

Perspectives and Experiences of Individuals Undergoing Predictive Testing for Hereditary Breast and Ovarian Cancer (HBOC) Syndrome in the Western Cape, South Africa.

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ABSTRACT

Breast cancer is the most common malignancy affecting females globally. Hereditary breast and ovarian cancer (HBOC) syndrome is caused by pathogenic variants in *BRCA1* and *BRCA2* and is seen in approximately 50% of families with a strong history of breast and ovarian cancers. Predictive testing (PT) is offered to unaffected individuals with a positive family history of HBOC, with an already identified *BRCA1* or *BRCA2* mutation in an affected family member. There is an overwhelming amount of research that has focused on the after-effects of diagnostic genetic testing for HBOC but there has been little investigation into how individuals experience the actual PT process. The present study therefore aimed to investigate individuals' decisions for undergoing and their experiences of PT for HBOC in a local context, by focusing on at-risk South African individuals residing in the Western Cape Province.

Sixteen participants were recruited retrospectively from the breast cancer and/or clinical genetics clinics at Groote Schuur Hospital, Tygerberg Hospital and private genetic counselling practices in Cape Town. Semi-structured interviews were conducted, and the interview transcripts were analysed using the framework approach for qualitative data analysis. Using this approach, five themes were identified relating to the perspectives and experiences of individuals undergoing PT for HBOC, in selected settings in the Western Cape.

While some participants felt that their decision to pursue PT was influenced by their family history of cancer and the associated cancer-related distress, others felt that their decision was made out of a sense of duty to their families or in solidarity with those that were affected or received a positive test result. Overall, the participants felt that the pre-test counselling was beneficial in allowing for an improved understanding of HBOC, however not all participants felt that the pre-test counselling prepared them for receiving their results. Receiving a negative test result was often accompanied by feelings of guilt and did not exempt participants from the fear of developing cancer. Some of the concerns raised by participants that received a positive test result were centred around prophylactic intervention and its effect on body image. Overall, participants felt empowered by their mutation status and felt that they were better able to manage their risk. The need for additional support, both practical and emotional support, was particularly evident amongst mutation-carriers. The findings of this study provide valuable insight into the perspectives and experiences of this population, which could potentially impact the services that are provided to individuals undergoing PT for HBOC in similar settings.

“... do all to the glory of God”

- 1 Corinthians 10:31

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“For I know the plans I have for you,” declares the Lord. “Plans to prosper you and not to harm you. Plans to give you hope and a future.” – Jeremiah 29:11

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LIST OF TERMS AND ABBREVIATIONS

BOADICEA – Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm

BRCA1 – Breast cancer gene 1

BRCA2 – Breast cancer gene 2

BSO – Bilateral salpingo-oophorectomy

GSH – Groote Schuur Hospital

HBOC – Hereditary breast and ovarian cancer

HD – Huntington disease

PT – Predictive testing

PVT – Private genetic counselling practice

RRBM – Risk-reducing bilateral mastectomy

SA – South Africa

TBH – Tygerberg Hospital

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CHAPTER 1: INTRODUCTION

1.1 CHAPTER INTRODUCTION

The first chapter outlines (1) breast cancer epidemiology, (2) the genetic aetiology of hereditary breast and ovarian cancer, (3) cancer risk associated with *BRCA1* and *BRCA2*, (4) *BRCA1* and *BRCA2* testing, and (5) management and surveillance options.

Literature was searched for using the Google Scholar and PubMed databases, using the following search terms: *breast cancer, ovarian cancer, hereditary, BRCA1, BRCA2, genetics, genetic counselling, family, predictive testing*, as well as permutations of these terms. As this is not a systematic literature review, the most informative literature was selected to present the background and rationale for this study.

1.2 EPIDEMIOLOGY OF BREAST CANCER

The global burden of non-communicable diseases continues to rise, with some of the contributing factors being increased lifespan, lifestyle changes and prolonged exposure to risk factors. Cancer is identified globally as one of the most important diseases. From an epidemiologic standpoint, cancer is particularly complex due to it being a multifactorial condition (Ghoncheh, Pournamdar & Salehiniya, 2016). It is a complex and heterogeneous disease with respect to the cellular origin, histology, disease progression, metastatic potential, mutations, response to therapeutics and overall clinical outcome (Cetin & Topcul, 2014). There are several risk factors that are recognised as being associated with the development of breast cancer. These include hormonal risk factors such as oestrogen and progesterone exposure, reproductive and obesity risk factors, as well as the role that the inheritance of highly penetrant high-risk genes play, amongst others (Cetin & Topcul, 2014).

Breast cancer is the most common malignancy affecting women globally (Seymour, *et al.* 2016). The cumulative incidence of breast cancer in developed countries suggests that approximately 1 in 10 females will develop breast cancer by the age of 70 years, and that there is a lifetime risk of approximately 10-12% (Schoeman, *et al.* 2013; Lalloo & Evans, 2012). Although the incidence of breast cancer is greater in developed countries, breast cancer-related death is higher in developing countries (Ghoncheh, Pournamdar & Salehiniya, 2016).

As in developed countries, breast cancer is the most prevalent cancer affecting females in South Africa (SA) (Schlebusch, *et al.* 2010). The incidence of breast and ovarian cancer in SA varies by time, location and ethnic group; however, there is supporting evidence to suggest that the incidence of breast cancer has increased over time (Hoffman, *et al.* 2000; NCR, 2011). Breast cancer accounts for approximately 22% of all cancers diagnosed nationally (NCR, 2012) and is associated with high mortality rates in South African women, believed in-part to be

due to delayed diagnosis (Murray, 2003; Walker, *et al.* 2004). Recent local estimates indicate that the lifetime risks of developing breast and ovarian cancer for women in SA are 1 in 26 and 1 in 391, respectively.

1.3 GENETICS OF HBOC

Approximately 5-10% of breast cancer has a strongly heritable component (Claus, Risch & Thompson, 1991; Newman, *et al.* 1988). Of all cancers, 4-5% are due to the transmission of Mendelian genes that are highly penetrant, in an autosomal dominant inheritance pattern (Fackenthal & Olopade, 2007; Lalloo & Evans, 2012). Two high penetrance genes, Breast Cancer Gene 1 (*BRCA1*) and Breast Cancer Gene 2 (*BRCA2*) are most frequently (~50% of inherited breast cancers) identified as monogenic causes for hereditary breast and/or ovarian cancers. However pathogenic variants in these genes are responsible for a small proportion of breast cancer cases, approximately 2%, and ovarian cancer cases overall (Lalloo & Evans, 2012). Despite being the minority, these cases are of particular importance. Individuals who carry a pathogenic variant in *BRCA1* or *BRCA2* are often described as having hereditary breast and ovarian cancer (HBOC) syndrome (Schoeman, *et al.* 2013; Seymour, *et al.* 2016).

As these names suggest, *BRCA1* and *BRCA2* mutations, in addition to breast cancer, confer an increased risk for ovarian cancer in females. Pathogenic variants in these genes are known to increase the risk of developing breast and ovarian cancer in women and breast and prostate cancer in men (Lalloo & Evans, 2012), amongst others detailed in section 1.4. The identification of the *BRCA1* gene in 1990 and the *BRCA2* gene in 1995, and the subsequent availability of predictive testing (PT), has afforded unaffected individuals with a family history of HBOC the opportunity to determine if they carry the mutation (Claes, *et al.* 2003). Consequently, inherited forms of breast and ovarian cancer have both a clinical and public health significance.

In some countries, such as SA, founder mutations have been identified in certain population groups and account for a significant proportion of *BRCA1* and *BRCA2* mutations locally (Seymour, *et al.* 2016). To date, three founder mutations have been identified in the Afrikaner population group, three in the Ashkenazi Jewish population group, one in the mixed ancestry and one in the Xhosa population groups (Schoeman, *et al.* 2013; Seymour, *et al.* 2016). Testing for founder mutations is based on specific institutional criteria and varies from one institution to the next.

Other than age, a positive family history is the strongest known factor associated with an increased risk for developing breast cancer. As the number of relatives affected with breast cancer increases, an individual's risk of developing breast cancer also increases. A woman's risk is approximately doubled by having one affected first-degree relative (Schoeman, *et al.* 2013). A detailed family history can be used to evaluate an individual's risk of

developing breast cancer together with the chance that there could be a hereditary component to the family's risk, thereby highlighting the importance of obtaining a comprehensive family history (Lalloo & Evans, 2012). Factors suggesting there is a familial susceptibility gene include a large number of affected individuals with breast, ovarian, or prostate cancer on one side of the family, a young average age at which these cancers were diagnosed, more than one primary cancer in one individual with an early age of onset, and the association of breast cancer with other related cancers in a family. These include early onset prostate cancer in male relatives and ovarian cancer in female relatives (Lalloo & Evans, 2012). The level of risk assessed can then be used to determine the subsequent testing and management options that are available to the individual and other at-risk family members (Lalloo & Evans, 2012).

Women at risk of developing breast cancer often require advice about their risk and how to be proactive when faced with this risk (Lalloo & Evans, 2012). This can be challenging when there is a limited amount of family history information available. Some studies have identified that the concept of cancer may be unfamiliar to some patients, therefore the communication between family members regarding the cause of death of an affected family member may not necessitate the knowledge of the type of cancer (De Vos, *et al.* 1999; Schoeman, *et al.* 2013; Walker, *et al.* 2004).

1.4 CANCER RISK ASSOCIATED WITH *BRCA1* AND *BRCA2*

BRCA1 and *BRCA2* are large genes that are expressed in several tissues, including breast and ovarian tissue. The proteins that are encoded by both *BRCA1* and *BRCA2* appear to have similar functions, justifying why mutations in these genes result in a similar and specific hereditary predisposition to breast and ovarian malignancies (Godet & Gilkes, 2017). Both genes function as tumour suppressor genes and are believed to be involved in transcription regulation and DNA repair. *BRCA1* also functions in regulating cell cycle progression and checkpoint control (Schlebusch, *et al.* 2010). Both genes are functionally recessive, meaning that both copies of the allele must be mutated in the cell for breast, ovarian or other associated cancers to develop (Godet & Gilkes, 2017).

Cells that possess germline mutations in *BRCA1* or *BRCA2* are vulnerable to DNA damage, which is a crucial feature in the progression of cancer formation (Kurian, 2010). Pathogenic variants in *BRCA1* and *BRCA2* each account for approximately 10% of hereditary forms of breast cancer. A summary of the cancer risks associated with germline pathogenic variants in *BRCA1* and *BRCA2* are detailed in table 1 below (Lee, Higgins & Qureshi, 2015; Petrucelli, Daly & Pal, 2016).

Table 1: Summary of lifetime cancer risks associated with pathogenic variants in BRCA1 and BRCA2

Cancer type	<i>BRCA1</i>	<i>BRCA2</i>
Female breast cancer	46-87%	38-84%

Ovarian cancer	39-63%	16.5-27%
Second primary breast cancer	83% by age 70	62% by age 70
Male breast cancer	~1%	5-10%
Prostate cancer	-	14-20%
Pancreas, biliary tree, stomach or melanoma		<1 in 20

In cases where there are multiple family members affected, the risk estimates at the upper end of the ranges displayed in table 1 are likely to be appropriate as a result of the co-inheritance of possible modifier genes and shared environmental exposures. There is also an increased risk of contralateral breast cancer in affected carriers, the highest being with the age of diagnosis being less than 40 years. This risk then decreases as the age of first diagnosis increases (Firth & Hurst, 2017). Ovarian cancer risks in *BRCA2* carriers are low before the age of 50 years. Importantly, breast cancer displays incomplete penetrance amongst *BRCA1* and *BRCA2* mutation carriers. Other factors such as age and gender, as well as nongenetic factors play an important role in developing breast cancer (Godet & Gilkes, 2017).

1.5 *BRCA1* AND *BRCA2* TESTING

According to Tygerberg Hospital (TBH) criteria, individuals who have been diagnosed with breast or ovarian cancer together with at least one first-degree relative with breast cancer at an age younger than 50 years or ovarian cancer at any age, or male breast cancer in a relative meet the family history criteria required to undergo full *BRCA1* and *BRCA2* screening in order to determine the cause of their cancer (Schoeman, *et al.* 2013). Testing for local founder mutations may be offered following appropriate risk analysis (Schoeman, *et al.* 2013). However, these guidelines may differ according to setting and across different clinical institutions. The criteria that is used to assess whether an individual is eligible to pursue full *BRCA1* and *BRCA2* screening or founder mutation testing also varies across different clinical institutions. These criteria are determined based on the availability of funding and the likelihood ($\geq 10\%$) of identifying a pathogenic variant.

While some settings base this decision on family history and the relation of the proband to an affected family member, others may use scoring systems such as the Manchester Scoring System or the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) risk assessment model to determine the likelihood of identifying a *BRCA1* or *BRCA2* mutation in the proband (Evans, *et al.* 2017; Lim, Borje & Allen, 2017). At Groote Schuur Hospital (GSH), individuals with a Manchester score of 15 or greater meet criteria to undergo full *BRCA1* and *BRCA2* screening. Founder mutation testing may be offered to individuals that come from a founder population but do not meet criteria to undergo full gene sequencing.

As a first-line testing option, individuals are offered testing for population-specific founder mutations, if appropriate. Additional molecular testing, including full *BRCA1* and *BRCA2* sequencing and analysis of large rearrangements, may be offered to individuals with a negative founder mutation result, should the family and clinical history warrant it (Seymour, *et al.* 2016). As genetic testing becomes routinely incorporated into the management of women diagnosed with breast and/or ovarian cancer and individuals who are at an increased risk for these diseases, it is important to take into account that mutations in other cancer susceptibility genes may contribute to an increased breast cancer risk. Therefore, there may be mutation carriers with less common high- and moderate-penetrance cancer susceptibility genes. Less is known about the management of these individuals when compared to *BRCA1* and *BRCA2* mutation carriers (Graffeo, *et al.* 2016). More recently, germline multigene panels have been used as a first-line testing option for individuals diagnosed with breast and ovarian cancer, however there is still limited availability of this option in the South African public sector. As with the eligibility criteria, these testing options may also vary across different institutions.

Since 2005 there has been a breast cancer genetic service in the Western Cape Province of SA which offers genetic testing for *BRCA1* and *BRCA2* mutations. Despite international institutions having established guidelines for the genetic counselling and testing process, there are still significant challenges (Robson, *et al.* 2010). In SA, although there is a lack of established guidelines, similar challenges arise. The local population comprises of diverse ethno-linguistic groups, with isiXhosa being the predominant one. White individuals of Afrikaner and non-Afrikaner ancestry and indigenous black South Africans each constitute a quarter of the population, while individuals of mixed ancestry constitute approximately half of the population (Schoeman, *et al.* 2013).

Formal South African guidelines have not yet been established to assist genetic counsellors in determining whether the analysis of founder mutations identified in a specific population group is sufficient or whether it is essential to pursue additional molecular analysis following a negative result (Seymour, *et al.* 2016). Unless full sequencing of *BRCA1* and *BRCA2* has been performed, a negative test result should be considered as being uninformative and not that there are no genetic mutations predisposing the individual to HBOC (Lalloo & Evans, 2012). The mutations in these genes may have simply been missed by the methods employed (Schlebusch, *et al.* 2010).

The isolation and identification of *BRCA1* and *BRCA2* has afforded individuals who are at an increased risk for developing HBOC the opportunity to learn whether they carry a risk-conferring mutation (Lerman, *et al.* 1998). Affected individuals who have tested positive for a *BRCA1* or *BRCA2* mutation are encouraged to inform all at-risk adult relatives about HBOC and to notify them of the possibility of undergoing PT to identify the familial mutation (Claes, *et al.* 2003). Raised awareness of these breast cancer susceptibility genes has resulted in an

increased number of women undergoing genetic testing to determine if they are at an increased risk of developing breast and ovarian cancer. This has been described in the media as the 'Angelina Jolie effect' (McCrea & McCutcheon, 2017).

PT is offered to unaffected individuals with a positive family history of HBOC with an already identified *BRCA1* or *BRCA2* mutation in an affected family member. These individuals are at 50% risk to have inherited the familial mutation conferring an increased susceptibility to cancer. It has been recommended that this be performed in a clinical setting as part of a genetic testing program (Seymour, *et al.* 2016). The delivery of genetic counselling plays an important role for at-risk individuals and their families during this time. Genetic counsellors are able to provide valuable support for those undergoing PT, guiding individuals through the rigorous decision making process and advise them on how best to manage their risk based on established clinical recommendations (McCrea & McCutcheon, 2017).

1.6 MANAGEMENT AND SURVEILLANCE OPTIONS FOR *BRCA1* AND *BRCA2* CARRIERS

An individual's *BRCA1* or *BRCA2* mutation status provides valuable insights with regard to prevention and treatment options (Godet & Gilkes, 2017). HBOC poses a considerable health burden on at-risk individuals and populations as a result of the significantly increased lifetime risks of developing breast and ovarian cancer. This can be greatly reduced through appropriate surveillance or prevention behaviours (Buchanan, *et al.* 2017). Management options for mutation carriers, both affected and unaffected, include regular surveillance, prophylactic surgery, such as risk-reducing bilateral mastectomy (RRBM) and/or bilateral salpingo-oophorectomy (BSO), prophylactic medication and risk avoidance (Laloo & Evans, 2012). The significantly increased breast cancer risk can be reduced by more than 90% with the uptake of a RRBM and by approximately 50% with the uptake of BSO in pre-menopausal women. A BSO can reduce the risk of ovarian cancer by 80-90% (Gilbert, *et al.* 2017; Hartmann, *et al.* 2001; Kauff, *et al.* 2008).

