lives *and* provided them with accurate risk information, women would be making fully informed choices, whether those choices were to have or avoid surgery.

**Reckoning with the Risks of Risk**

The findings from this study can also inform the current debate in genetic medicine over whether there should be population screening for BOC mutations. While some experts have expressed caution about adopting population-wide testing (Leib, Olopade, Pal, Rebbeck, & Vadaparampil, 2015; Yurgelun, Hiller, & Garber, 2015), several prominent clinicians and scientists have recently advocated for population genetic screening for BRCA mutations (M. C. King et al., 2014; Leib et al., 2015; Manchanda et al., 2018; Manickam et al., 2018; M. F. Murray, 2018). For example, Mary Clare King, one of the scientists who discovered the BRCA1 gene, has been a vocal advocate for population testing for BRCA mutations in light of robust evidence that demonstrates their risks and the survival benefit conferred by RRSO (M. C. King et al., 2014). More recently, researchers studying whole exome[61] or whole genome sequencing have argued that population screening would be beneficial because such testing catches mutations in people who do not meet current testing guidelines (Manickam et al., 2018; M. F. Murray, 2018).

Clinicians and scientists who support population screening assume that identifying more people at risk is better, but this study suggests that is not always the case. The net effect on women's health might be negative if, as was the case for many women who participated in this project, the effects of medically-induced menopause are systematically under-treated and moderate genetic risk for breast cancer is over-managed with mastectomy and followed with reconstruction. Moreover, there is, in fact, a greater likelihood that the net health effect of genetic risk knowledge would be harmful among people currently deemed at "average" risk. The lifetime

[61] The exome is the coding-portion of the genome.

risk estimates of developing cancer among carriers of BOC mutations are subject to ascertainment bias, as these percentages have largely been derived from studies that included women at the highest end of the risk spectrum, such as women who had already developed breast cancer or those from “cluster” families with extensive cancer histories. Hence, the lifetime risk estimates of BRCA mutation carriers in the general population are likely to be notably lower. Given that it is unclear whether RRM confers a survival advantage even among BRCA1 and BRCA2 mutation carriers in the highest-risk populations, mastectomy is unlikely to reduce mortality among a broader population of women with overall lower risk. In addition, learning they have a mutation might trigger anxiety in women in the general population who previously had no reason to constantly be “waiting for cancer to come.” Hence, both the physical and mental health benefits of genetic risk knowledge and risk-management interventions are likely to be lower among women who do not meet current genetic testing criteria.

The millions of dollars annually that population BRCA testing would require could instead be devoted to research aimed at developing effective screening tests for ovarian and pancreatic cancers and non-surgical approaches to preventing breast and ovarian cancers. As Susan Domchek, the medical oncologist who directs the Basser Center, recently stated in an article on RRM in the *Journal of the American Medical Association* (JAMA), “Women deserve better choices” (S. M. Domchek, 2019, p. E2). Indeed, they do, and significant financial and scientific resources should be devoted to developing those choices. But until those better, non-surgical "treatment" options exist, offering BOC genetic testing to all women over 30 would expose vast numbers of women to the potential harms of mastectomy, reconstruction, and RRSO. Steve, an oncologist, addressed that potential for harm when he discussed his hesitance about population screening:

> [I]f you really want to make this a cost-effective intervention, everybody has to have surgery. And that's a weird world. I don't think that's what people meant when they started thinking about genetics. And if that model gets built in for that, where does that stop? CHEK2? ATM? And so, we need to come to some agreement about what the downstream consequences are going to be. *(Steve, Oncologist)*

I spoke with Steve early in this study, before I interviewed women with MRMs and learned that we are, in fact, *not* stopping at CHEK2 and ATM. But his concerns are even more salient now that whole genome sequencing is making its way into clinical care (Manickam et al., 2018; M. F. Murray, 2018). Cancer genetics is the subspecialty within US genetic medicine that is supported by the greatest volume of data and research. Yet, as this project has highlighted, the expansion of BOC genetic testing from sequencing two genes to sequencing 30 has generated notable uncertainty, confusion, and mismanagement among patients. As we look toward a future in which people's *entire genomes* might be sequenced and genetic risk is explored in areas of health with a weaker knowledge base than cancer, the downstream consequences Steve mentioned years ago will be exponentially magnified. This study has illustrated that producing and managing genetic risk for cancer generates new health risks and consequences. Hence, as the scope of genetic screening tools continues to expand, the primary challenge for BOC genetic medicine will be grappling with and addressing the risks of making risk even more visible.