Breast cancer surveillance is available to women who are carriers of a risk-conferring mutation in *BRCA1* or *BRCA2* as well as their first-degree relatives. Surveillance recommendations are diverse and vary from one institution to the next. With the appropriate management and surveillance, mutation carriers have the opportunity to detect or prevent cancer at early stages when there is an increased likelihood for successful treatment outcomes (Godet & Gilkes, 2017). Many surveillance programs start before the age of 30 years and include annual clinical breast examination, breast magnetic resonance imaging (MRI), annual mammography screening and breast ultrasonography (van Zelst, *et al.* 2017).

Mammography aids in detecting *in situ* carcinomas that may not be visible in MRI images. Early detection of malignancy is important for women with *BRCA1* or *BRCA2* mutations as they are more likely to develop more aggressive forms of breast cancer (van Zelst, *et al.* 2017). Some surveillance options, such as mammography screening and MRI, are limited in their ability to detect the disease early enough or to prevent the disease (Lalloo & Evans, 2012). Risk avoidance activities that could be undertaken include smoking cessation, reduced caloric intake, avoiding obesity, increased physical activity, avoiding exposure to carcinogens and attendance of regular health check-ups (Agnihotri, *et al.* 2014).

1.7 CHAPTER SUMMARY

In this chapter breast cancer is introduced, both epidemiologically and within the context of SA. The genetics of HBOC are discussed in detail and the cancer risks associated with mutations in *BRCA1* and *BRCA2* are described. The testing options for *BRCA1* and *BRCA2* are explored and addressed in a South African context. Management and surveillance options are introduced. In the next chapter, PT for HBOC is presented as it provides a rationale for the current study. The aim and objectives of this study are also presented.

CHAPTER 2: PREDICTIVE TESTING FOR HBOC

2.1 CHAPTER INTRODUCTION

In this chapter, PT for HBOC is outlined. In particular, (1) the complexities of PT, (2) the psychosocial challenges related to HBOC, and (3) the role of pre-test counselling in PT for HBOC. The rationale for this study will be contextualised prior to introducing the aim and objectives of this study.

2.2 PREDICTIVE TESTING IN SA

There is a considerable lack of specialised clinical services in SA. One area in which this is particularly evident is genetic services. With only three urban centres in the country that offer a fully integrated genetic service, including clinical, diagnostic and genetic counselling services, and two centres that offer clinical genetic services with some laboratory support, the lack of genetics professionals results in a significant proportion of the South African population not having access to the appropriate genetic services. These services are aimed at assisting individuals whose lives may be affected by a disorder with a significant hereditary component (Beighton, *et al.* 2012).

In a South African context, very little is understood about how effective the PT process is at preparing individuals for receiving their test results and how family members who are found to have a *BRCA1* or *BRCA2* mutation use the knowledge of their status (Schoeman, *et al.* 2013). The PT process in SA typically involves pre-test counselling, molecular genetic testing and post-test counselling during which the results are returned to the individual. In most cases, pre-test counselling of individuals undergoing PT is carried out by a genetic counsellor or a suitably trained healthcare professional. These individuals are uniquely positioned to obtain a comprehensive family history and focus on the individualised needs of the person, while providing tailored information in a supportive environment. Pre-test counselling aims to establish a foundation for a discussion pertaining to the information about the condition, genetic concepts, inheritance patterns, the DNA test and the testing process. The primary focus of pre-test counselling is to assist at-risk individuals in taking the necessary time to work through the pre-test information in order to facilitate informed decision-making about pursuing PT and to explore the emotional impact of all possible testing outcomes (Arning, *et al.* 2015).

2.2.1 THE COMPLEXITIES OF PREDICTIVE TESTING

PT differs in fundamental ways from traditional forms of genetic testing that have been used solely for diagnostic purposes. PT aims to identify asymptomatic individuals, that are at an increased risk for a specific disease, early in an attempt to reduce the morbidity and mortality associated with the disease through the use of appropriate

screening, surveillance and prevention behaviours. Despite having considerable potential for accurate risk assessment, the clinical utility of PT for different conditions is variable (Evans, Skrzynia & Burke, 2001).

Conventional diagnostic testing has important implications and benefits for family members that are at risk for having inherited the pathogenic variant. One of the uncertainties associated with PT, in general, is that the outcome of the result is unable to determine whether the condition will develop, by what age it will develop or the severity of the condition (Claes, *et al.* 2005; Evans, Skrzynia & Burke, 2001). However, the benefit of individuals knowing their mutation status lies in their ability to take proactive steps towards reducing their risk and being in a position to detect cancer early enough to allow for better health outcomes.

For Huntington disease (HD), a positive predictive test indicates with certainty that the individual will develop the condition, but there is still a component of uncertainty about when it will appear and the severity of the phenotype. In addition, the interventions that are available to individuals at risk are often recommendations that are made on the presumed benefit and not always based on tested outcomes. Individuals are often misconstrued into believing that the genetic risk obtained from PT is highly predictable and determinant of disease outcomes. These inherent uncertainties are a limitation for PT (Evans, Skrzynia & Burke, 2001).

PT for HBOC is useful to identify individuals that are at an increased risk for developing cancer but the utility of the testing has several limitations (Evans, Skrzynia & Burke, 2001). There is great uncertainty about the predictive value of the testing, with penetrance estimates for breast cancer in women ranging from approximately 40-85% and ovarian cancer ranging from approximately 30-60% (Lalloo & Evans, 2012). Female mutation carriers may develop breast or ovarian cancer, or neither or both, and the age at which cancer develops is largely variable. Environmental effects, genetic modifiers and the nature of a specific mutation are all factors that may further contribute to the development of the condition (Claes, *et al.* 2005; Evans, Skrzynia & Burke, 2001). In cases where the PT result is negative, this means that these individuals do not possess the allele conferring an increased risk for HBOC in that particular family and their risk is therefore the same as that of the general population (Seymour, *et al.* 2016).

The utility of PT is further limited when taking into consideration surveillance and prevention strategies. The efficacy of starting annual mammography screening between the ages of 25 and 35 years is unknown and due to the fact that mammography screening is generally recommended for women over the age of 40 years, information pertaining to genetic susceptibility would be less relevant for older women. In addition, routine surveillance for ovarian cancer is not available. Consequently, the knowledge of an inherited predisposition for HBOC does not result in a clear and uncomplicated solution to reduce risk (Evans, Skrzynia & Burke, 2001). In spite of these limitations, PT has helped some individuals manage some degree of uncertainty related to their

genetic situation (MacLeod, *et al.* 2014). It is important to tailor pre-test discussions about testing to the individual's needs or preferences and to ensure that they are fully informed about the utility and limitations of the testing (Evans, Skrzynia & Burke, 2001).

Owing to the fact that PT is used to identify exact mutations it is relatively inexpensive and cost effective, however medical aid schemes may not always cover these costs and state patients may be charged a portion of this testing based on their income (Seymour, *et al.* 2016). A study by Watson, *et al.* (2004) explored the psychosocial impact of HBOC PT in a multicentre cohort in the United Kingdom. When exploring the topic of insurance discrimination amongst female participants, 20% of female mutation carriers reported experiencing some form of insurance discrimination after their genetic testing. While some women reported difficulties in getting life insurance after testing, most women reported difficulties obtaining health insurance. Some women also reported that their insurance premiums had increased following testing (Watson, *et al.* 2004). This has not been investigated in SA.

2.2.2 PSYCHOSOCIAL CHALLENGES RELATED TO HBOC

One of the main concerns of doing PT for HBOC in a clinical setting is the possibility of adverse psychological effects particularly when patients are confronted with a result that is unexpected or unfavourable (Claes, *et al.* 2005). Longitudinal research efforts are essential to evaluate the psychosocial impact of PT (Claes, *et al.* 2005; De Vos, *et al.* 1999). Research carried out in women with a family history of breast and/or ovarian cancer has indicated that women who are most interested in undergoing PT are also the most worried and distressed, and are perceived to be the most vulnerable for adverse psychological outcomes (Claes, *et al.* 2005; Lerman and Croyle, 1996). Many studies have investigated variables, other than the genetic testing result, that are associated with distress following genetic testing (Claes, *et al.* 2005; Decruyenaere, *et al.* 2000a). These variables include the test results of siblings, spousal and family support, pre-test distress as well as underestimation of the emotional impact of the genetic result. Other studies have focused on the perception of risk and the perceived seriousness and controllability of the disease (Claes, *et al.* 2005; Decruyenaere, *et al.* 2000a).

Early detection, surveillance and prevention behaviours have the greatest impact on the associated morbidity and mortality for *BRCA1* or *BRCA2* mutation carriers (Buchanan, *et al.* 2017). *BRCA1* and *BRCA2* mutation carriers often face difficulties when making decisions regarding the best approach to manage their breast cancer risk. They need to decide between screening, undertaking risk reducing surgery or prophylactic treatments such as chemoprevention. This decision is often made without clear guidance as to which option is best for them. Mutation carriers are likely to misinterpret their lifetime cancer risks and perceive them to be a short-term risk, anticipating a cancer diagnosis in the near future (Brunstrom, Murray & McAllister, 2016). Conversely, in some

cases mutation carriers can also underestimate their lifetime cancer risk, therefore complicating the meaning of being at-risk (Hesse-Biber, 2014).

Individuals who are found not to carry the familial mutation are alleviated from the unnecessary worry associated with the increased risk of breast and/or ovarian cancer and will return to the average population risk for breast/ovarian cancer. They do not need to undergo increased surveillance or make a decision about undergoing prophylactic surgery, however, they do still have to deal with family members who are at increased risk for cancer after testing positive for causative mutations which may have other psychological consequences such as dealing with survivor guilt, feeling isolated from positive mutation carriers or being worried about family members that carry the mutation (Claes, *et al.* 2005).

Women from a breast cancer family are likely to have an increased interest in pursuing genetic testing, particularly in cases where the affected persons are first degree relatives (Pasacreta, 2003). Individuals who have lost relatives to breast cancer are more likely to seek genetic testing (van der Meer, *et al.* 2012). Young women are more likely to consider genetic testing at a younger age if they have a family member diagnosed with breast cancer at a young age (Hesse-Biber, 2014; Brunstrom, Murray & McAllister, 2015).

Women who know that they are at an increased risk of developing breast cancer may feel that they have a responsibility to undergo genetic testing in order to assist them in managing this risk, not only for their own benefit but for the benefit of their family members (Brunstrom, Murray & McAllister, 2015; Hallowell, 1999). The choice to pursue PT for *BRCA1* or *BRCA2* may be motivated by factors such as planning for the future or making decisions about reproduction. Women may feel strongly about not wanting to transmit such a mutation on to their children or be at risk for dying early and leaving their children without a mother. Some women are likely to feel that not knowing is not an option, as they would need to know for the benefit of their family members or their own future family. The decision is often no longer perceived to be a personal choice, but rather one that is made on behalf of their children or future children (Brunstrom, Murray & McAllister, 2015, d'Agincourt-Canning, 2006).

Young adults, in particular, may feel that they are less likely to make the decision to pursue PT independently, owing to the fact that they are more likely to be emotionally and financially dependent on their family, when compared to older adults (Brunstrom, Murray & McAllister, 2015). There is no consensus on the age at which to undergo PT. Other factors such as career, relationship status, family history of cancer, familial influence and family planning, social support, and the age at which at-risk individuals perceive their cancer risk to be the greatest, are taken into consideration (Hesse-Biber, 2014; Brunstrom, Murray & McAllister, 2015, Macrae, *et al.* 2013).

There are a number of factors that may influence an individual's decision to undergo PT for HBOC. These include the removal of uncertainty, empowerment and familial obligations (Brunstrom, Murray & McAllister, 2015). Removal of uncertainty refers to the fact that individuals at risk may choose to pursue testing in an attempt to eradicate the fear and anxieties of not knowing if they are a mutation carrier and that regardless of the result, it would be better than not knowing (Brunstrom, Murray & McAllister, 2015, d'Agincourt-Canning, 2006). By having the PT result, individuals may feel better prepared to deal with their risk and take control of their situation, achieving an overall sense of empowerment. Having children has been shown to play a significant role in an individual's decision to be tested. Some at-risk individuals may believe that undergoing PT for HBOC is what is expected of them based on their family history (Brunstrom, Murray & McAllister, 2015; d'Agincourt-Canning, 2006).

When exploring the perceived benefit or advantages of PT for HBOC, studies have shown the counselling process to have a positive impact as at-risk individuals have an improved knowledge and awareness about the effects of being a *BRCA1* or *BRCA2* mutation carrier, raising awareness about surveillance and having a positive influence on an individual's health and lifestyle choices (Brunstrom, Murray & McAllister, 2015). Genetic counselling is able to ensure that the correct information be provided and that individuals are less reliant on seeking out any necessary information themselves, information which may be incorrect and result in unnecessary worry. Genetic counselling is also able to assist in improving the accuracy of risk perception and distinguishing individuals that are likely to be carriers from those that aren't (Brunstrom, Murray & McAllister, 2015). In contrast, some individuals feel that because of their mutation status, they are forced into making difficult and unexpected decisions. Decisions such as deciding when or if to have risk reducing surgery or whether to have children (Donnelly, *et al.* 2013). In some instances, the outcomes of the testing may be unexpected and pre-test anxieties are replaced with other anxieties following result delivery (Brunstrom, Murray & McAllister, 2015).

In light of the fact that PT for HBOC is a relatively complex process with various associated uncertainties as well as the possible adverse psychological effects associated with this form of testing, it has been suggested that PT for HBOC be offered in a multidisciplinary counselling context (Seymour, *et al.* 2016). This would include genetic counselling and possible psychological counselling, in the case of the patient displaying signs of depression and/or psychological distress, prior to mutation analysis. Genetic counselling provides individuals with an opportunity to receive information about the condition, how the condition is inherited and the chances of other individuals in the family carrying the same genetic mutation. They also receive information regarding the cancer risks, the options available for undergoing PT and its associated implications, as well as the available options and their associated risks and benefits for early detection, surveillance and prevention. The genetic counsellor is

required to enable the individual to make informed decisions about their genetics and undergoing PT while also focusing on individual emotional support (Seymour, *et al.* 2016).

2.2.3 THE ROLE OF PRE-TEST COUNSELLING IN PREDICTIVE TESTING FOR HBOC

It is important that individuals that are eligible for PT are managed in a manner that ensures their ability to make well informed decisions regarding their risk and that any psychological distress experienced during this period is minimised. Less HBOC-related knowledge and risk awareness is associated with adverse psychological effects during PT. Males from HBOC families are less likely to undergo PT owing to their low risk of developing cancer. Denial or minimalization of the risks may also contribute to the reduced uptake of PT amongst at-risk males (de Wit, *et al.* 1996; Foster, *et al.* 2002).

During pre-test counselling for *BRCA1* or *BRCA2* mutations, it is important to ensure that the decision to pursue testing is not influenced by cancer-related distress alone, but that the individuals are well informed so as to avoid individuals making poorly informed and impulsive decisions regarding testing. Concerns related to HBOC need to be addressed before undergoing testing. Given the family history, it is natural to expect concerns related to the development of cancer but it is important to be aware that some individuals may be more likely to require additional psychological support. The increased accessibility of genetic testing necessitates that individuals receive comprehensive counselling prior to testing in order to address their concerns, allowing them to make well-informed decisions and to support them both medically and psychosocially (Foster, *et al.* 2002).

One area that has not yet been fully explored is the extent to which pre-test counselling adequately prepares and supports individuals undergoing PT (MacLeod, *et al.* 2014). It has been suggested that further studies should focus on examining both the content and the quality of the counselling interaction during this period (Meiser & Halliday, 2002). In a qualitative study exploring the experiences of PT in 36 individuals younger than the age of 25 years at risk for HD, familial cardiomyopathy or HBOC, the usefulness of pre-test counselling was seen in providing personalised information in a manner that could be easily understood. Across all three groups of conditions, individuals did not view the pre-test counselling as useful in facilitating the decision-making process. Some individuals took issue with the lack of information tailored to their specific situation and felt that the length of time between appointments could have been shortened. However, none of the participants believed that the age limit of testing should be lowered to under the age of 18 years for HBOC and HD (McLeod, *et al.* 2014).

There is an overwhelming amount of research that has focused on the after-effects of both predictive and diagnostic genetic testing for HBOC but there has been little investigation surrounding the actual PT process (Claes, *et al.* 2005). By exploring what these individuals' experiences and perceptions are, and the factors that

influenced their decision to undergo PT for HBOC, we are better able to understand their evaluation of the actual PT procedure. Perspectives refer to their overall attitude towards the process or the manner in which they regard the PT process, whereas experiences refer to these individuals' direct observation of the events that have occurred during the PT process (Claes, *et al.* 2005).

To the best of our knowledge, there are no studies that have been conducted in a South African context, looking at the PT process, nor the factors affecting decision making, for HBOC. South African research efforts have largely focused on healthcare disparities and breast cancer survival (McKenzie, *et al.* 2016). Rayne, *et al.* (2017) recently explored the psychosocial stress affecting women already diagnosed with breast cancer in SA. The study concluded that increased fears at diagnosis were associated with the treatment of breast cancer and its adverse effects, as well as fears of dying. Affordability of cancer treatment was found to be the only significant socio-economic factor to be associated with increased concern (Rayne, *et al.* 2017). Fear is an important factor that has been found to contribute to delayed treatment amongst individuals diagnosed with cancer (Otieno, *et al.* 2010; Rayne, *et al.* 2017).

Hallowell, *et al.* (2005) explored the factors influencing PT decisions in at-risk men in the United Kingdom. The study concluded that all the men in the study felt obliged to undergo predictive genetic testing for the benefit of their family members, their children in particular (Hallowell, *et al.* 2005). Research efforts have yet to focus on the characteristics of individuals, both men and women, and the psychosocial factors that affect their decision to undergo PT for HBOC (Sweeny, *et al.* 2014). The present study will aim to address this in a local context by focusing on South African individuals residing in the Western Cape Province. These individuals would have undergone PT for HBOC as a result of an already identified mutation for HBOC in an affected family member.

This study will focus on the perspectives and experiences of individuals that have undergone PT for HBOC with the aim of assisting genetic counsellors and other healthcare professionals working with this group of individuals to provide more focused PT counselling sessions tailored towards the unique needs of these individuals in an attempt to better prepare them for receiving their results.

2.3 AIM AND OBJECTIVES

2.3.1 AIM OF THIS STUDY

The aim of this research project is to qualitatively explore the perspectives and experiences of individuals who have undergone PT for HBOC in the Western Cape, South Africa.

2.3.2 OBJECTIVES OF THIS STUDY

The aim of this study will be achieved through the following objectives:

1. To explore the participants' experiences of undergoing a predictive test for HBOC.
2. To explore the participants' perceptions about undergoing PT for HBOC.
3. To explore the factors that influence the participants' perceptions and experiences of undergoing PT for HBOC.
4. To explore what factors influenced the participants' decision to undergo PT for HBOC.
5. To explore how each participant perceives the PT process could be improved.

2.4 CHAPTER SUMMARY

In this chapter, PT for HBOC was discussed in further detail and the rationale for this study was presented. The study aim and objectives were presented. The methods employed in this study are explained in detail in the preceding chapter.

CHAPTER 3: METHODS

3.1 CHAPTER INTRODUCTION

This chapter includes (1) an outline of the research design and a rationale for the use of qualitative methodologies, (2) details of the study population and sample, data collection and analysis and (3) ethical considerations.

3.2 RESEARCH DESIGN

3.2.1 QUALITATIVE RESEARCH

This study has been designed to be an in-depth qualitative study of the perspectives and experiences of individuals undergoing PT for HBOC. Since the aim and objectives of the study were to explore individuals' perspectives and experiences of the PT process with regard to HBOC, a qualitative research approach was found to be most appropriate. Qualitative methodologies allow for the researcher to understand a phenomenon in a setting that is context-specific, natural and experienced by the participants themselves, a phenomenon that otherwise may be poorly understood (Golafshani, 2003). It allows for the contextualisation and understanding of peoples' experiences in a real-world context, placing emphasis on their actions, thoughts and reflections, and investigates questions pertaining to their psychological and social interactions (Henwood, 2014).

In addition, as only a limited amount of knowledge is available on this topic in the context of SA, an exploration of this phenomenon is initially needed, which is only possible using qualitative questioning of the phenomenon in order to find the significance that individuals place on this process. Qualitative research allows for the possibility of guiding clinical practice and improving service delivery in order to make a difference in the lives of those who are faced with similar situations (Merriam, 2009; Redlinger-Grosse, *et al.* 2015). In order to understand the phenomenon under study, it is important that the researcher set aside any prejudgements and previous experience of the phenomenon (Al-Busaidi, 2008).

Genetic counselling necessitates that psychosocial aspects are addressed by a counsellor that has sufficient experience in dealing with emotional issues. A significant proportion of genetic counselling training and clinical practice is associated with interacting with individuals regarding sensitive and complex topics related to genetic conditions, similar to the skills that are required to conduct interviews. In addition, the skills, that are gained during the preparation of cases for presentation to colleagues and during patient follow-up, correspond to the skills that are required for information synthesis and analysing and evaluating data in qualitative research

(MacFarlane, Veach & LeRoy, 2014). Genetic counselling research therefore encompasses many of the objectives of qualitative research (Redlinger-Grosse, *et al.* 2015).

3.3 STUDY POPULATION AND STUDY SAMPLE

3.3.1 STUDY SETTINGS

Research study participants were recruited retrospectively from the breast cancer and/or clinical genetics clinics at GSH, TBH and private genetic counselling practices in Cape Town (PVT). Individuals that have undergone PT for HBOC are seen through these genetics services. GSH and TBH are state-funded tertiary academic hospitals in the Western Cape that serve patients referred by less-specialised primary or secondary healthcare services. Both hospitals serve patients from different geographic regions in the Western Cape. Private genetic counselling practices serve patients that have private medical insurance or those that are able to pay private rates. It was important to recruit participants from multiple genetics services in the Western Cape so that the findings from this study could be representative of the perspectives and experiences of individuals undergoing PT for HBOC in the Western Cape and not just a reflection on the perspectives and experiences of individuals that had been through the process at one institution.

Genetic counselling referrals for patients diagnosed with cancer are generally made by specialist physicians such as oncologists, gynaecologists or breast surgeons. Patients that are found to carry a *BRCA1* or *BRCA2* mutation are encouraged to notify their relatives about their risk of having inherited the same mutation and the availability of PT. Potential study participants were identified following a search of the various clinical databases and patient files. Participants that fit the study inclusion criteria (described in 3.3.2) were contacted if they had been seen by a healthcare professional and if they had completed the PT process for HBOC.

3.3.2 STUDY POPULATION

Participants, both male and female, were included to participate based on the following criteria: they needed to have undergone PT for HBOC and they needed to be older than the age of 18 years at the time of recruitment. These participants had positive family history of HBOC. All study participants that underwent PT for HBOC would have been at 50% for having inherited the familial risk-conferring variant prior to being tested. In addition, participants needed to have completed the PT process and received their results at least a month prior to the interview. Owing to the sensitive nature of the results, it was decided that this would be an appropriate time to allow participants to process their results and deal with the initial impact of what their results mean for them and their families. Participants were excluded from this study if they were cognitively impaired due to health complications. It was important to exclude individuals that are cognitively impaired because there is concern

that these individuals could be vulnerable to coercion or in the case of severe cognitive impairment, may lack the capacity to provide truly informed consent (Berg, 1996).

In order to reduce the chance of introducing potential bias that accompanies the decision to only interview English speaking participants, it was important to provide the option of a suitably appointed translator and translated supplementary documentation for participants who did not feel comfortable communicating in English. Interviews were offered in English, Afrikaans or isiXhosa, the three main languages spoken in the Western Cape.

3.3.3 SAMPLING METHOD

The sampling method used in this research study was purposive sampling. Purposive sampling is a non-probability sampling technique that may be subjective in nature but can be useful when the purpose of the research is not aimed at making generalisations that pertain to an entire population. Purposive sampling may be advantageous in smaller scale research and in instances where there are limited resources and time (Etikan, *et al.* 2016), such was the case in this research study. The participants in this study were selected based on the aim and objectives of this study as well as the knowledge and experience of undergoing PT for HBOC that each participant possessed. It was expected that each participant would be able to provide information that was both unique and valuable. The purposive sampling strategy used in this study was homogeneous sampling as the group of participants selected had some similar and defining characteristics (Bernard, 2017; Savin-Baden & Howell Major, 2013).

Purposive sampling is most often associated with qualitative research as it allows for the identification of the most informative cases, with particular characteristics, that aid in achieving a depth of understanding about a particular phenomenon (Etikan, *et al.* 2016). With purposive sampling, the sample size is dependent on the point at which data saturation is reached (Wu Suen, Huang & Lee, 2014). This is the point at which novel themes and explanations no longer emerge from the data (Francis, *et al.* 2010; Marshall, 1996). Regardless of the technique employed, validity and efficiency are paramount (Morse & Niehaus, 2009).

The original genetic counsellor, who performed the PT for each individual, was contacted telephonically or via email and was asked to contact potential interview participants informing them about the research project, its aims and objectives. This was ethically important as it protected the anonymity of these individuals, particularly in cases where they were not interested in participating, as well as their autonomy, as it may have been easier for them to make an autonomous decision about participating when asked by someone who they were familiar with. The genetic counsellors contacted each participant telephonically or via email in order to obtain their

consent for the researcher to contact them. Individuals willing to participate were contacted by the researcher, telephonically or via email, the research aims were discussed further, and an interview date and time was set up at the participants' earliest convenience.

3.3.4 SAMPLE SIZE

Sixteen participants were recruited to participate. The emphasis of qualitative methodologies is placed on the participants' lived experiences and does not aim to enumerate. A large sample size and statistical representativeness is not regarded as an important requirement in qualitative research, and in some cases, may be impractical. The sample size is dependent on the purpose of the study as well as the availability of resources and the time constraints (Patton 2002). Qualitative research methods aim to collect information-dense data. Conversely, quantitative methods are deductive in nature and aim to obtain a breadth of understanding (Etikan, *et al.* 2016; Patton, 2002). During the interview process one interview was excluded from this study as it was found that this participant had been diagnosed with breast cancer a number of years prior to her testing, meaning that she had in-fact undergone diagnostic genetic testing and not PT. The remaining 15 interviews were analysed further during data analysis.

I aimed to recruit 10-20 participants overall, from both the public and private sectors. As the aim of this study was not to identify differences between the public and private sectors but rather to obtain a comprehensive understanding of the perspectives and experiences of individuals in the Western Cape undergoing PT for HBOC, equal representation of the two sectors was not necessary. This predicted sample size was subject to change as the number of required participants became apparent as the interview process progressed and until data saturation was reached. Data saturation was reached after the 14th interview, not including the excluded interview. This was the point at which the interviews no longer provided new information on the phenomenon under investigation. A 15th interview was conducted and data analysis was able to confirm that data saturation had in-fact been reached. Qualitative analysis of research content during the data collection period allows the researcher to better navigate between the development of concepts and the collection of data. This is helpful in directing subsequent data collection so that it may be more useful in addressing the intended research question (Miles & Huberman, 1994; Zhang & Wildemuth, 2016).

3.4 DATA COLLECTION

Data was collected through the use of short socio-demographic questionnaires as well as face-to-face or telephonic interviews. Prior to the interview, consenting participants were given a socio-demographic questionnaire (appendix A). This questionnaire consisted of closed-ended questions aimed at collecting general

demographic information that could be used as data for analysis. Interviews were conducted by the researcher using a semi-structured interview guide (appendix B). The questions in the interview guide were created based on information obtained from published literature pertaining to the subject of breast cancer. The interview guide included open-ended questions that were focused on the PT process for HBOC in the Western Cape.

A semi-structured interview is characteristically based on flexible parameters that provide open-ended questions that are able to explore participant experiences and perceptions (Turner III, 2010). The advantage of the loose structure of open-ended interview questions is that they enable the interviewer to explore new areas that have not yet been explored by the researcher and enrich their data, as well as enabling them to build rapport with the participants (Al-Busaidi, 2008).

The interview guide was reviewed by the study supervisors to ensure rigour of the study. Two test interviews were carried out in order to determine whether there were any limitations or weaknesses with the interview design and necessary changes to the questions were made prior to the implementation of the study. Open-ended questions were used to allow participants to fully express their perspectives and experiences. These questions were carefully worded to remove bias and ensure neutrality (Turner III, 2010). Follow-up probing questions were used as a means of eliciting additional responses or to provide context.

These interview questions aimed to explore how the participants experienced and perceived the PT process. Based on the fact that interviews are aimed at exploring more sensitive issues, they were conducted in a quiet and private setting in an attempt to minimise distractions and to further encourage full disclosure of information. All of the interviews were conducted by the researcher and audio-recorded. Field notes were used by the researcher during the interview process in order to assist in taking note of both physical and verbal behaviours of the participant, as well as any features of the setting that may be useful during the data analysis (Mulhall, 2003). By observing how people behave and physically interact in a particular setting and taking note of the emotions that are felt and expressed, the researcher is able to gain a better understanding of the social situation under study (Wolfinger, 2002).

When arranging an appropriate time and place for the interviews, prospective participants who were willing to participate but were unable to travel to a suitable location for a face-to-face interview, or their working hours made it impossible for them to be available for a face-to-face interview, were given the option of having a telephonic interview. All participants were also given the option of having the interview conducted in a language other than English.

3.5 DATA ANALYSIS

3.5.1 APPROACH TO QUALITATIVE DATA ANALYSIS

The framework approach was chosen for this research study. This approach allows for in-depth exploration of the data set and facilitates effective and transparent interpretation of the research findings. The systematic manner in which this analytical method is conducted is well suited for beginner qualitative researchers as it ensures academic rigour (Smith & Firth, 2011). This approach to qualitative data analysis was developed by social policy researchers during the 1980's and has been increasingly used as a means of performing qualitative data analysis for healthcare related research. The framework method is part of a broad conglomerate of data analysis methods that are often referred to as thematic analysis (Smith & Firth, 2011). This approach is an analytical method that is guided by the original observations of the research participants and is open to change and amendment throughout the analysis process. Data analysis is conducted systematically through an interconnected four stage process, while allowing the researcher to re-visit and rework ideas afforded by the rigorous and transparent management of data (Smith & Firth, 2011). The researcher is able to move back and forth throughout the data to allow for the constant refinement of themes and subsequent development of a conceptual framework matrix (Spencer, Richie & O'Connor, 2003).

Initially, the data analysis procedure requires that the researcher become immersed in the data that has been generated in an attempt to start sorting the raw data and determining themes that will then be applied to the data (Gale, *et al.* 2013). The interview recordings, field notes and interview transcripts were reviewed and read multiple times. This process was helpful in allowing the researcher to become familiar with the interviews and the data generated during the interviews. This first step is known as familiarisation and is important for subsequent data analysis (Spencer, Richie & O'Connor, 2003). Next, the data obtained from the first five interview transcripts was then carefully read and portions of the interviews that were relevant to the study were assigned codes which described the interpretation and the importance of the passage. Coding allowed for the data to be classified so that it could be compared systematically with other parts of the data set in order to identify recurrent themes and emerging ideas that were raised by the research participants throughout the interviews. These codes were then sorted and grouped into categories in order to construct a detailed index based on the issues that were raised in the interviews. These included issues that were introduced via the interview guide and new issues that were raised by the participants themselves based on the recurrence of specific experiences or perspectives. During this second step of data analysis a working thematic framework is identified and constructed (Spencer, Richie & O'Connor, 2003).

The working thematic framework that was constructed in the previous step was then applied to the remainder of the data set. The complete data set was systematically coded according to the predetermined categories in this working thematic framework. This allowed for the visualisation of categories and allowed for these

categories to be summarised, linked to one another and grouped into specific themes (Gale, *et al.* 2013). The categorised data was then reorganised according to the appropriate theme which the information referred to. This allowed for the researcher to develop a holistic view of the data from each interview that pertained to each issue or theme that arose throughout the interview process. In this way, charting, which is the final step of the process, allows for the identification of themes and sub-themes in the data so that the findings may be addressed in context of the aims and objectives of the study and the emergent themes (Spencer, Richie & O'Connor, 2003).

3.5.2 DATA ANALYSIS PROCEDURE

The audio-recorded interviews were transcribed verbatim by the researcher to be used in subsequent data analysis. Each participant was assigned an alpha-numeric code in order to ensure privacy and confidentiality and any information that may have contributed to the identification of the participants was removed during the transcription. Field notes were taken during and after the interviews. A personal reflection was also noted by the researcher after each interview. All recordings, notes and supplementary documentation associated with the research was kept on a password-protected computer and backed-up to private cloud storage or kept under lock and key.

The transcribed interviews were rigorously examined to identify themes according to the framework approach, in close discussion with the project supervisors. Thematic analysis is a non-linear, theoretically flexible method for analysing qualitative data that allows for the coding of data and describes the data set in detail (Braun & Clarke, 2006; Vaismoradi, *et al.* 2013). As described in the previous chapter, analysis and categorisation of data occurred simultaneously with data collection. This process was important to inform future interviews to explore issues that were raised in previous interviews. By listening to interview recordings and the ongoing reading of interview transcripts, early thoughts and ideas could be generated. Being able to engage with data is an important starting point in gaining familiarity, insight and understanding of the data generated and becomes the foundation for the data analysis (Mauthner & Doucet, 2003).

The data obtained from the research project was coded and managed using the NVivo11 (QSR International) software program. This software was chosen as it facilitates qualitative research methods and it has been designed to facilitate the organisation and manipulation of data, enables the researcher to perform more complex searches, to visually explore the thematic framework and themes that have been generated and the security of the data is maintained, all in a time efficient manner (Al-Busaidi, 2008).

The themes and sub-themes were developed according to the steps outlined in 3.2.2 and were developed in accordance with the aims and objectives of the study, as well as any emergent issues raised by the study

participants. Table 2 below is the framework matrix used to analyse the data. The framework matrix provides a visual representation of the initial categories and the codes assigned to each category that were developed during step two. The refined categories were then derived from the initial categories and in some cases, were derived from more than one of the initial categories. The final themes were then derived from the refined categories. The themes and sub-themes were discussed and reviewed by the researcher and study supervisors. Excerpts of the interviews were selected based on their representativeness of the ideas raised from the interview guide as well as emerging ideas for the presentation as results of this study.