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# Appendices

## Appendix A: Acronym Glossary

| Acronym | Referent |
|---|---|
| ACMG | American College of Medical Genetics and Genomics |
| AMP | Association for Molecular Pathology |
| ATM | Moderate-risk gene |
| BARD1 | Moderate-risk gene |
| BOC | Breast and ovarian cancer |
| BPM | Bilateral prophylactic mastectomy |
| BRCA1 | High-risk gene |
| BRCA2 | High-risk gene |
| CA-125 | Blood test used in ovarian cancer management and screening |
| CDH1 | High-risk gene |
| CHEK2 | Moderate-risk gene |
| CPM | Contralateral prophylactic mastectomy |
| DNA | Deoxyribonucleic acid |
| EUS | Endoscopic ultrasound |
| GYN/ONC | Gynecologic Oncologist |
| HRT | Hormone replacement therapy |
| IVF | In vitro fertilization |
| MRI | Magnetic resonance imaging |
| MRM | Moderate-risk mutation |
| MUYTH | Low-risk gene |
| NCCN | National Comprehensive Cancer Network |
| NGS | Next generation sequencing |
| OB/GYN | Obstetrician/Gynecologist |
| PALB2 | Moderate-risk gene |
| PGD | Preimplantation genetic diagnosis |
| RRM | Risk-reducing mastectomy |
| RRP | Risk-reducing pancreatectomy |
| RRSO | Risk-reducing salpingo-oophorectomy |
| SDHA | Low-risk gene |
| STS | Science and technology studies |
| USPSTF | US Preventative Services Task Force |
| VUS | Variant of uncertain significance |

## Appendix B: Research Methods and Approach

This research project, originally envisioned as a study of young, healthy carriers of BRCA mutations, began in the spring of 2012, approximately one year before Jolie's op-ed, the *AMP v. Myriad* decision, and the shift to panel testing. However, during preliminary fieldwork at scientific cancer genetics meetings in 2013, and through conversations with key informants I met at those conferences, it became clear that BOC genetic science and medicine were undergoing major transformations, and I turned my gaze toward exploring the consequences of those important shifts. Between the fall of 2013 and spring of 2017, I conducted over three years of qualitative research that included participant observation at both professional and patient-centered cancer genetics conferences; in-depth interviews with health professionals working in US BOC genetic medicine and women with BOC variants and mutations; and document analysis of laboratory reports, industry and advocacy group educational and promotional materials, and scientific and clinical guidelines. The data I collected through participant observation, document analysis, and interviews informed one another; combining methods enabled me to test and refine my working hypotheses on how BOC genetic risk is produced and managed in the United States in the era of panel testing. Because qualitative research is both iterative and dialectical, data collection and analysis were conducted concurrently, with interviews and field notes being transcribed and coded soon after they were completed and preliminary findings informing subsequent data collection.

### *Participant Observation*

Between the fall of 2013 and spring of 2017, I engaged in participant observation at over 40 different professional and patient-centered events. These included seven national scientific conferences for genetics professionals, four regional or national advocacy conferences for people

with BOC mutations, 21 webinars for scientists and providers working in cancer genetics, and nine webinars or symposia on cancer genetic risk aimed at the lay public. I also regularly attended monthly research seminars focused on cancer genetics at a major academic medical center between 2014 and 2016. My preliminary fieldwork began in the fall of 2013, just months after the *Myriad Genetics v. AMP* ruling and as multi-gene panels were being adopted throughout US BOC genetic medicine. This timing provided unique insights into the social, scientific, and practice concerns about panel tests and variant classification at a key moment of transition in cancer and clinical genetics. The first national professional meeting I attended in the fall of 2013 included a full-day pre-conference session focused on panel tests, and in subsequent years there were both breakout and plenary sessions at scientific conferences that centered on the issue. These sessions highlighted ongoing debates and disagreements among experts about the benefits and limitations of multi-gene panel tests and variant classification and reporting.