Table 2: Framework matrix detailing the development of the final themes

Initial Categories	Codes	Refined Categories	Final themes
Family history of cancer	<ul style="list-style-type: none"> • Impact of family history • Personal scares • Family support and communication • Awareness of risks 	Family history of cancer and factors influencing the decision to undergo testing	To test or not to test
Factors influencing decision to do testing	<ul style="list-style-type: none"> • Family and children • Fear of cancer • Being supported • Personal experiences 		Consequence of knowing
Influence of knowledge	<ul style="list-style-type: none"> • Feeling empowered • Wanting to know • Attitude towards results • Residual risk • Family dynamics 	Post-test distress and feeling empowered by knowledge	Head knowledge versus emotional knowledge
Predictive testing process	<ul style="list-style-type: none"> • Number of sessions • Follow up and support • Provision of information • Other cancers • Timelines 	Being prepared, being supported and being informed	What now? Perceptions of the process
Religion and personal beliefs	<ul style="list-style-type: none"> • Religion • Feeling guilty • Effect on work and personal life • Attitude about being tested • Culture 	Post-test perceptions	Support and its role in the predictive testing process
Surveillance and taking care of yourself	<ul style="list-style-type: none"> • Screening and check-ups 	Support and not being free of cancer risk	

	<ul style="list-style-type: none"> • Advantages and disadvantages of knowing results • Lifestyle changes • Seeking support • Prophylactic intervention 		
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3.6 VALIDITY AND RELIABILITY

Qualitative research is centred around non-numerical information and the manner in which this information is interpreted and made sense of. This interpretation relies on human emotions and perspectives of both the researcher and the participants, and is therefore subjective (Leung, 2015). The validity of qualitative research refers to the manner in which an account is interpreted by the researcher and whether it is an accurate representation of the phenomenon to which it relates. It addresses whether the research process and data are appropriate for answering the aim and objectives of the study. The choice of methodology needs to enable the detection of credible findings in an appropriate context in order for it to be valid. The interpretations and inferences made by the researcher needs to be rational in the context of previous research findings as well as being supported by the research (Waterman, 2013).

The validity of a deduction is achieved when the interpretation is not made subjectively, but rather, the researcher has analysed the data and considered various possible cases so that a valid interpretation can be made (Silverman, 2015). Strategies for enhancing the credibility of qualitative research can be employed to produce more valid findings. These include reflexivity and reflections on the perspectives of the researcher, repeated reanalysis of the data to assess emerging ideas and remaining true to the accounts of the participants, and actively exploring deviant cases (Noble & Smith, 2015). To ensure validity, the researcher and study supervisors worked in collaboration to critically evaluate the data. Three of the interview transcripts were examined by independent supervisors and each generated their own codes. These codes were then reviewed with the researcher in order to challenge the researcher’s ideas and to ensure validity. These differences in interpretation were discussed until there was 100% agreement between the coders and the framework matrix was modified prior to it being applied to the remainder of the dataset.

During the data analysis process, it was important that the researcher be reflexive and use reflective techniques in order to ensure that her own values and biases did not impinge on the manner in which the data was analysed. As a practicing genetic counselling student intern doing research on a condition that is seen in clinic, it was important for the researcher to be reflexive throughout this study. One of the important elements of reflexivity is that the researcher places themselves socially and emotionally in response to the participants in the study

(Mauthner & Doucet, 2003). During the interview process, it was important for the researcher to set aside any personal beliefs and training experience in order to ensure that they did not affect the manner in which the interviews were conducted and the data was analysed. Additionally, it was important to be aware of the impact that the study findings could have on the researcher's ability to conduct PT pre-test counselling sessions in clinic and to reflect on them after the sessions. Although the researcher was making a conscious effort to consider the impact of being a practising genetic counsellor and researcher at the same, it is acknowledged that some would still remain.

Reliability refers to the consistency within the analytical procedures that have been employed and the future replicability of the research. These include taking account of any biases, personal bias and bias in the research methodology, that could have influenced the research findings. Reliability is achieved through a transparent and clear description of the research procedure, including the data analysis and reporting of findings. The framework approach to qualitative research is well-suited to achieving reliability. It is important that pauses, body language and subtle nuances are noted when audio-recorded interviews are transcribed in order to strengthen the reliability of the interpretation. Incorporating fieldnotes and observations into written transcripts and transcribing verbatim, including interviewer questions, will further strengthen the reliability of the study (Silverman, 2015). Discussion of emerging themes with the research team in an interactive process where inferences can be challenged to reach a consensus interpretation. This is important for achieving consistency within the analytical process (Noble & Smith, 2015). These strategies were applied to this study to ensure that the outcomes were consistent and reliable.

3.7 ETHICAL CONSIDERATIONS

According to the Declaration of Helsinki developed by the World Medical Association, some of the essential ethical principles for medical research involving human participants include respect for the individual, the right to make an informed choice as to whether or not to participate in the research, as well as the individual's right to autonomy. These principles are paramount not only upon the commencement of the study but throughout the duration of the research (World Medical Association, 2011). It is important to remain mindful that the well-being of the participant must always be prioritised over the interest of science and society. Ethical considerations should always take priority over laws and regulations.

3.7.1 ETHICAL APPROVAL

Ethical approval was granted by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (HREC REF: 564/2017) (appendix E).

3.7.2 CONSENT

Research participants were informed both in writing and via verbal communication that they would be enrolled in a research study in which the main objective was to assess how adults in the Western Cape, who have undergone PT for HBOC, perceive and experience the PT process. Each participant was notified that participation in the research was voluntary and that they were able to withdraw from the study at any given time without this affecting their current or future medical care. Participants were made aware that all interviews would be conducted in a private setting and that the duration of each interview would be approximately an hour. They were also notified that the interviews would be conducted in English and would be audio-recorded. Each participant was notified that should they require a translator, an appropriately suited translator would be made available to them at the time of the interview.

All potential participants were provided with an information sheet (appendix C) outlining the details and purpose of the research and were required to consent (appendix D) to their involvement in the research in writing by signing consent forms. Each participant received a copy of the information sheet and the signed consent form. All participants chose to have the interview conducted in English and all supporting documentation did not need to be translated into another language.

Informed consent is integral to medical research and is essential to ensuring the autonomy of the participant. Participant authorisation is granted based on the fact that they have a clear understanding of what the research activity entails and that they are not persuaded by others. Information pertaining to the research needs to be disclosed in a manner that can be comprehended by the prospective research participant so as to facilitate informed and autonomous decision-making. In some cases, it may necessitate the translation or further explanation of the consent form where necessary (Grady, 2015).

3.7.3 PRIVACY AND CONFIDENTIALITY

Ensuring the privacy and confidentiality of research study participants is imperative in research ethics. Every effort should be made to protect the privacy of study participants and keep their personal information confidential. In order to minimise the violation of participant privacy and confidentiality, only the data that is pertinent to this research topic was reported (Morse & Coulehan, 2015).

All completed documentation, including consent forms and socio-demographic questionnaires, as well as audio recordings of the interviews were stored on a password-protected computer or under lock and key, to which only the researcher had access. All participants were assigned a de-identifying alpha-numeric code which would appear in both the data obtained and throughout the research. Each participant was advised that the data

obtained during the research process would only be made available to the researcher, supervisors and examiners directly involved in the study.

Following completion of the recruitment and interview process, all hard copies of documentation were converted to electronic copies, anonymised and stored on a password-protected computer. All documents and recordings will be retained by the minor-dissertation supervisor until such time that the data obtained from this study is published in peer reviewed journals.

3.7.4 RISKS AND BENEFITS TO PARTICIPANTS

Prior to obtaining consent, participants were advised that the information obtained would be for the sole purpose of conducting research. Some of the interview questions were of a particularly sensitive nature and may have evoked an emotional response that they may not have felt comfortable exploring. This was a potential risk to participants in this study. Cultural competency and the use of empathy were used to minimise these risks. Participants were also allowed to terminate the interview and withdraw from the study at any time, as well as seek counselling from a qualified genetic counsellor if deemed necessary. Participants were informed that if they chose to no longer participate in the study, for any reason, their decision would not in any way affect the standard of healthcare that they receive from the respective institutions.

Providing participants with an opportunity to share their stories and with a platform to more effectively make sense of their condition and their lives, may be a benefit of participating in this study. Storytelling has long been used as powerful instrument of communication. Storytelling has been shown to have therapeutic benefits for patients living with cancer and enabling them to cope with their diagnosis (Chelf, *et al.* 2000). Storytelling has also allowed for groups of individuals, with similar conditions or in similar situations, to be heard (Koch, 1998). The information that was obtained during the interview process will aid in improving our understanding of patient perceptions and experiences of the PT procedure for HBOC. This information will be beneficial for health care practitioners, including genetic counsellors, to understand and assess the efficacy of the PT procedure as well as the interventions that are employed to prepare patients for receiving their test results.

3.8 CHAPTER SUMMARY

The study methodology was outlined in this chapter. Qualitative research methods were used for this study and the rationale was explained. The study population and recruitment have been described in detail. The methodology has been described in full and the ethical considerations have been discussed. The subsequent chapters will serve to present the results and discussion.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 CHAPTER INTRODUCTION

This chapter will (1) include a summary of the socio-demographic characteristics of the study participants, (2) describe the themes and sub-themes that have been identified during data analysis, and (3) present and discuss these themes in the context of the current research, providing interview excerpts in support of the findings. Where appropriate, existing research is presented to further the interpretation of the themes.

4.2 SOCIO-DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS

The intention of this study was to recruit participants that had undergone PT for HBOC in the Western Cape, South Africa. Twenty-two participants were originally recruited for this study. All study participants were originally from SA. The age of participants ranged from 19-79 years and most were in a stable relationship. The majority of the participants were female (12/15). Five of the participants did not have children, while the number of children in the remaining participant's family ranged from one to four. Nine of the participants went through the PT process at GSH, two at TBH and the remainder through a private genetic counsellor. Fourteen of the fifteen participants had received their results between 1-2.5 years prior to being interviewed and one participant had their result for 2 months prior to being interviewed. Participants 11 and 16 were the only two participants whose first language was Afrikaans. The remainder of the participants' first language was English. A summary of the sociodemographic data of the participants is presented in table 3.

Table 3: Summary of socio-demographic information of study participants

Code	Age	Gender	Stable Relationship	Children	Employed	Education	Mutation Status	Institution
P1	37	F	N	0	Y	Tertiary	Negative	GSH
P2	39	F	Y	4	Y	Tertiary	Positive	GSH
P3	33	F	Y	2	Y	Tertiary	Negative	GSH
P4	40	F	Y	3	Y	Secondary	Negative	GSH
P5	33	M	Y	3	Y	Secondary	Negative	GSH
P7	34	F	Y	2	Y	Tertiary	Positive	PVT
P8	79	F	N	4	N	Primary	Positive	GSH
P9	36	F	Y	2	Y	Secondary	Negative	GSH
P10	58	F	N	0	Y	Tertiary	Negative	PVT
P11	40	F	Y	2	Y	Secondary	Negative	TBH

P12	19	F	N	0	Y	Secondary	Negative	GSH
P13	30	M	Y	0	Y	Tertiary	Negative	PVT
P14	51	M	Y	0	Y	Secondary	Positive	GSH
P15	51	F	Y	3	Y	Tertiary	Positive	PVT
P16	35	F	N	1	N	Secondary	Positive	TBH

F: Female, M: Male, Y: Yes, N: No

Nine participants were from three different families (P1, P2 and P3; P4, P5 and P9; P8, P12 and P14). The relationships between these individuals are depicted in the pedigrees below. The cancer affected status and carrier status of family members have been deliberately omitted so as not to allow for the identification of families.

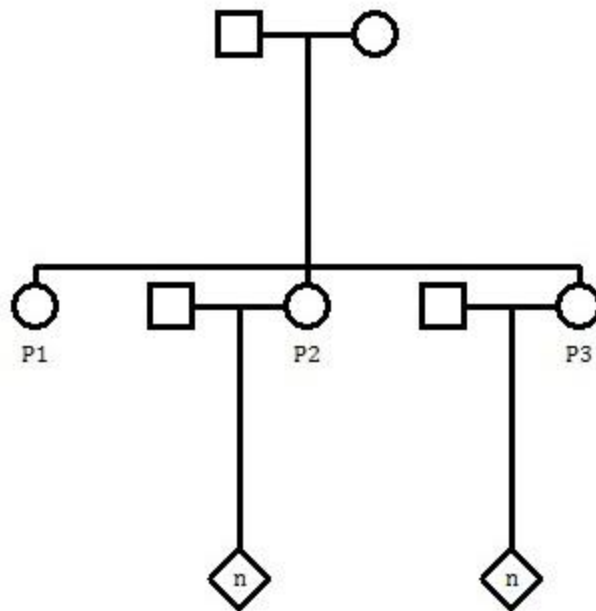


Figure 1: Pedigree showing the relationship between P1, P2 and P3. Circles represent females, squares represent males and diamonds represent 'n' number of individuals of unknown gender.

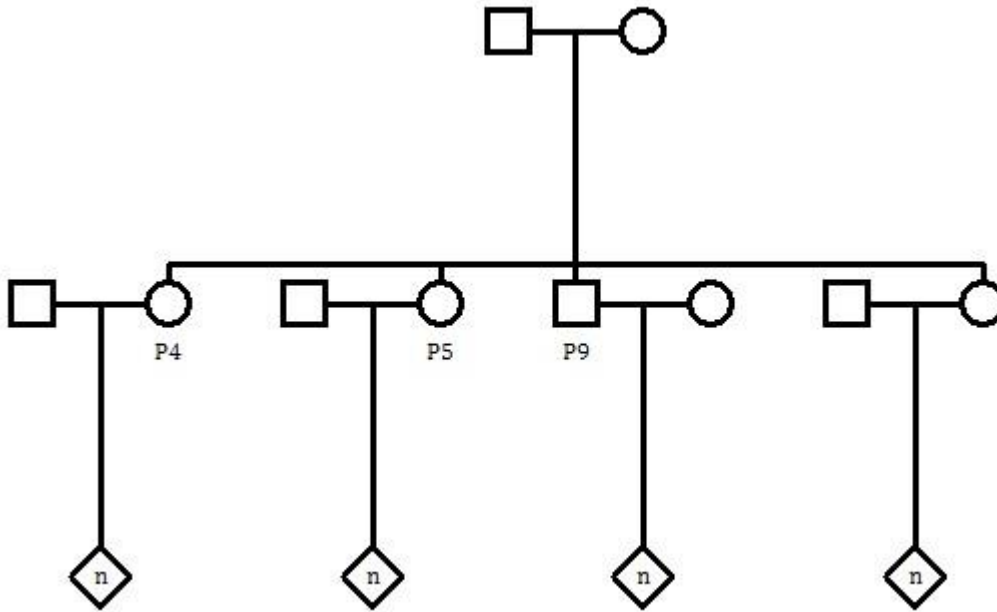


Figure 2: Pedigree showing the relationship between P4, P5 and P9. Circles represent females, squares represent males and diamonds represent 'n' number of individuals of unknown gender.

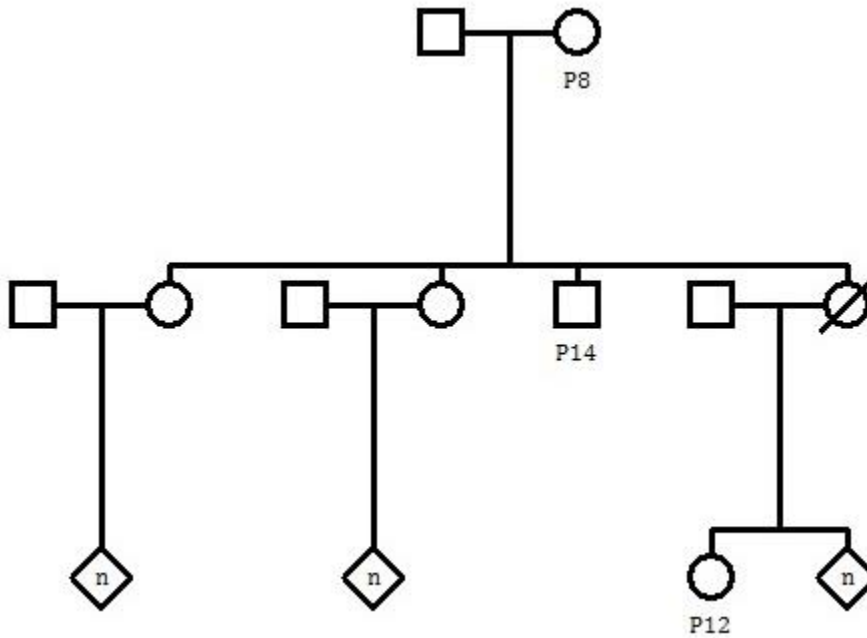


Figure 3: Pedigree showing the relationship between P8, P14 and P12. Circles represent females, squares represent males and diamonds represent 'n' number of individuals of unknown gender.

4.3 IDENTIFIED THEMES

The following themes and sub-themes were identified as described in chapter 3 and are summarised in table 4 below. Each of the themes and sub-themes will be discussed in the sections to follow.

Table 4: Themes and sub-themes identified

Theme	Sub-themes
To test or not to test	<ul style="list-style-type: none">- Sense of duty- Reconciled to being positive
Head knowledge versus emotional knowledge	<ul style="list-style-type: none">- One hour isn't enough- The bigger picture
What now? Perceptions of the process	<ul style="list-style-type: none">- Additional support- It should have been me
Consequence of knowing	<ul style="list-style-type: none">- I'm not cancer-risk free- It's the disfigurement- Empowered by knowledge
Support and its role in the predictive testing process	

4.4 THEME 1 – TO TEST OR NOT TO TEST

Participants are often introduced to the concept of PT for HBOC once a molecular genetic diagnosis has been made in an affected family member. In cases where there is a significant family history of cancer, individuals may be aware that they are at an increased risk from a young age. The findings presented in this theme illustrate the role that cancer burden plays in an individual's perception of developing cancer and the sense of duty to take action, either to prevent a cancer diagnosis or to allow for the detection of cancer as early as possible. The findings will also highlight the beliefs that people develop based on their family history of cancer. Participants in this study felt that their decision to pursue PT was motivated out of a sense of duty to their children or families or as a result of their family history of cancer and the associated cancer-related stress.

4.4.1 SENSE OF DUTY

Genetic testing for cancer susceptibility in healthy at-risk individuals affords them the opportunity to be informed about their mutation status and they are able to potentially benefit from the preventative surveillance and prophylactic options that are available to mutation carriers (Menko, *et al.* 2018). PT has provided individuals with new ways to manage their health and allow for informed family planning (Hallowell, 1999). There are also

important consequences for individuals who test negative for the familial pathogenic variant. A negative test suggests that the individual is not at an increased risk for developing cancer and that preventative surveillance and preventative measures are not necessary. It also implies that any present or future children of these individuals have no increased cancer risk (Menko, *et al.* 2018).

While exploring the factors that influenced the participants' decision to undergo PT and what worried them most about not knowing their mutation status, many of the participants explained that they felt a sense of duty to their children or their families to know whether they carried the disease-causing mutation or not. They said that they had a responsibility to the current and future generations to determine their risks. This is illustrated in the following quotes:

"The other reason for me is that my kids are small, I can't be dumb. I need to take care of myself in order to take care of them. If I have cancer like in five years' time it's okay they're older, you know what I mean, it'll be easier, I'm not saying its ... Ja¹ ... but it'll be easier then. If I can do something to help myself now I must do it." (P2)

"So, you've got all this questions, so, for me it was more about myself and my family and my children because my boys are so young and I was weak. How could I leave them behind so young and I still have to teach them so much?" (P9)

"For my girls. So, for, as I said, for what I've passed on and for me being a young mom, it's always been in the back of my mind knowing that my mom's strong family history and then I'm a girl, not to say that it's only girls" (P7)

The above quotes also illustrate how the female participants with young children felt that it was important to know their risks and take action where necessary because their children still needed to be taken care of. The right to know one's genetic information is often relinquished in cases where the individuals feel that they have a duty to their families to determine the extent of their risk and the risk to other members of their family (Biesecker, *et al.* 2000; Hallowell, 1999). While the knowledge obtained as a result of PT is perceived to be empowering, this freedom to choose becomes constrained as individuals, women in particular, may feel that their increased risk means that they have a responsibility to engage in risk-reducing behaviours. Additionally, there is a presumed responsibility to protect the health of future generations (d'Agincourt-Canning, 2006; Foster, *et al.* 2002; Hallowell, 1999).

¹ "Ja" means yes in Afrikaans

Most of the female participants who had children felt that, as mothers, it was their duty to determine and manage their risks for the benefit of their children, and particularly in cases where they were aware of the fact that if they were to test positive their children would also be at risk of inheriting the mutation. These participants expressed that they feared the idea of their children having to grow up without a mother or with a mother who was suffering from cancer. Society positions women as being responsible for taking care of others, particularly their children (Hallowell, 1999; Hallowell, *et al.* 2006). These women ascribed to these notions and felt that they had a responsibility to determine their risks and engage in medical interventions in order to alter their risk status so that they could fulfil their duty to care for others. Meijers-Heijboer, *et al.* (2000) demonstrated that being a parent was a strong predictor for the uptake of PT in both men and women. This is seen in the following quote by participant 7:

“So, after having my two girls my, it was very important for me to go and get tested, it had always been something that I had wanted to do” (P7)

The notion that individuals are at increased risk and that these risks can be managed suggests that individuals have a responsibility to try and modify these risks where possible (Foster, *et al.* 2002; Hallowell, 1999; Scott, *et al.* 2005). This perceived obligation to know one’s risk for the benefit of others threatens the concept of autonomous or independent decision-making suggesting that the needs and well-being of family members are seen as an integral part of the individual (d’Agincourt-Canning, 2006; Hallowell, 1999; Kenen, 1994).

Some of the participants who did not have children expressed similar feelings. They felt it was important to establish their risk status so that it would allow for informed family planning. By simply knowing that other family members carried the mutation, there was a perceived responsibility to determine their own risk and the risk of their future children. Men, in particular, most often define their decision to undergo PT as a moral duty to their family, especially their children. The choice to pursue PT is motivated by the desire to avoid causing children future harm, something that can be achieved by knowing one’s mutation status (Hallowell, *et al.* 2006). One participant described that knowing whether his future offspring would be at risk was an important factor influencing his decision:

“like I wouldn’t want to have kids and then be like oh well maybe they do maybe they don’t” (P13)

In cases where an individual’s sibling or close family member has been diagnosed with cancer or has been found to carry the mutation, there may be a perceived responsibility to also be tested. Some study participants explained that they had chosen to pursue PT in solidarity with those family members who had either tested positive for the mutation or those that had been diagnosed with breast or ovarian cancer:

“What motivated me, I think it was more and this may sound silly but, but more to show solidarity with my sister and my sister-in-law. Who am I to say no I don’t care, I can have the gene it’s got nothing to do with me, I thought yeah, I think it was more for them, I just realised.” (P10)

“I think it was mostly for my sister. You know what, she was so strong. She was stronger than all of us.” (P4)

Similarly, participant 14’s comment explains how the decision to pursue PT was based on providing moral support for a family member:

“I decided to go with my niece and get tested as well but more as a support for her, not thinking about myself” (P14)

Even for those individuals that expressed that having a positive test result would cause them distress and that they weren’t sure how they would cope with the diagnosis, they chose to pursue testing in solidarity with a family member that had been diagnosed with cancer or because all their other siblings were being tested and they felt that, regardless of the outcome, it was the right thing to do. A study by Biesecker, *et al.* (2000) found that individuals from cohesive families were more likely to pursue PT. These individuals presumably had a greater amount of support that could be a beneficial resource during stressful events (Biesecker, *et al.* 2000). This finding is supported by the presence of participants from three different families in this study and is illustrated in the following quote by participant 3 who was tested with her siblings:

“The three of us went together for the counselling, so that was quite nice, you know, we would know that we are in it together.” (P3)

Many participants who underwent PT alongside family members found comfort in the fact that they were not on their own and that they were able to share the experience and support one another.

4.4.2 RECONCILED TO BEING POSITIVE

Fears about developing cancer and being at an increased risk for developing cancer were amongst some of the most common factors influencing the participants’ decision to pursue PT. It has been seen that having a positive family history of cancer can result in increased cancer-related distress. Experiencing a parent, sibling or family member being diagnosed and living with breast or ovarian cancer, or both, can alter the way in which individuals perceive their risks for developing the same condition (Biesecker, *et al.* 2000; Hirschberg, Chan-Smutko & Pril, 2015; Scott, *et al.* 2005).

It was found that the long awareness of a family history of cancer and the integration of increased cancer awareness into routine family life can alter the way in which a family functions and how individuals within these families perceive their personal risk for developing cancer. This finding is in agreement with Hirschberg, Chan-Smutko & Pril (2015) who identified that experiencing the loss of a relative to hereditary cancer, especially young children losing a parent, can have a significant effect on the development of psychological distress during the period of predictive genetic testing for cancer susceptibility. The following interview excerpts demonstrate how family history impacted the decision to test:

“And so, it suddenly became like really real and frightening, you know. It was a big thing for us. Suddenly instead of having like our cousins get together at home playing 30 seconds, we were visiting people in hospital and just praying that they be okay.” (P2)

“there’s a long line, so all the females on my mom’s side have suffered from breast cancer or ovarian. So, the family history was extremely strong and that’s why I went to go and see [the genetic counsellor].” (P7)

The experience of cancer in a family can influence an individual’s perception of their own vulnerability to developing cancer or worrying about other relatives developing cancer (Foster, *et al.* 2002). While PT is useful in identifying individuals that are at an increased risk for developing cancer, there is great uncertainty surrounding the predictive value of the testing. The penetrance estimates for *BRCA1* and *BRCA2* mutations and the age at which the cancer develops are largely variable. One of the aims of pre-test counselling is to address these uncertainties and to present these risks in probabilistic terms. Prior knowledge of the familial mutation allows for more tailored risk communication, including gene-specific penetrance estimates and age-related risks (Evans, Skrzynia & Burke, 2001; Lalloo and Evans, 2012). However, many of the participants felt that developing cancer was more of a certainty rather than a probability. The probabilities communicated to the participants during the pre-test counselling did not appear to alter their perception of risk, which is likely influenced by an extensive family history of hereditary cancer.

During his interview participant 13 explained how when he had been given a lifetime risk estimate of 30% chance for developing breast cancer he felt that the decision to not pursue testing would be too much of a gamble. He explained how his experiences of regularly finding out that another one of his relatives had been diagnosed with breast cancer or tested positive for the mutation had made the 30% risk feel like it was higher than it actually was. Below is an excerpt from his interview:

“When you look at it, it’s 30% and you think you can take a chance. I suppose anything under 10% you think okay well that’s unlikely but 30% on its own just feels like a certainty. As much as I understood that just because you have this you can still live and that it might never materialise, it I think for me it felt like at some point you’re going to get cancer.” (P13)

This finding supports literature which suggests that it is more common for patients to overestimate rather than underestimate their risks relative to the genetic risk values communicated to them (Scott, *et al.* 2005). Previous studies have also identified that some individuals attending genetic counselling sessions perceive their risk estimates as being binary, suggesting that the given condition will either develop or not (Hallowell, 1999). The perception of risk is largely influenced by social and personal factors, including family history (Scott, *et al.* 2005). Similar observations were made in this study which suggested that in many cases the individual’s perceived risk was influenced by experiences of cancer in the family.

Experiencing the death of close relatives diagnosed with cancer or having a family member diagnosed with cancer appeared to influence the perceptions of being ‘at-risk’. Participant 12, who underwent testing alongside a family member, explained how living with the thought of possibly having cancer was scary. By experiencing the death of her mother at a young age, she believed that she would be more likely to test positive.

“I was expecting a positive result, so I was expecting to have the gene because of my mother passing away of cancer. So, I thought okay, I thought I was going to be the only one that would come out positive.” (P12).

Other factors influencing the participants’ decision to undergo PT included preconceived ideas about the aetiology of cancer and the influence of personal health factors such as previous cancer scares, having other serious medical conditions and the effects of how living a stressful lifestyle could impact the development of cancer. Many participants explained that the cancer-related worry that they experienced while attending annual mammography and gynaecological screening is what influenced their decision to know whether they carried the mutation or not. Participant 1 explained that an initial breast-cancer scare at a young age is what prompted her decision to pursue testing:

“I think because I had my initial scare when I was twenty, that just spurred me on.” (P1)

“To test or not to test” illustrates the participants’ initial journey prior to undergoing PT. While each participant’s experience is distinct, the factors influencing the decision to pursue testing were largely centred around increased cancer-related distress as a result of having a family history of cancer or a sense of duty to family

members and children. Theme 2 addresses the experiences of the predictive testing process and how it prepared the participants for receiving their results, once the decision to undergo testing had been made.

4.5 THEME 2 – HEAD KNOWLEDGE VERSUS EMOTIONAL KNOWLEDGE

The second theme identified was the participants' experiences of the pre-test counselling. The participants, overall, expressed having a positive experience with the counselling process. The participants reflected on how they felt the pre-test counselling prepared them for receiving their results. The findings presented in this theme illustrate how the provision of tailored information during pre-test counselling may not always be sufficient to preparing individuals emotionally for receiving their result. The findings will also highlight the perceived distinction between what it means to be prepared as a result of being equipped with accurate information and what it means to be emotionally prepared for the impact of the test result. Some participants in this study felt that the one hour of pre-test counselling was not sufficient in preparing them emotionally to receive their result.

4.5.1 ONE HOUR ISN'T ENOUGH

As discussed in theme 1, the diagnosis of breast or ovarian cancer in a family can create a significant amount of distress in individuals that are closely related to the affected individual. While the majority of participants only had a single, one hour long pre-test counselling session, a few participants did attend more than one session prior to receiving their results, in most cases because they were accompanying other family members who were going through the process at the same time. Most participants explained that they were happy with the pre-test counselling session and that they felt that the counselling had prepared them to receive their results, regardless of the outcome:

"I was completely happy. And, you know, we had the opportunity at all points to ask questions. So, yes that obviously helps. It wasn't a one-sided conversation, it was quite good." (P3)

"I was prepared for whatever was going to happen. Whether it was positive which I really thought I was going to be or negative, which I am, so I was very prepared for whatever was going to come." (P12)

However, there were some participants that felt that while the pre-test counselling helped them insofar as to have an opportunity to improve their knowledge by meeting with someone who could provide them with the necessary information, in terms of risk estimates and inheritance patterns, it was the support from their families and their personal experiences in dealing with a family history of cancer that helped prepare them for receiving their results. This was not specific to receiving a positive result and is depicted in the following statements:

"I think because I was at the end of a, not the end, but after a number of other people I think their experience was more helpful to me. So, I think the notes and all the broad strokes of it I understood. So,

it was good to speak to her and get the specifics but I think a lot of the counselling aspect had been done by, through discussion with different family members beforehand.” (P13)

“I think the most important part that prepared me for getting my results is my family. That was the most important part.” (P9)

“If I had to go alone then I would be in a mental state because I wouldn’t know what to expect, what would they ask, what do I do, where do I go. So, I would say that the family support structure prepared me for the overall thing.” (P5)

Having had the opportunity to talk about it as a family and understanding what the testing process entailed based on the experiences of other family members, as well as the support of family members whilst going through the PT process is what helped in preparing these participants to receive their results. In addition to these comments, one participant explained that the counselling session didn’t help prepare her for the possibility of obtaining a positive result:

“I wouldn’t say that the time with her, I enjoyed speaking to her and listening to her and get some more information, understanding and knowledge but I wouldn’t say that really prepared me. I would say that, if I recall correctly, that was more clinical, this is what it’s about, the gene test. It was something that I had to work through in my own head.” (P10)

“I really enjoyed the session and she is a kind person and yeah it was good for me to be there but I can’t say that that hour or half an hour whatever time it was, that that helped me to deal with the possibility of a positive, I can’t recall that.” (P10)

The above quotes illustrate how participant 10 was grateful for the opportunity to consult with a specialist and improve her knowledge about HBOC, but she felt that the pre-test counselling was an interaction that involved the communication of clinical information. Dealing with the possibility of receiving a positive test result was something that she felt she had to work through in her own time and not during the pre-test counselling. The distress that individuals experience while going through predictive genetic testing and following result delivery has been previously studied by Hirschberg, Chan-Smutko & Phil (2015). They identified that distress is influenced by several factors including availability of support and coping styles. Personal experiences in dealing with a family history of cancer and the support of family members are described in this study as a means of preparing individuals to receive their results.

A study by Cox (2003) explored how individuals at risk for HD make the decision to request PT. The author describes how five of the 16 study participants that chose to pursue PT felt that the decision was something that they had evolved towards. Living with a long awareness of a family history of HD and having an affected parent in the preceding years resulted in participants experiencing increased levels of anxiety about learning that they were at risk for HD and possibly having inherited the mutation as well as the imminent onset of the condition. There is often a period of weighing up the usefulness of knowing one's mutation status and deciding whether or not to know if they have inherited the disease-causing mutation, therefore suggesting that the decision to pursue testing is often made prior to starting the PT process (Cox, 2003).

It is possible that these findings would also apply to participants undergoing PT for HBOC. Similarly, some participants in the present study felt that their decision to pursue testing was influenced by their family history of HBOC, experiencing the death of an affected relative or living with a relative diagnosed with breast or ovarian cancer. Their long awareness of the condition and their personal experiences is what influenced their willingness to know and be tested when PT was made available to them. Considering the fact that all study participants had undergone testing and received a result, they must have, at some stage, contemplated the benefits of knowing their mutation status. Interestingly, all of the participants that felt that the pre-test counselling was not sufficient in helping prepare them for receiving their results were also identified in the previous theme as choosing to pursue testing out of a sense of duty to their families or in solidarity with family members that had already been tested. This may mean that these individuals had not thoroughly explored the possibility of receiving a positive test result as their motives for doing the test were focused on supporting a relative. In addition, the one hour of pre-test counselling would not have been enough to prepare them for the possibility of receiving a positive test result. The role of pre-test counselling in the PT process will be discussed in further detail in the following sub-theme.

4.5.2 THE BIGGER PICTURE

As introduced in the previous theme, there are numerous factors that were found to influence an individual's decision to pursue PT for HBOC. These included a family history of cancer, cancer-related distress and a perceived sense of duty to family members and children. While some study participants felt that the pre-test counselling sufficiently prepared them to receive their results, there were other participants who didn't feel the same way. For some participants, as demonstrated in the previous sub-theme, it was the support from their family members and their family history of breast and ovarian cancer that helped prepare them. Participant 10 said that the possibility of receiving a positive result was something that needed to be worked through on her own.

It is important to consider the bigger picture and where the pre-test counselling session fits into it, in the context of the individual and their unique story. It is also important to understand what factors prepare a patient for receiving their result. Having a better understanding of the factors motivating individuals to pursue testing, their personality traits and coping mechanisms used when facing the possibility of receiving a positive test result, the effectiveness of pre-test counselling may be enhanced (Biesecker, *et al.* 2000). A study by Lodder, *et al.* (2003) found that distress is more likely to occur in individuals at risk of being carriers if they have experienced the serious repercussions of cancer in their family. Considering prophylactic intervention and anticipating that their problems will increase if they are identified as a carrier, were amongst some of the factors found to increase distress in these individuals. In some cases, individuals may decline testing because they feel that they are not emotionally prepared to deal with the consequences of receiving a positive test result (Lodder, *et al.* 2003).