Initially, data from fieldwork helped me to develop my research questions and working lists of themes to explore and to design semi-structured guides for in-depth interviews. In addition, at conferences and events, I built relationships with key staff at cancer genetics clinics and in advocacy groups, and I had numerous conversations and interactions with women with mutations. These connections were helpful in recruiting women with mutations or variants for interviews and meeting other relevant experts. Once I began conducting semi-structured interviews, participant observation data were used to triangulate and refine the findings that were emerging in the interviews. During conference sessions, webinars, and meetings, I took photographs and detailed field notes on the content of the presentations and the tools and language experts used to communicate genetic risk information. In the exhibit areas and other less structured public spaces, I observed interactions among attendees, which I recorded in

ethnographic "jottings" (Emerson, Fretz, & Shaw, 1995) and expanded into detailed field notes within 24 hours. I also gathered brochures and informational materials for document analysis from genetics laboratories and patient advocacy groups that exhibited at meetings. Throughout my fieldwork, I paid special attention to how risk was enacted and made visible, questions that were asked and the answers provided, issues or concerns that arose in discussions, tensions between patients' and professionals' priorities, how women with mutations and health care providers were responding to new developments in the field, and the processes of active problem solving that occurred in interactions.

Observing, firsthand, the actual interactions among and between scientists, health professionals, and women with mutations at conferences provided insight into the social and structural contexts of genetic medicine, the ways in which information was communicated (as opposed to how individuals recalled it being communicated), the immediate feelings and concerns of mutation carriers, and any competing logics and disputes between patients and providers. The events for scientists and health professionals shed light on how experts communicated with one another about BOC genetic risk, clinical and scientific developments in the field, and the topics and issues of importance to genetics professionals. The patient-centered and public seminars and conferences were rich sources of data on the issues of importance to women with mutations, whether and how mutation carriers were forming biosocial identities and communities, and the ways in which experts communicate and translate complex genetic risk information to people with mutations and lay publics.

***Document Analysis***

Genetics laboratories and scientists are integral to the production and visibility of BOC genetic risk. They devote significant resources to researching links between genetic mutations

and cancer, develop the classification criteria for genetic variants, design computer models for evaluating individuals' cancer risks, produce informational materials for both patients and providers, and generate reports for genetic counselors and clinicians that identify and summarize patients' risks. During fieldwork, I gathered and systematically analyzed publications, brochures, webpages, and reports produced by the five major US laboratories that perform most BOC genetic testing in the United States: Ambry Genetics, Color Genomics, GeneDx, Invitae, and Myriad Genetics. Similarly, cancer advocacy groups, genetics professional organizations, and government agencies such as the Centers for Disease Control and Prevention (CDC) and the National Cancer Institute (NCI) create risk assessment tools and produce educational materials for the public. In addition, the positions and guidelines issued by these groups influence health policy, allocation of research funds, research priorities, and the attitudes and actions of providers and women with mutations. Hence, I also examined materials published by key advocacy groups for BOC mutation carriers, professional societies involved in BOC genetic medicine, and federal institutes or agencies that provide funding, resources, information, and data on cancer or genetics. For all documents and materials, I explored what information they highlighted, what they omitted, the images and language they used to convey risk, the audiences they targeted, the references they drew on, and any tensions in their narratives in order to uncover their encoded themes and values. I then triangulated those findings with data collected in interviews and participant observation.

***Interviews***

Concurrent with fieldwork and document analysis, I conducted a total of 85 in-depth, semi-structured interviews: 75 with women with BOC mutations or variants and 10 with health professionals working in cancer genetics. One-on-one interviews are especially useful for

uncovering the meaning and significance of events or situations for participants, providing data not only on what happened, but also on how people make sense of their experiences (Creswell, 2007; Kvale & Brinkman, 2009; Rubin & Rubin, 2005; Warren & Karner, 2010). Thus, these lengthy conversations with women with BOC mutations or variants provided opportunities to elicit rich, detailed narratives from them about their experiences navigating US BOC genetic medicine; their beliefs, understandings, and feelings about BOC genetic risk; and their risk management decisions. Throughout the interviews with women, I paid careful attention to the language, logics, and evidence that they used to explain their experiences and choices and to similarities and differences between women with high- and moderate-risk mutations. The interviews with genetic counselors and clinicians both provided important insights into the processes involved in producing genetic risk and making it visible and facilitated an analysis of agreements and disjunctures between professionals' and patients' descriptions of the practices of US BOC genetic medicine.