Pre-test counselling for individuals undergoing PT for HBOC is focused on collecting relevant medical and psychological information about the patient, providing the patient with information about HBOC and the testing process and exploring the impact that the testing could have on the individual and their lives going forward. In some cases, medical management options are discussed and patients are encouraged to get their affairs in order with regard to life insurance and medical insurance in an attempt to prevent future insurance discrimination (Lerman & Shields, 2004).

While the pre-test counselling content is tailored for each individual, the genetic counsellor or clinician providing the service is not familiar with each individual's unique life story nor do they administer personality assessment tools to obtain a better understanding of the individual's personality or coping styles. These healthcare providers are reliant on the information that their patients are willing to share with them or that they are aware of themselves. Therefore, it is impossible to be aware of all the factors influencing an individual's decision. Genetic counsellors from the various institutions sampled in this study describe a similar approach to pre-test counselling, covering the same content. This is illustrated in the following interview excerpt by participant 3:

"I think the process was very good because we went in there first having to state what we know about it, what were our expectations, etc. What would we do if we were to test positive, what we would do if we were to test negative, why we doing this. So, we were very ... so you either well informed or you are not. So, I think she helped guide us and make sure we were going in the right direction with what we are thinking about. It was good, it was really good, it was very informative. And it helped prepare you for either outcome, so, even if you were negative, it doesn't mean you are, it doesn't mean you will never get breast cancer or ovarian cancer, so, the process was quite good, I think, and it helped us prepare well."
(P3)

When asked about the provision of psychological support during the pre-test counselling period one genetic counsellor explained that unlike the South African PT protocol for HD, which necessitates that individuals undergoing PT consult with a clinical psychologist prior to receiving their results, there are no formal South African guidelines for individuals undergoing PT for HBOC. Therefore, the decision to refer patients for additional psychological support is at the discretion of the clinician or genetic counsellor providing the service. In some cases, patients may request a referral or personally seek out additional psychological support.

Emotional distress is an important factor to consider in the PT process. Higher levels of emotional distress have previously been found to be associated with decreased satisfaction with information provided during pre-test counselling, as were familial dysfunction and greater perceived cancer risk (O'Neill, *et al.* 2017). The provision of information can be an effective way in which to manage uncertainty. Patients are able to increase their knowledge and understand their situation, which provides them with a greater sense of control and facilitates informed decision making (Dean, *et al.* 2017). In line with this, some participants in this study felt that the information provided during pre-test counselling helped them to cope with their situation:

"It helped me, expanded my knowledge about everything and yeah they just helped me cope a bit more, I felt better." (P12)

However, there were participants that explained that should they have received a positive result they weren't sure if they would have coped. This is illustrated by the following quotes by participant 13:

"And then again, you know, positive [mutation-negative] it was fine, there was nothing to worry about. Whereas if it was negative [mutation-positive], maybe I would've regretted it, maybe I would've regretted it, you know, I don't know, maybe I would have been unprepared, I don't know how I would've responded in that situation." (P13)

"But again, my results came out as being okay. If I had found out that I did have this gene, I'm not sure I would've been, you know, I don't know how I would have dealt with it. And I thought oh I would've done this I would've done that but I don't know how emotionally prepared I would have been to receive a no." (P13)

Based on the various responses received from participants in this study, additional psychological support prior to result delivery may not benefit all patients undergoing PT for HBOC but it may be beneficial to some. It is important to take into account the fact that while the majority of participants felt that the pre-test counselling sufficiently prepared them to receive their results, many of these participants were found not to carry the mutation. As illustrated in participant 13's quote above, their perceptions may have been different if they were

found to be mutation carriers. It is important to therefore consider what each participant believes what it means to be prepared. For some, it was the factual information and improved understanding and for others it was knowing that they had the support of their family members.

One of the study participants described this a difference between “head knowledge” and “emotional knowledge”. While the provision of information tailored towards the specific needs of the client may prepare participants for the possibility of receiving a positive result, it is difficult to determine beforehand if they are also emotionally prepared. The pre-test counselling may be sufficient in improving “head knowledge” but based on the findings of this study, in some cases, it may be lacking in improving “emotional knowledge”. The capacity to improve this “emotional knowledge” is limited by the time constraints of the pre-test counselling session and the healthcare provider’s ability to identify aspects of an individual’s personality and their coping styles within this time frame.

The second theme encompasses the participants’ experiences of the PT process, in particular the role of pre-test counselling in preparing individuals to receive their results. While most of the study participants felt that the pre-test counselling sufficiently prepared them for receiving their result, there were some participants that felt that it was their personal experiences in dealing with their family history of cancer and support from their family members that prepared them for receiving their results. The tailoring of pre-test counselling content may not always be sufficient in preparing individuals emotionally for receiving their result. As discussed in this theme, it is important to consider the bigger picture and the unique factors influencing an individual’s decision to pursue testing. Following the pre-test counselling, the participants then chose to proceed with molecular genetic testing and then received their results once they were available. The participants’ post-test perceptions will be further explored in theme 3.

4.6 THEME 3 – WHAT NOW? POST-TEST PERCEPTIONS

Participants that received a positive result felt that they required additional support following result delivery, this included practical, emotional and social support. These findings also highlight the fact that receiving a negative result does not always minimise distress as some individuals felt guilty about not carrying the mutation. One participant described her experience of feeling isolated as a positive mutation-carrier.

4.6.1 ADDITIONAL SUPPORT

A significant sub-theme that arose, particularly amongst the positive mutation carriers, was the need for additional support following a positive diagnosis. This included both practical and emotional support. Concerns were raised about the fact that there is no holistic service geared towards supporting individuals who are mutation-positive. *BRCA1* and *BRCA2* mutation carriers often face difficulties when making decisions regarding the best manner in which to manage their breast cancer risk. They need to decide between screening or prophylactic intervention. This decision is often made without clear direction as to which option is best for them. (Brunstrom, Murray & McAllister, 2015). This is highlighted in the following quotes by participant 2:

“This lady that I go to now, she does mammograms but it’s not a holistic service geared towards supporting you as a person who is BRCA positive. So, I feel that is lacking. Like afterwards I was a fish now out of water trying to be a professional in something that is not my profession. I now had to say ... and then I had to convince my husband who is this, you know, who is now basically standing there saying okay what are you doing, how do you know what you’re doing is right? I don’t know but I’m doing the best that I can.” (P2)

“So, that I feel is lacking and so now it’s up to me to make sure that I do things. So, I feel like, you know, if I’m missing something or if there’s something new or whatever, unless I go and dig, I’m not going to find it. Whereas if I go to a professional that provided a holistic service, I would feel more at ease, if that makes sense.” (P2)

Similarly, other participants expressed that they wanted additional support from established support structures or individuals that had been through similar experiences. This is illustrated by participant 7:

“But if I had someone to talk to and maybe someone who is like me, it could help and to say okay well, you know, you might feel this you might feel that, you might have to have that extra procedure or even if this person was just having one operation and be like well why do you feel so scared, it’s not actually that scary, I found a Caesarean more painful, I don’t know, it’s help, it helps because there’s nothing like

human, kind of interaction and someone's experience, you know because no one experience is the same but, and everyone's lives are different, but if you can help in anyway and it's you know, by talking to someone then I think that would be helpful." (P7)

Participant 2, in the above quote, describes how not only did she feel overwhelmed by the test results, but she felt that she would have benefitted from consulting with a medical professional who provided a holistic service geared towards the surveillance of individuals who are mutation positive or by having a formal support structure to help guide her in making sure that she was taking the necessary steps and precautions to manage her risk. Similarly, participant 7 felt that she would have benefitted from an experienced individual's guidance and support. The need for additional support after a positive predictive test is also supported by the finding that there were some participants who sought out additional emotional support and psychotherapy after receiving their result.

Genetic counselling has been shown to play an integral role in managing the levels of anxiety and distress amongst these individuals by empowering them to make informed and autonomous decisions about possible treatment, engaging in preventative behaviours and managing the perceptions of risk (Scott, *et al.* 2005). The uncertainties associated with being neither sick nor healthy can create new concerns for these individuals as they attempt to integrate their risks into their way of life. There is an increased awareness that they may develop cancer within a particular time frame without knowing if or when it will happen (Harmsen, *et al.* 2015; Scott, *et al.* 2005).

A study by Harmsen, *et al.* (2015) analysed the effect of medical decision making on the quality of life of women with a *BRCA1* or *BRCA2* mutation. Females with a *BRCA1* or *BRCA2* mutation were shown to present with increased cancer-related distress and worry and an increased perception of risk within the first year following receiving their genetic testing results. Distress levels do tend to fluctuate around times of surveillance visits and abnormal screening results. Decreased levels of distress and cancer-related worry were observed following risk-reducing interventions. Females that opted for prophylactic surgery displayed high levels of satisfaction with their decision (Harmsen, *et al.* 2015). These findings support the findings of the present study as participants who were found to be mutation carriers felt that they had higher cancer-related distress following a positive diagnosis and that around the time of surveillance visits they were highly distressed. Participants that underwent prophylactic surgery felt that they had decreased levels of cancer-related distress and were happy with their decision.

One of the most robust predictors of future psychological distress is the distress present at baseline. Individuals that have greater baseline distress are at an increased risk for future psychological distress (Hirschberg, Chan-Smutko & Pril, 2015). This is illustrated in the following interview excerpt:

“It was that kind of trauma that just, it was just an ongoing thing and people always say to you sometimes forewarned is forearmed, they say that, but with that also don’t tell you is that when you have the kind of anxiety that I have, you have a tendency to want to know more and sometimes the more you know the worse for you because then your brain starts playing all the signs.” (P14)

“When you’re lying down watching TV and all of a sudden something comes to mind, now I’ve been carrying that two heavy bags from where I live to the hospital and back. So now I’ve obviously pulled a muscle in my back or something, and now I’m lying watching TV and I’m like hey what’s that pain, and my God could this be the start of it. And then I’ll start Googling.” (P14)

Participant 14 was the only male participant that was found to be mutation-positive. The above quote illustrates that knowledge of his mutation status resulted in increased levels of anxiety and cancer-related distress. This participant also explained that as a naturally anxious person, the positive result had a negative effect on his psychological well-being. This participant also felt that he is now constantly aware of changes to his body and that he may perceive normal pains as being possible signs of developing cancer.

Hesse-Biber (2014) found that the perceived risk of developing cancer amongst female study participants was not based on the statistical risk values provided by a physician or genetic counsellor but rather reframed in the context of important factors including family history, personal experience of living with a relative that had been diagnosed with cancer or died from cancer and the availability of support and information from family, friends and other social relationships. Findings from the present study support these findings as the perception of cancer risk was found to be influenced by a family history of breast or ovarian cancer and the participants’ personal experiences in dealing with their family history. The availability of both formal and social support was found to influence the perceived controllability of developing cancer.

During the interviews, most of the participants reflected back on their experience of the PT process, how the pre-test counselling prepared them for receiving their result and how emotionally difficult it was for them to wait for their results. Participants tested in private typically waited between a week and two weeks to receive their results, while in most cases participants that had testing done through a public institution waited approximately six to eight weeks to receive their results. Most participants described the period of waiting for their results as being very stressful and that they experienced heightened levels of anxiety. Despite most

participants feeling that they were prepared to receive their results, some of them felt that in retrospect they may have benefitted from receiving additional support from a psychologist or someone from a mental health background while waiting to receive their results. This was particularly evident, but not exclusively, amongst participants who tested positive.

“When I think back I feel many people can benefit if, say [my genetic counsellor] or whoever is on the other side, to say listen this is a hard week awaiting you, I recommend you just go and see a therapist or here are two names, that always helps, they work with people going through this. I think it will help a great lot with many people just to go and sit there and, you know, just help them go through, sort out stuff all the thoughts and emotions that go through because I went through that.” (P10)

Hirschberg, Chan-Smutko & Pril (2015) have argued that at any point in the genetic testing procedure there are opportunities to identify individuals that are distressed and make appropriate psychology referrals. Genetic counsellors need to evaluate an individual’s psychological functioning during the first pre-test counselling session and assess their ability to provide truly informed consent, as this may be impaired during periods of psychological distress. During pre-test counselling, patients should be allowed to explore the possible testing outcomes and anticipate thoughts and emotions about the possible results. By imagining the possible consequences of the testing results in the various facets of their life, they are better able to engage their coping mechanisms to try and modulate distress and to engage in preparatory planning (Hirschberg, Chan-Smutko & Pril, 2015). Although these suggestions have been made with affected individuals presenting for genetic testing in mind, similar considerations would apply for asymptomatic individuals undergoing predictive genetic testing.

The delivery of genetic counselling plays an important role for at-risk individuals and their families during this time. Genetic counsellors are uniquely positioned to provide support to individuals undergoing PT and assist in guiding them through a complex decision making process to enable them to manage their risk (McCrea & McCutcheon, 2017).

4.6.2 IT SHOULD HAVE BEEN ME

PT for *BRCA1* and *BRCA2* mutations has been shown to have an impact on family functioning and relationships. A negative testing result can result in feelings of guilt, particularly in cases where other family members have been found to carry a *BRCA1* or *BRCA2* mutation. This is a phenomenon that is referred to as ‘survivor guilt’ (d’Agincourt-Canning, 2001; Douglas, Hamilton & Grubs, 2009).

Some study participants expressed that they felt guilty because they had received a negative result. Despite being alleviated from the cancer-related distress, some individuals experienced feelings of guilt knowing that

they did not test positive, suggesting that it would have been fair to at least carry the mutation. The quotes below illustrate some of these responses:

"I said I'm negative I know and I started crying. They asked me 'why' and I said because I was hoping I'm gonna have it." (P4)

"I wanted to be like my sister. I didn't want her to go through it alone, I really didn't want her to go through it alone." (P4)

"So, for me, yeah that was also very hard that, that's why I just realised I must go test myself but I actually thought it should've been me. And I, I, I think I said to her at one stage I almost want to ask you for forgiveness is that it's you and not me." (P10)

"Yeah, it wasn't fun, it wasn't fun and then I actually felt guilty when I was not. It should've been fair for me to at least have the gene or, just not have cancer." (P10)

Participant 12 expressed how she hadn't accepted the fact that everyone else in her family that had been tested was found to carry the mutation and that she was the only one who tested negative.

Interviewer: *"And how did their positive results have an effect on you?"*

P12: *"I don't think I've actually accepted it yet. I don't know why. I don't think I've accepted it yet, like I don't know."*

Survivor guilt has been associated with profound effects on family relationships and difficulties in communication (Hallowell, *et al.* 2006; Huggins, *et al.* 1992). These individuals may find it difficult to communicate information about their mutation status to relatives that are mutation-positive and have difficulty with knowing how to support these relatives (Hallowell, *et al.* 2006; Goelen, *et al.* 1999). Conversely, there were also individuals that felt isolated as mutation carriers. These individuals felt that it was difficult to talk to family members that had tested negative. Participant 2's quote below illustrates this:

"So, initially that first six months it was really hard. And I couldn't speak to anybody about it. It's just, my sisters don't have it, my parents and the older generation they just go about their life they're not into checks and research and what not. But afterwards it's just, now it's just something on my list to do and I do it." (P2)

Family members who receive a positive test result can manifest a variety of strong emotions including shock, fear, anger and guilt. A positive test result can cause individuals to feel isolated within their family structures, especially if they find it difficult to communicate with other family members (Douglas, Hamilton & Grubs, 2009; Phelps, *et al.* 2007). This was particularly evident for participant 2 as she was the only sibling that received a positive test result. This concept of individuals testing positive and feeling isolated in their families is not unique to HBOC as it has also been described in families with HD and familial adenomatous polyposis (Douglas, Hamilton & Grubs, 2009; Duncan, *et al.* 2008).

Some of the positive mutation-carriers that had children explained that they didn't realise that their children could potentially be at risk and that once they had been informed of this possibility they felt distressed. This is demonstrated in the following quotes:

"And for me one of the saddest things is that at some point I'm going to have to tell my sons and my daughter that potentially they have this." (P2)

"Initially I got a fright about that because I didn't think about it. When I first got the result, I wasn't thinking about my children and then it suddenly, you know, I was like oh my God my daughter, never mind the boys, my daughter, I mean and the boys." (P15)

"I know how [my mother] feels because my son is growing up, everything, you know, we're feeling his breasts also now because he's young but he can have it too. And he can give it too." (P16)

Several studies have shown that affected parents feel guilty or distressed about transmitting genetic mutations to their children and that they blame themselves for having put their children at risk of disease. This is not only seen in *BRCA1* or *BRCA2* mutation cases, but has also been documented with conditions such as myotonic dystrophy and cystic fibrosis (d'Agincourt-Canning, 2001; Faulkner & Kingston, 1998; Fanos & Johnson, 1995; Hallowell, *et al.* 2006).

The participants' post-test perceptions and experiences were highlighted in this theme. Upon reflection, some participants felt that they may have benefitted from additional psychological support while they were waiting for their result. Participants that received a positive diagnosis felt that they required additional support, both practical and emotional support, after receiving their result. Survivor guilt appeared to be a common consequence of receiving a negative result. The period following result delivery can elicit a variety of emotions and for some necessitate a call to action. The consequences of knowing one's result are explored further in theme 4.

4.7 THEME 4 – CONSEQUENCE OF KNOWING

The fourth theme addresses some of the post-test perceptions and attitudes of the participants after they had received their testing results. Despite receiving a negative test result, many participants felt that they had the same concerns and that their result did not mean that they were risk free. These findings will also illustrate the participants' attitudes towards breasts and prophylactic intervention and address the power of knowledge.