Typical interviews lasted approximately one hour and 15 minutes, but they ranged from as short as 35 minutes to as long as two hours and 15 minutes. All interviews were conducted via telephone or computer video-chat applications (e.g., Skype, FaceTime, or Google Hangout) and were digitally audiorecorded in order to capture participants' exact responses. I also made ethnographic jottings (Emerson et al., 1995) during interviews about occurrences or visual details not captured on audio, including body language and nonverbal exchanges, and then expanded those into detailed field notes and memos immediately after the interviews concluded. In accordance with the procedures approved by Columbia University's Institutional Review Board (IRB), participants were emailed a combined study information sheet and HIPAA form in advance of their interview, and then verbal consent to both participate in the interview and to

audio record the discussion were obtained at the beginning of each conversation. I continued conducting interviews with genetics health professionals and women with BOC mutations or variants until my findings reached saturation in each group (J. A. Maxwell, 2005; Warren & Karner, 2010).

Utilizing a modified, constructivist approach to grounded theory (Charmaz, 2006; Corbin & Strauss, 2008), I developed semi-structured guides for the interviews that drew on topics and themes I had identified through preliminary fieldwork and existing literature on BOC genetic medicine and risk. For women with mutations or variants, these broad topics included their experiences with genetic testing, understandings of genetic risk, feelings about being at risk, decisions about risk management, interactions with providers and the health care system, and involvement with advocacy and support groups. I also incorporated questions about if and how being at BOC genetic risk affected their identities, feelings about their bodies, and their social and familial relationships. For experts, the initial topics and themes I explored in interviews included the tools they used to identify risk and explain risk estimates and classifications; how they communicated about VUSs; the risk management guidance they provided to women with high- and moderate-penetrance mutations; their feelings about and responses to recent developments in the field, including the use of multi-gene panels; their interactions with other genetics and medical professionals; and their perspectives on future directions or challenges for the field. As is common practice in qualitative research, I used the data I gathered in initial interviews to refine and modify the questions on the interview guides so that they focused on the themes and associations that were most strongly emerging in the data (Kvale & Brinkman, 2009; Rubin & Rubin, 2005; Warren & Karner, 2010). For example, I modified the guides for women with mutations to include additional questions on insurance coverage and the costs of care, the

decision to have breast reconstruction or stay flat and not reconstruct, and preparation for and knowledge about the side effects of oophorectomy because these topics surfaced as important themes in early interviews.

***Recruitment and Sampling***

The ten health professionals with whom I conducted in-depth interviews—eight genetic counselors and two physicians—were recruited during fieldwork at scientific and professional meetings and through relationships I built at those meetings with key informants. The primary way women with mutations or VUSs were recruited into the study was through cancer genetic counselors. The genetic counselors I partnered with were located throughout the United States, as I met them either at national conferences or in the online cancer special interest group (SIG) of one of the national professional associations for genetic counselors.[62] I joined the cancer SIG based on the recommendation of one of the genetic counselors I met early in fieldwork who became a key informant. She suggested that I share information about the study in their SIG's online listserv when recruitment of women with moderate-risk mutations (MRMs) and VUSs was slow. Genetic counselors who were interested in the project secured permission from their institutions to share the study's IRB-approved recruitment flyers in the patient information packets they distributed to their clients. These flyers provided brief information about the purpose of the study, the eligibility criteria, and my contact information where interested patients could follow up.

In addition, I recruited women through a modified snowball approach to sampling. At the

[62] This organization has a membership category for professionals who are not genetic counselors but do work related to genetic counseling. In all communications in this group, I was transparent about being a researcher studying the consequences of panel testing and the production and management of BOC genetic risk.

end of each interview, I asked women who had participated if they would be willing to share information about the study with other women they knew with BOC mutations or VUSs. I then shared the IRB-approved flyers with those who agreed. Many women I interviewed belonged to private online social media groups for individuals with similar mutations or for women making breast or ovarian surgical decisions, and some offered to share the study flyers in those groups. Thus, the snowball approach was particularly effective in finding eligible women in subgroups that were less prevalent within the population of women at BOC genetic risk but had formed online support groups, such as women with MRMs or VUSs, women who chose to stay flat after risk-reducing surgery, and women who opted for surveillance.

Finally, I recruited patient participants through national education and advocacy groups that serve people with BOC mutations. One group maintains an online database of active research projects that people with mutations can access to find studies in which they would like to participate. That group added this study to their database, posted the IRB-approved flyers for the project on social media, and added a link to the study flyer in their monthly email update. Another advocacy group allowed me to put recruitment flyers on information tables at their annual national meetings. That same group maintains online message boards for individuals at genetic risk for cancers and their allies, and I obtained permission from them to post links to the study flyers in appropriate threads, including one for research projects, one for people with MRMs, one for younger women with mutations, and one for individuals with VUSs. Summary characteristics for the 75 women who participated in the study are provided in Tables 7 and 8: Table 7 summarizes their genetic information and surgical decisions, while Table 8 provides their demographic characteristics and cancer information.

| Genetic Information and Surgical Decisions | N | % |
|---|---|---|
| **Risk Penetrance Group** | | |
| Variant of Uncertain Significance (VUS) or Conflicting Interpretation (CI) | 4 | 5.3% |
| High-Risk Mutation (HRM) | 33 | 44.0% |
| Moderate-Risk Mutation (MRM) | 38 | 50.7% |
| Total | 75 | 100.0% |
| **Mutation Gene** | | |
| BRCA1 | 17 | 23.9% |
| BRCA2 | 16 | 22.5% |
| CHEK2 | 30 | 42.3% |
| PALB2 | 4 | 5.6% |
| ATM | 4 | 5.6% |
| Total | 71 | 100.0% |
| **Any VUS** | | |
| Yes | 14 | 18.7% |
| No | 61 | 81.3% |
| Total | 75 | 100.0% |
| **Breast Surgery** | | |
| Had/Having | 52 | 69.3% |
| Declined/Undecided | 22 | 29.3% |
| Not Offered | 1 | 1.3% |
| Total | 75 | 100.0% |
| **Breast Reconstruction** | | |
| Had/Having | 43 | 82.7% |
| Declined/Undecided | 9 | 17.3% |
| Total | 52 | 100.0% |
| **Ovarian Surgery** | | |
| Had/Having | 36 | 48.0% |
| Declined/Undecided | 9 | 12.0% |
| Not Offered | 30 | 40.0% |
| Total | 75 | 100.0% |

**Table 7: Participants' Summary Genetic Information and Surgical Decisions**

| Demographic Characteristics and Cancer Information | N | % |
|---|---|---|
| **Age** | | |
| 20 - 29 | 6 | 8.0% |
| 30 - 39 | 27 | 36.0% |
| 40 - 49 | 19 | 25.3% |
| 50 - 59 | 11 | 14.7% |
| 60 - 64 | 10 | 13.3% |
| 70 - 79 | 2 | 2.7% |
| Total | 75 | 100.0% |
| **Race/Ethnicity** | | |
| White | 69 | 92.0% |
| Other | 6 | 8.0% |
| Total | 75 | 100.0% |
| **Education (Highest Level Completed)** | | |
| High School | 10 | 13.5% |
| College | 32 | 43.2% |
| Graduate School | 32 | 43.2% |
| Total | 74 | 100.0% |
| **Children** | | |
| Yes | 56 | 74.7% |
| No | 19 | 25.3% |
| Total | 75 | 100.0% |
| **Cancers** | | |
| Unaffected | 42 | 56.0% |
| Single Cancer | 27 | 36.0% |
| Multiple Cancers | 6 | 8.0% |
| Total | 75 | 100.0% |
| **Cancer Type** | | |
| Breast | 27 | 81.8% |
| Thyroid | 4 | 12.1% |
| Ovarian | 2 | 6.1% |
| Endometrial | 2 | 6.1% |
| Kidney | 2 | 6.1% |
| Colon | 1 | 3.0% |
| Skin | 1 | 3.0% |