4.7.1 I'M NOT CANCER-RISK FREE

The impact of genetic counselling content on health behaviour was investigated in the United States of America by Kelly, *et al.* (2015). The researchers were able to conclude that following genetic counselling and receiving a positive diagnosis, women were more likely to consider prophylactic surgeries and cancer screening, ovarian cancer screening especially. Interestingly, those that received genetic counselling followed by a negative result continued to opt for age-related population screening. It was postulated that the decision to continue cancer screening was likely as a result of genetic counsellors discussing the implications of cancer screening, highlighting the critical role of genetic counselling in genetic testing (Kelly, *et al.* 2015; Scott, *et al.* 2005). Similarly, the current study also showed that those receiving a negative test result also opted for continued cancer surveillance due to residual cancer worry. This is illustrated in the following quotes:

“So, I readily go for, I do breast examinations and I ask the doctor to check because despite my results I have to be vigilant because we live in a time and a space, you know, you still have to be vigilant and take care of yourself.” (P1)

“Because colon cancer is the other one that is rife in our family so obviously, that is something that you can't let just park so we were encouraged that okay your risk is less for this one but just remember that that little bugger is still waving his hello flag on that side of the guy so just to be vigilant regarding that.” (P1)

“So, I feel my risk has definitely lessened but at the rate that cancer is prevalent, especially breast cancer in women at the moment, there is no guarantee. I'm well aware that the risk is still there and ja, I know my risk is lessened but it's still a risk.” (P3)

“I have the same concerns. I just know that I don't have that weakness in my body. That's the only thing I know I don't have. But it is possible that my mother died of another cancer. So, and many other people died because of cancer that's got nothing to do with the gene that I don't have. No, and

therefore I go for my tests just to be grateful that it's negative or otherwise to pick it up if it's there. No, I have the same risks. Yeah.” (P10)

As can be seen, receiving a negative result does not exempt individuals from experiencing distress as there is still some remaining uncertainty. This was particularly evident in cases where there were other types of cancer in the family. Many participants explained that receiving a negative result did not mean that they were free from any cancer risk and that based on their family history they felt there would always be some residual risk. The above quote by participant 10 illustrates how the PT result simply excluded one type of cancer but it was still important to remain vigilant for other types of cancer. She felt that her negative result did not reduce her risks for developing cancer.

There are often conflicting emotions of relief, guilt and fear, amongst others, associated with receiving a negative result. Some studies have shown that these individuals will continue to have some residual cancer-related worry and seek out additional cancer screening, particularly at those younger ages (Hirschberg, Chan-Smutko & Pril, 2015; Macrae, *et al.* 2013). In keeping with the findings by Hirschberg, Chan-Smutko & Pril (2015), this highlights the importance of ensuring that individuals have an accurate perception of their risk and emphasising that the risk of developing cancer is not binary, not only during the PT process but also after receiving their results.

4.7.2 IT'S THE DISFIGUREMENT

Concerns have been raised regarding the psychological harm of PT for *BRCA1* and *BRCA2* mutations and undergoing prophylactic surgery. Risk-reducing strategies can influence levels of anxiety and psychological distress, as well as overall physical health (Harmsen, *et al.* 2015; Stan, *et al.* 2013). RRBM is a visibly disfiguring and permanent intervention that has the potential to affect an individual's sexual functioning and body image (Harmsen, *et al.* 2015; Meijers-Heijboer, *et al.* 2000).

Three of the six study participants that tested positive for a familial *BRCA1* or *BRCA2* mutation had undergone prophylactic surgery in an attempt to manage their risks. Two participants underwent a RRBM and one participant underwent a BSO. All three participants expressed that they were relieved that their risk following prophylactic surgery was reduced. The remaining mutation-positive individuals had opted for regular surveillance as a means to manage their risk. Of the three participants that opted for regular surveillance, one participant was male and the remaining female participants chose not to have surgery because they were concerned about the disfigurement of having their breasts removed. Harmsen *et al.* (2015), identified factors influencing female mutation carriers' decision to choose prophylactic surgery, which included a younger age, having had children, a

strong family history of cancer and increased cancer-related distress. These were the same factors identified in the present study.

One of the greatest concerns raised by the study participants with regard to prophylactic intervention is that unlike a prophylactic hysterectomy or BSO which is 'internal' and not physically visible to the outside world, the RRBM was referred to as being 'external' and that the physical disfigurement can be seen. This is consistent with what is described in some literature which shows that females that are mutation-positive are more likely to opt for a prophylactic BSO when compared to prophylactic RRBM (Johns, *et al.* 2017). The majority of female participants, regardless of their mutation status, expressed fears about feeling like less of a woman and that their breasts were central to how they identified themselves and how they felt their husbands identified them.

"So, ja, I was scared about feeling like less of a woman and then the other thing is the ovarian cancer where they say you can have your, have a what, a hysterectomy but then you go into menopause and I'm like hell no, you know. I just wasn't ready to do that, I don't think I'll ever be ready to do it unless I need to. It's like if you have a bad tooth, you first try and fill it before you pull it out." (P2)

"Yes, I mean as a woman to not have breasts, my husband loves breasts, like I think he's obsessed with breasts, you know. So, imagine if I didn't have breasts." (P2)

"I would never be able to, I won't have nipples, ja. So, that kind of, that kind of threw me." (P15)

Importantly, in addition to participant 15's quote above, she explained how the decision to have a prophylactic BSO was an easy one because it was not something that would be outwardly visible. The thought of not having breasts and specifically nipples is what influenced her decision to not have a RRBM and to opt for regular breast surveillance instead.

Participant 13 explained how, as a male, his concerns were centred around the disfigurement of breast surgery. He recalled how difficult the experience was for his male relatives who had undergone mastectomies following a diagnosis of breast cancer and that prior to learning about his family history he had always assumed that breast cancer was only associated with being female.

"I think it's not so much for me, it's not saying oh well I have breast cancer, I think it's the disfigurement of surgery, the cosmetic side of it and then people looking at you and going, it's just an odd place to have scars if you're a man, I think, and if it's uncovered. I mean, my dad's got his scars and it's not too noticeable, he just doesn't have nipples which is odd." (P13)

Despite the fears associated with body image, the two mutation-positive female participants who had opted for having a RRBM felt strongly about their decision and did not regret the choices that they had made. For these participants, the cancer-related worry that was associated with not having the surgery far outweighed their fears about their change in body image. This is illustrated in the following interview excerpts:

“And I was, you know, I was lucky, I was done with that tissue, I’ve been a mom, I’ve breast fed, I’ve done it all and not to say that I wouldn’t have looked at some form of augmentation later on anyway.” (P7)

“I was petrified for this, I was petrified, but I would rather like take something out that could go bad and that for me was just like my approach and how I just felt about it.” (P7)

This is in agreement with previous literature which found that women who opted for a RRBM, after receiving a positive PT result and adequate counselling, were relieved from the fear of developing cancer and rarely expressed regret regarding their decision (Meijers-Heijboer, *et al.* 2000). The two mutation-positive female participants who opted for RRBM expressed that the decision to not have a prophylactic BSO was based on the fact that they were concerned about having to go through menopause at a young age. Following a recommendation by her gynaecologist, one of these two participants had opted to have her fallopian tubes removed as an additional prophylactic measure.

4.7.3 EMPOWERED BY KNOWLEDGE

Most of the participants felt that the PT process had a positive impact in that it allowed them to increase their knowledge and understanding about what it means to be a *BRCA1* or *BRCA2* mutation carrier and it provided them with an opportunity to receive the correct information. They felt empowered by the knowledge that they had received as a result of undergoing PT.

“So, we realised that, you know, we’ve got something that our aunts and grandparents didn’t have and that’s the power of knowledge.” (P1)

“That’s the thing, you know, if you, I mean I understand we don’t all know how or when or what we are going to be, what we could get with different cancers or this or that, heart disease, but if you can find out what you are predisposed to, it’s about having that knowledge, knowledge is power, like for me that’s what I felt, I felt really strongly about.” (P7)

These findings are similar to those identified in previous studies in which the perceived advantages of receiving genetic counselling and genetic testing were that individuals felt that they had an increased knowledge of HBOC,

improved awareness about their breasts and feeling more in control about managing their risks (Brunstrom, Murray & McAllister, 2016; Hamilton, Lobel & Moyer, 2009).

Some participants felt that by knowing their mutation status and their cancer-related risks, they could better manage their risks and take precaution where necessary. For those that tested negative, they felt that they could live their lives without worrying about whether they were at risk.

“I feel much better, I feel happier because I don’t have to take that extra precaution and I can actually live now because I’m obviously young still and the thought of me, if I did have it, removing my breasts or my ovaries for example. I mean, I obviously want to have children one day and that was quite scary, so yeah. It helped me a lot.” (P12)

“So, I feel lucky that I know because I’ve been able to take steps and I’m still taking steps now” (P15)

Individuals knowing that they are potentially at risk for HBOC, based on information provided by family members, may experience fear and uncertainty about their personal risks, but the knowledge of one’s mutation status and risk values can be empowering and a beneficial outcome of doing the test. Individuals potentially at risk are likely to seek out advice from genetic counsellors or healthcare professionals in order to improve their understanding of HBOC, determine their risks and take action to prevent cancer or manage their risks, where necessary (Brunstrom, Murray & McAllister, 2016; Crotser & Dickerson, 2010).

Many participants explained that by going through the PT process, they experienced a change in their family dynamics. It forced individuals to have difficult conversations and allowed them to open up about their family history. Many described that their families grew stronger as a result, regardless of the outcome of the testing. This is illustrated in the following interview excerpts:

“That’s why I said it forced people to have difficult conversations which is a good thing in our ... community, to put it that way. Everything is always under the wraps in the big ... we don’t speak about illness ever.” (P1)

“And let’s be honest, we are much stronger than ever before. I’m feeling now like we much closer, we much open. The bond now is even stronger.” (P4)

“The main results for me is that we became much, much closer as a family and that we learn something, something very valuable and that we can share with other people and I think no one can take that away from us.” (P9)

The discovery of a cancer-predisposing mutation in a family has previously been shown to have a positive effect on some family relationships. For some families, it may serve as a means to engage in conversations about cancer or to allow for increased contact between family members (Douglas, Hamilton & Grubs, 2009). Conversely, in some cases individuals may feel isolated within their families or feel that they have been forced to pursue testing. Individuals who receive a positive test result may find it difficult to disclose their results to family members who are still at risk or have received a negative test result (Van Riper & McKinnon, 2004). In a study by d'Agincourt-Canning (2001) which explored the experiences of genetic risk, the research participants found that genetic testing allowed for the strengthening of relationships amongst family members due to the importance of the information that had been disclosed. Similarly, McInerney-Leo, *et al.* (2005) reported that there was a perceived improvement of family cohesiveness, regardless of whether individuals had chosen to pursue PT.

In summary, the participants' post-test perceptions and the consequences of knowing one's result are explored in the fourth theme. Participants in this study felt that a negative test result did not mean that they were free from risk for developing cancer and that there was some remaining uncertainty. Concerns were raised about the psychological and physical harms associated with prophylactic intervention and particularly the visible, physical disfigurement of a RRBM. Overall, participants felt that they were empowered by knowing their mutation status and they could better manage their risks and take precaution where necessary and some experienced a positive change in their family dynamics. However, the need for support throughout the PT process appeared to be a recurrent theme, regardless of the testing outcomes. The role of support in the PT process will be explored in the subsequent theme.

4.8 THEME 5 – SUPPORT AND ITS ROLE IN THE PREDICTIVE TESTING PROCESS

In this study, support has been identified as an overarching theme. Support from healthcare providers, from families, the need for additional practical and emotional support following a positive diagnosis and the need for support in the period leading up to receiving their results. Several participants expressed their gratitude for the support that they had received throughout the PT process, not only by the healthcare providers but also by their family members. The following quotes illustrate how the study participants felt supported by the healthcare providers throughout the PT process:

“So, it’s all thanks to you guys, for helping, for assisting us. You guys were there supporting us, the family, the counselling. I mean from the beginning of this process, it really was a big help to the family. If it wasn’t for you guys we would have been lost. If it wasn’t for the counselling, I don’t know. I don’t think we would have survived it.” (P4)

“They were very sympathetic, I was like in tears and you could see that, you could see the concern and you could actually feel the love man and the support when they talk to you. They didn’t just talk to you, you could see that they really cared and I think that made me feel more at ease because I was very supported.” (P9)

The need for additional social and emotional support was raised by several participants, both prior to receiving their results as well as following result delivery. The need for emotional support following result delivery was raised almost exclusively by positive mutation carriers, however there was one participant who received a negative result but felt that there could have been additional support following result delivery:

“And then what I also wanted, suggestions or whatever, they could just every year at least just to keep us positive phone us and find out how you feel. I mean, but now after the test and the results it was just quiet. Nobody phone back and say do you still remember you came for this test and how do you feel, are you still okay and all that, but they don’t.” (P11)

Mutation-carriers felt that they could benefit from increased support and follow up as well as continued interaction with healthcare providers following result delivery:

“And then afterwards, once the result is out, if somebody could speak to you. Like in my case, I had other things going on in my mind, then to say okay, you know, maybe this is what you could do or look into, or whatever the case is.” (P2)

"I even phoned my medical aid. I said to them look, you know like you have a cancer program, what do you have to support somebody in my situation? They say no you can only register on the cancer program once you have cancer, you see. So, that was another door closed. There wasn't somebody that I could speak to there, which is wrong." (P2)

"Maybe having a little bit of a support with regard to the psychology aspect. Also, maybe as a person who's been through it, if you could get matched up with someone perhaps within the same so socio-economic group, or demographic, or maybe not, I don't know, there's different people and we all react differently." (P7)

Men and women that undergo predictive genetic testing for hereditary cancer syndromes may experience psychological distress during the time that they are going through the process of testing or following identification of their mutation status, differently (Hirschberg, Chan-Smutko & Pril, 2015). Individuals that are said to be 'at-risk' are asymptomatic mutation carriers that are aware of the potential of a disease becoming reality. As a result, these individuals occupy a unique position within the healthcare system, redefining what it means to be a patient. Given that the risk values are not absolute and that there is variability in the penetrance estimates, they are constantly confronted with the possibility of future suffering. These individuals often find themselves in a position where they are neither healthy nor affected, but rather a hybrid of the two (Scott, *et al.* 2005).

In addition to participant 2's quote above, she explained how she had subscribed to overseas newsletters and joined forums which support unaffected mutation carriers and that after extensive research she could not find any similar services in SA. Similarly, the following participants explained how they would have benefitted from talking to individuals that have been in a similar position:

"So, and you're dealing with human beings, you know, and a hell of a lot emotion and is specially for a female and maybe their kids haven't had kids, I don't know, there is a lot to it all, so it's hard to put a box and say this is how they must be treated, but as I say, maybe having a little bit of a support with regard to the psychology aspect but also maybe at person who's been through it, if you could get matched up with someone perhaps within the same so socio-economic group, or demographic, or maybe not, I don't know, there's different people and we all react differently." (P9)

"The questions I had is like, somebody that goes through it, I want to speak to somebody like that. A psychiatrist doesn't know. They can say okay fine I'm so sorry to hear it and good luck with it and how do

you feel. It's not that. You want to know, the stuff I wanted to know are if it's sore, what will I expect afterwards, did you have nausea, what's going to happen, are you depressed.” (P16)

The lack of desired support for mutation carriers has been illustrated in the above comments. As cancer risk assessment and PT for hereditary cancer syndromes becomes more readily available, it is essential that service providers meet the mental health needs of these at-risk, but otherwise unaffected individuals (Hirschberg, Chan-Smutko & Pril, 2015). Genetic counsellors, in particular, are well suited to provide pre-test and post-test counselling in a supportive environment, as well as assisting patients in making sense of what their results mean for them and their family members and addressing the emotional impact throughout (Arning, *et al.* 2015). In SA, however, there are only approximately 25 practicing genetic counsellors which means that this service is also largely offered by other healthcare professionals (Ormond, *et al.* 2018). It is therefore important that all healthcare professionals offering this service are able to identify individuals that require additional psychosocial and practical support and make the necessary referrals or recommendations.

4.9 CHAPTER SUMMARY

In summary, the study results were presented. The results were discussed and linked to the aim and objective of the study. Following analysis of the interview data five themes were identified. These themes were explored through interview excerpts and were supported by published literature. In the final chapter, the conclusions of the study are presented, as well as the strengths and limitations of the study. Recommendations will be presented for future research relating to PT for HBOC.

CHAPTER 5: CONCLUSIONS, STRENGTHS AND LIMITATIONS OF THIS STUDY AND RECOMMENDATIONS FOR FUTURE RESEARCH

5.1 CHAPTER INTRODUCTION

This chapter will include (1) a summary of the relevant findings of the research, (2) the researcher's personal reflection, (3) a discussion of the strengths and limitations of this study, (4) practical implications of this research and (5) recommendations for future research.

5.2 CONCLUSIONS

This qualitative research study aimed to explore the experiences of individuals undergoing PT for HBOC in the Western Cape, SA and their perceptions of the PT process. By investigating these individuals' perspectives and experiences of undergoing PT for HBOC, this research aimed to understand what factors influence an individual's decision to pursue PT, how effective the pre-test counselling is in preparing them to receive their result and their post-test perceptions. Fifteen individuals that underwent PT for a familial *BRCA1* or *BRCA2* mutation were interviewed in this study. The interviews were transcribed verbatim and thematic analysis was performed using the framework approach. Five themes were identified from the participants' accounts as they related to the aim and objectives of this study.