**Table 8: Participants' Summary Demographic Characteristics and Cancer Information**

The initial recruitment plan was designed using systematic ethnographic sampling (Hirsch et al., 2009), which is a purposive approach that is guided by variables previous research

has found to be relevant to the experiences being studied. Like all purposive or theoretical sampling approaches for qualitative research, systematic ethnographic sampling is not intended to ensure statistical representativeness or to capture the experiences of individuals in any one particular cell in the sampling distribution (M. N. Marshall, 1996). Rather, this approach helps researchers explore similarities and differences along broad social axes of interest. The initial sampling frame for the study was structured along three key axes of interest: race/ethnicity, socioeconomic status/education, and genetic variant classification (i.e., high risk, moderate risk, or of uncertain significance). I also planned to limit participation among women to those who were age 45 or younger and unaffected by cancer. Younger women with BOC mutations face unique challenges because the risk-reducing surgeries that are recommended for women at increased risk of ovarian cancer limit reproductive functioning and cause medically-induced menopause (Hamilton et al., 2009; Werner-Lin, Hoskins, Doyle, & Greene, 2012). Similarly, the risk-benefit ratios of surgical risk management options for women diagnosed with cancer, who usually already require some type of surgery, are different from those for healthy individuals (Dagan & Goldblatt, 2009).

There are several groups of individuals who have been underrepresented in BOC research: men, women of color, younger women, unaffected women, and economically disadvantaged women. Their underrepresentation is, in part, linked to the uneven demographic distribution of clinical genetic testing clients in the United States, who have been disproportionately white, female, highly-educated, post-menopausal, and afflicted with cancer (Armstrong et al., 2015; Suther & Kiros, 2009; Underhill et al., 2016). However, science studies scholars have illustrated how the skewed demographics of patients in genetic medicine are, themselves a reflection of the field's early engagement with Ashkenazi Jewish and other

European populations (Mozersky & Joseph, 2010; Wailoo & Pemberton, 2006). Scientists created databases of genetic samples from these populations that were used for early genetic research, which concentrated knowledge on variants more commonly seen among Ashkenazi Jews and other people of European ancestry. Greater knowledge about cancer genetic risk in those populations has sedimented racialized ideas about who is and is not at risk and, in turn, influences who tends to use genetic testing services (Montoya, 2011; Mozersky & Joseph, 2010; Wailoo & Pemberton, 2006). One of the outcomes of this history is that the population of women who gets tested for BOC mutations is much whiter than the population of women who develops breast cancer (Armstrong et al., 2015; National Cancer Institute, 2018d; Suther & Kiros, 2009; Underhill et al., 2016).

I originally intended to target recruitment among women in some of these underrepresented groups. I was particularly interested in interviewing women of color because both VUSs and certain BOC mutations have a higher prevalence among US women of color than among non-Hispanic white women (A. W. Kurian, 2010; Pal et al., 2014) and because several studies have shown that race and ethnicity affect perceptions and practices related to managing risk (Callon & Rabeharisoa, 2004; Cragun et al., 2017; A. W. Kurian, 2010; Shaw, 2011). However, this dissertation is focused on women who had already had BOC genetic testing and either received a positive or uncertain result. Prior to initiating the project, I had not fully appreciated how choosing that population as my sampling frame meant that it had already passed through multiple filters of racialization and would limit my ability to recruit women of color. Early in the project, I actively attempted to bolster recruitment among women of color by partnering with genetic counselors and local chapters of advocacy groups based in urban areas with greater patient or member racial/ethnic diversity and reaching out to cancer support or

advocacy groups that specifically serve women of color. In the future, to avoid producing additional research on genetic risk among white women, I would consider recruiting from among cancer patients at baseline because black women develop breast cancer at similar rates to white women (National Cancer Institute, 2018d).

The rapid and widespread adoption of panel tests, which have been identifying more women with VUSs and MRMs, coincided with my preliminary research, and it quickly became apparent that the most important axis of difference in the sample was the penetrance classification of people's genetic variants. Multi-gene panels were not only placing more people into a category of *unknown* risk, but also were generating new tiers of risk among individuals who tested positive for mutations, and these shifts in the zones of risk were transforming practices in the field. Yet because MRMs have lower population prevalence than BRCA mutations (Couch et al., 2015; PDQ® Cancer Genetics Editorial Board, 2019) and because, as I will highlight in Chapter One, genetics experts actively attempt to de-medicalize VUSs, recruiting women in these categories also proved challenging.