The first theme focused on the pre-test period. In particular, the influence of their family history of cancer and the factors influencing their decision to pursue PT. It was found that participants mainly chose to have testing because they felt a responsibility to their families and their children or future children to know their risk and manage it where possible. Some participants chose to be tested out of a sense of duty to their family members affected by breast or ovarian cancer, or both, or because their family members were being tested at the same time. Experiencing a family member being diagnosed with cancer or the loss of a family member resulted in increased cancer-related distress amongst participants. Most participants felt that their family history of cancer increased their risk perception and influenced their decision to test.

The second theme identified addresses how the participants felt the pre-test counselling prepared them to receive their results. While most participants felt that the information provided during pre-test counselling helped prepare them to receive their result, there were some participants that felt that while the pre-test counselling was informative, it wasn't what prepared them to receive their results. Some participants felt that the support from their family and their experiences in dealing with a family history of cancer is what prepared them for their results. Some participants felt that their perceptions of the pre-test counselling may have been different if they had been found to be mutation-carriers.

It was found that some participants felt guilty about receiving a negative result. Survivor guilt was evident amongst individuals who were tested concurrently with other family members and amongst those who had a living relative diagnosed with breast or ovarian cancer. It was also found that some individuals who tested negative felt that their result did not exempt them from experiencing cancer-related distress and that based on their family history they were still at risk for developing cancer. Some individuals experienced shock and grief by learning that their children could also be at risk.

One of the greatest concerns raised by the study participants with regard to prophylactic interventions was the disfigurement of a RRBM. Most female participants, regardless of their mutation status, expressed fears about feeling like less of a woman and that their breasts were central to how they identified themselves and how they felt their husbands identified them. One male participant felt that it was an odd place for a male to have scars. Despite these fears, three female participants had proceeded with a RRBM and did not regret their decision.

Overall, most participants felt empowered by the knowledge of their mutation status and that they were able to better manage their risks and take precaution where necessary or live their lives without worrying about whether they were at risk. Some participants explained that by going through the PT process, they experienced a positive change in their family dynamics and that there was improved family cohesiveness.

The need for additional support, both practical and emotional support, was particularly evident amongst mutation-carriers. Mutation-carriers need to make difficult decisions about how to best manage their risk going forward, deciding between surveillance and prophylactic options. Concerns were raised about the lack of a holistic service geared towards supporting individuals who are found to be mutation carriers, particularly those that chose surveillance over prophylactic intervention. Some participants felt that they would have benefitted from formal psychological support, while others felt that they would have preferred to talk to someone that had been through a similar experience.

In conclusion, the findings of this study indicate that there is a need for additional support both throughout the PT process, as well as following result delivery irrespective of the setting in which the service is provided. While the pre-test counselling content appears to be sufficient in facilitating informed decision-making, individuals are not always emotionally prepared to receive their result and to deal with what their result means in the context of their unique situation. In SA, there are no formal guidelines or testing protocols in place for individuals undergoing PT for HBOC, meaning that the PT process, including the counselling content and provision of support before and after result delivery, may vary across the institutions and genetic counsellors that offer this service. In other countries, such as Belgium, there are established PT protocols for HBOC which include a psychological framework and medical and psychological follow-up following result delivery (Decruyenaere, *et al.* 2000b). As

found in Belgium, it is evident that the individuals in this study have support needs beyond what is being offered to them or what works best for them. The participants clearly communicated a need for more emotional support and this should be addressed in our local setting. In addition, they communicated a need for informal support such as support group. This has been highlighted by several studies. These have highlighted the benefits of support groups and organisations that are focused on providing support for individuals that receive a positive PT result for HBOC. These less formal support structures are able to connect individuals share similar experiences (Hoskins, Roy, & Greene, 2012).

This need for further support could be addressed by adapting current PT protocols. While these findings do not suggest that there is a need for a uniform PT protocol for all individuals undergoing PT for HBOC in SA, healthcare providers in this setting need to be able to recognise where additional support is required and make recommendations where necessary. As seen in the present study, psychological challenges can arise throughout the process, from decisions to pursue testing, to making decisions based on the outcomes of the PT results. Based on the findings of this study and literature by Hirschberg, Chan-Smutko & Pril (2015), the guidelines in table 5 below have been proposed to assist genetic counsellors and healthcare providers offering PT for HBOC in meeting the psychosocial needs of the individuals being tested.

Table 5: Proposed pre-test and post-test counselling consultation guidelines

Pre-test counselling consultation	Post-test counselling consultation
<ul style="list-style-type: none"> • Explore why the patient is there and their reasons for wanting to pursue PT • Obtain a comprehensive family history taking note of any children/other relatives that may be at risk • Provision of information on HBOC and cancer risks associated with the familial mutation <ul style="list-style-type: none"> - Clarify that this is a genetic predisposition and not a test to determine if the individual will develop cancer or not • Encourage individual to explore possible testing outcomes and what they would do if they tested positive or negative • Discuss management options if positive (surveillance and risk-reducing surgery) • Discuss possibility of life insurance discrimination • Explore psychosocial impact of positive and negative result • Explore how the result would affect future decision-making and planning • Explore their support system • Discuss information dissemination/risk communication in family • Provide emotional support • Discuss testing approach and practical arrangements (turn-around time, plan for result delivery, etc.) and offer support during waiting period • Decide on whether they want to proceed with testing or delay it • Consider referral for additional psychosocial support in the following cases: <ul style="list-style-type: none"> - Increased baseline distress or anxiety - History of depression or mental illness - Elevated risk perception - Complicated grief - Individuals with children - Loss of a relative to hereditary cancer • Provide written information • Plan for follow-up 	<p data-bbox="911 260 1458 289"><i>Individuals who receive a negative test result:</i></p> <ul style="list-style-type: none"> • Discuss screening for early detection according to general population recommendations • Consult family history to determine if other family members should be tested and if/how they need to be notified • Consider referral for additional psychosocial support in the following cases: <ul style="list-style-type: none"> - If individuals display signs of depression - Survivor guilt • Open invitation for follow-up <p data-bbox="911 877 1458 907"><i>Individuals who receive a positive test result:</i></p> <ul style="list-style-type: none"> • Re-discuss risk implications (cancer and familial risks) • Provide emotional support • Discuss management options • Refer to breast specialist and gynaecologist to discuss surveillance and/or risk-reducing surgery options and plan for follow up • Provide summary letter • Consult family history to determine if other family members should be tested and if/how they need to be notified • Consider referral for additional psychosocial support • Consider referral to support groups (including overseas if none available locally) • Follow-up call after 6 months

Although some of the findings in this study are similar to those identified in previous international literature, the outcomes of this study have provided valuable insight into the perspectives and experiences of individuals undergoing PT for HBOC, which has not yet been explored in this local setting. The findings of this study are able to potentially impact the services that are provided to individuals undergoing PT for HBOC. The strengths and limitations of this study are listed below.

5.3 STRENGTHS OF THIS STUDY

- This study is the first to employ qualitative research methods to explore the perspectives and experiences of individuals undergoing PT for HBOC in a South African setting.
- The use of a semi-structured interview guide, including open-ended questions, encouraged participants to answer questions openly and without restriction.
- Several of the participants felt that despite the emotional nature of their experiences, the interview process allowed them to share their story, an opportunity that many of them hadn't done before, and found it to be helpful and therapeutic.
- The use of purposive sampling aided in the recruitment of individuals that highlighted novel issues that are specific to the selected settings in the Western Cape, and may be relevant to other settings in SA and countries that provide the same service.
- Owing to the fact that there are small numbers of genetic counselling students in SA conducting qualitative research pertaining to genetic disorders, these findings are valuable in contributing to the growth of this field locally.

5.4 LIMITATIONS OF THIS STUDY

- While the aim of undertaking qualitative research methods was for practical growth of the researcher, this was the researcher's first attempt at qualitative research and interviewing. The consequence is that there was variability in the quality of the interviews.
- All of the interviews were conducted in English. Not all of the participants' first language was English and despite being offered to include an interpreter, they chose to have the interview conducted in English. The participants whose first language is not English may not have been able to express themselves fully.
- There may have been some ascertainment bias as the perspectives and experiences of those unwilling to participate or those that are less communicative are not included. This is commonly associated with purposive sampling.
- One of the limitations of recruiting individuals from both the public and private sectors is that there is a greater volume of individuals receiving medical and health services in the public sector than there are in

the private sector. Every attempt was made to have adequate representation of participants from both groups. However, the main objective was to obtain as comprehensive a view on the PT process for HBOC as possible in the Western Cape and not to make comparisons between the two sectors.

- The fact that the researcher is undergoing genetic counselling training at one of the institutions sampled in this study may have affected the responses obtained from individuals sampled from the institution.

5.5 PRACTICAL IMPLICATIONS OF THIS STUDY

Certain aspects of this research may have future practical implications and are recommended below:

- Increased provision of formal emotional support for participants that are undergoing PT for HBOC, prior to result delivery and once the results have been delivered, as it is important that participants feel supported throughout the PT process and post-delivery of results.
- Establish a formal referral protocol which ensures that mutation-positive individuals are referred to the appropriate specialist services for further management. This will allow them to feel secure in knowing that they are taking the necessary steps to manage their risk in an informed way.
- The formation of a support group for mutation carriers which would create a forum for mutation carriers to openly discuss issues or concerns that they have, to share experiences and to gain insight from individuals that have been in a similar position.
- It is important that clinicians and genetics healthcare professionals providing this service and supporting mutation carriers understand the perspectives and experiences of individuals undergoing PT for HBOC, in order to meet the specialised needs of these individuals and to work towards improving service delivery.
- There is evidence from this research to suggest that guidelines should be drafted with recommendations to assist with the provision of additional psychosocial support throughout the PT process.

5.6 RECOMMENDATIONS FOR FUTURE RESEARCH

The following recommendations have been made in an attempt to guide future research:

- Although it would possibly be difficult, it would be beneficial to explore the experiences of individuals that have a family history of HBOC but choose to decline to pursue PT and the reasons for doing so.
- Exploring the perspectives and experiences of individuals undergoing PT for HBOC between the ages of 18 and 25 years. Several international studies have highlighted that young adults are particularly vulnerable in that they are at a stage in their lives where they are building a career, developing

partnerships and possibly becoming parents. Having one participant in this age group was not sufficient to evaluate the impact of presymptomatic testing for HBOC in young adults.

- Exploring the perspectives and experiences of individuals that undergo PT for mutations in genes other than *BRCA1* and *BRCA2*, which are associated with an increased risk for developing breast cancer.
- The financial implications of PT did not appear to be of significant concern amongst the individuals sampled in this study. Interestingly, concerns were raised about the financial implications of increased surveillance and prophylactic intervention amongst mutation-positive participants. Future research should explore this topic in a local setting and make comparisons between the public and private sectors.
- Explore the topic of insurance discrimination amongst individuals in SA that have received their PT result.

5.7 CHAPTER SUMMARY

In this chapter, conclusions have been made based on the research outcomes, the strengths and limitations of this study have been presented, as well as the practical implications of the research and recommendations for future research.

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APPENDICES

APPENDIX A: SOCIO-DEMOGRAPHIC QUESTIONNAIRE

Socio-Demographic Questionnaire

To be completed by the participant:

1. Name:
2. Age:
3. Gender (please circle): Male/Female
4. Are you in a stable relationship (please circle): Yes/No
5. Do you have any children? If yes, how many:
6. Country of origin:
7. Employment status (please circle): Employed/Unemployed

If employed, what work do you do?
8. Highest Education level (please circle): Primary school/high school/tertiary education/none

To be completed by the researcher:

9. Mutation status (if optionally provided by participant):
10. Private/public and institution:

APPENDIX B: INTERVIEW GUIDE

- Tell me about yourself and your experiences with cancer
 - Prompts:
 - Which of your family members were affected by breast or ovarian cancer?
 - How old were they when they were diagnosed?
 - How old were you when they were diagnosed?
 - How did their diagnosis impact you?
- Tell me about your emotional/social support system
 - Prompts:
 - How did your family members feel about your decision to undergo predictive testing for HBOC?
 - Were there people that you chose not to tell or couldn't tell?
- Why was it important to you whether you carried the mutation?
 - Prompts:
 - What factors influenced your decision to undergo predictive testing?
 - Do you feel that you are independent or do you rely on the advice or guidance of friends to family members?
- How do you feel now that you know your result?
 - Prompts:
 - What do you think the main advantages and disadvantages are of knowing your predictive testing result?
- Tell me about the process that you underwent
 - Prompts:
 - What worried you the most about not knowing your mutation status?
 - What medical professionals were involved in this process?
 - How do you think the process prepared you to receive your result?
 - How do you feel your concerns were addressed?
 - What was the result that you were expecting?
 - How do you feel about your risk for developing breast or ovarian cancer?
 - What socio-economic factors or barriers do you think were present at the time that you were undergoing predictive testing?
- Do you feel that you needed anything else during the process?

- Prompts:
 - Additional sessions
 - Psychologist
- What was the actual information that was conveyed to you?
 - Prompts:
 - What was said about the implications of the results?
 - Do you feel that you were sufficiently informed?
- What worries or concerns did you have during this process?
 - Prompts:
 - What did you do or who did you speak to about your worries or concerns?
 - How have your concerns changed since knowing?
- How did this process prepare you for receiving your results?
 - Prompts:
 - Do you think anything could have been done differently during this PT process?
- Have you told anyone about your mutation status?
 - Prompts:
 - How did you feel about telling them your mutation status?
- Is there anything that you felt I did not cover?

Participant Information Sheet

STATEMENT BY PARTICIPANT

I, _____ confirm that:

1. I have been invited to be involved in the above-mentioned research project which has been initiated through the division of Human Genetics at the University of Cape Town. I understand that 15-20 other adult participants will be involved in the study and that my name and other personal information will not be discussed with the other participants or with anyone else not involved in the study.
2. I understand that the objective of the study is to understand how individuals, in the Western Cape Province of South Africa, perceive and experience the predictive testing procedure for hereditary breast and ovarian cancer (HBOC).
3. I understand that the interview will take place in a private setting at Groote Schuur Hospital (GSH), Tygerberg Hospital, a private genetic counselling practice (PVT) or telephonically, on a pre-scheduled date and time that is agreeable for me, the participant, and the researcher.
4. I understand the interviews will take approximately 60 minutes. Should it be required that the interview run for longer than this allocated time, I, the participant, would be invited to reschedule at my earliest convenience to continue the interview.
5. I understand that I voluntarily choose to participate in this study and if I choose to no longer continue that my decision will not in any way affect the health care services I currently receive at GSH, Tygerberg Hospital or UCT Private Academic Hospital.
6. I understand that the questions may cause emotional reactions and that I may choose not to answer any questions if I do not wish to do so. I understand that I may decide to stop with the interview process at any point if I feel uncomfortable or too emotional and that this will not impact on my pre-existing and future healthcare in any way. A genetic counselling session can be arranged if I would like to discuss anything further.

7. I understand that my involvement in the study may contribute to health care professionals having a better understanding of the impact of predictive genetic testing for HBOC on individuals in the South African public and private healthcare systems. This information will assist health care professionals in understanding how various medical, counselling and therapeutic options can be adjusted accordingly to the needs of these individuals.
8. I understand that all information collected will remain confidential and will be used for research purposes only.
9. I understand that the interview will be recorded for research purposes. All audio recordings will be safely stored under lock and key and information stored on a password-protected computer. I understand that only the researcher, her supervisors and examiners will have access to the data. All recordings will be destroyed upon completion and publication of this study and all identities will remain anonymous.
10. I understand that the interview will take place in English and that the researcher will be administering the interviews herself and if I do not feel comfortable communicating in English and require a translator, a suitably trained individual will be used to translate the interview and supplementary documentation.
11. I understand that this study has been approved by the registered Human Research Ethics Committee at the Faculty of Health Sciences at the University of Cape Town. I have been given contact details should I wish to contact the committee about how I was treated as a research participant.
12. I have the researchers contact details in the event that I would like to contact her regarding further questions about this study.
13. _____ has explained the information of this study in English or in _____ through the use of a suitably trained translator and I understand this information.

APPENDIX D: PARTICIPANT CONSENT FORM

Participant Consent Form

I hereby declare that I have voluntarily agreed to participate in the above-mentioned research study and that the interview can be audio-recorded.

Signed at:

(Address of venue) _____ on _____ 2018.

Participant Name

Witness Name

Participant Signature

Witness Signature

If you have any questions regarding your rights as a research participant, please contact the Human Research Ethics Committee at the Faculty of Health Sciences of the University of Cape Town.

Professor Marc Blockman (Chairperson of the Human Research Ethics Committee):

Tel: (021) 406 6496

If you have any questions regarding the research or the research procedure, please contact the researcher or her supervisor:

Monica Rodrigues Araujo (Researcher): Tel: 083 406 2350 | Email: arjimon001@myuct.ac.za

Dr Tina-Marié Wessels (Supervisor): Tel: (021) 406 6304 | Email: tina.wessels@uct.ac.za



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20 October 2017

HREC REF: 564/2017

Dr TM Wessels
Human Genetics
Room 4.23
Falmouth Building-FHS

Dear Dr Wessels

PROJECT TITLE: PERSPECTIVES AND EXPERIENCES OF INDIVIDUALS UNDERGOING PREDICTIVE TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER (HBOC) SYNDROME IN THE WESTERN CAPE, SOUTH AFRICA (MSc CANDIDATE - MS M RODRIGUES ARAUJO)

Thank you for your response letter dated 06 October 2017, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30 October 2018.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Monica R Araujo will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate Institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

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