The restrictions among women by age and cancer status compounded the difficulties of recruiting women with MRMs and VUSs; however, I later discovered that these eligibility criteria were less relevant than I initially theorized, particularly in these populations. According to current research and clinical guidelines, women with MRMs and VUSs do not meet evidence-based eligibility criteria for surgical approaches to ovarian cancer risk management, such as risk-reducing hysterectomy (RRH) or risk-reducing salpingo-oophorectomy (RRSO). I had limited participation in the study to women age 45 or younger because of the clinical impact of those surgeries, but that restriction was not relevant among women with BOC MRMs or VUSs. Furthermore, a majority of breast cancers are diagnosed in Stage 0 or Stage 1, when typically,

patients are candidates for lumpectomy. Thus, while there are still differences in the decision-making processes for women who are already affected by breast cancer and women who are not, women in both groups who opt for double mastectomies are electing to undergo several additional surgical procedures that, based on current evidence, do not significantly improve their chances of survival (S. M. Domchek et al., 2010; A. W. Kurian et al., 2010; Li et al., 2016; Portschy, Kuntz, & Tuttle, 2014). Moreover, no matter whether women's RRM procedures were BPM or CPM, once they had breast surgery, they faced the same decisions about breast reconstruction and endured the same complications and side effects from reconstruction procedures, which also emerged early in the study as important themes. Thankfully, with the partnership of cancer genetic counselors from the Cancer SIG and after modifying the eligibility criteria to allow women with MRMs and VUSs to participate regardless of age or cancer status, my efforts at targeted recruitment in these groups were successful.

***Data Analysis***

Because qualitative research is both iterative and dialectical, I conducted ethnographic data collection and data analysis concurrently in this study so that I could I could reformulate study and interview questions and modify the samples and approaches in response to emerging themes (Charmaz, 2006; J. A. Maxwell, 2005; Warren & Karner, 2010; Wolcott, 2009). Interviews were transcribed as soon as possible after completion, and those transcripts and my field notes were coded on an ongoing basis throughout the project. I primarily drew on a constructivist grounded theory approach to coding (Charmaz, 2006; Corbin & Strauss, 2008). In the initial phases of analysis, I developed a priori codes based on the existing cancer genetics literature, my preliminary fieldwork, and the study's main research questions (Miles & Huberman, 1994). I then allowed patterns and hypotheses to emerge inductively from the data

and checked them against new data and findings.

In looking for themes and patterns, I primarily used the constant-comparative method, which involves triangulating and exploring the similarities and differences between data from the interviews, participant observation, and document analyses (Charmaz, 2006). In combination with the a priori codes I had established, I began with open coding, which requires going through the data line by line, labeling the actions and processes that are apparent, and looking for emergent themes. I searched for data that confirmed and challenged my working hypotheses, paying particular attention to any strong language, repetitions, transitions, gaps, and unusual or extreme cases (Miles & Huberman, 1994). I then moved to focused coding, in which I organized, refined, and further developed the initial codes by comparing them with new data. I searched for relationships between codes, paying particular attention to similarities or variations along theoretical and conceptual axes of interest. Throughout data analysis, I wrote memos in which I defined codes, explored themes and conceptual relationships, and reflected on the research process (Emerson et al., 1995). I used MaxQDA 18.1, robust qualitative data management software, to transcribe interviews, organize and store documents and memos, assign codes to text segments, trace associations between codes and themes, and explore similarities and differences in the data.

***IRB, HIPAA, and Privacy***

This research project followed the human subjects guidelines of Columbia University's Morningside Institutional Review Board (IRB), including all procedures for obtaining informed consent, protecting the anonymity of study participants, securing data, and compliance with HIPAA. Careful measures were taken to ensure that the privacy and confidentiality of participants were protected and that all data remained confidential. Any handwritten field notes

were scanned and then shredded, and all audio recordings, interview transcripts, and field notes were stored on my encrypted and password-protected laptop in password-protected folders. Once the audio-recordings were transcribed, they were moved to a password protected and encrypted external hard drive. All identifying information was removed from transcripts, field notes, and memos, and any data used in publications and presentations has also been de-identified. Each participant was assigned a unique ID code and pseudonym, and only those were used to label audio-files and transcripts. A master list matching these codes and pseudonyms to participant names and contact information were stored in a password protected file on a password protected and encrypted external drive to which only I had access. I altered any quotations or descriptions used in the preceding chapters that contained potential identifying information, such as unique elements of their life stories, to protect the confidentiality and privacy of participants.