Decisions surrounding risk-reducing salpingo-oophorectomy (RRSO): Experiences of *BRCA*-positive women

by

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ABSTRACT

Women with pathogenic or likely pathogenic variants in *BRCA1* or *BRCA2* ("*BRCA*-positive") have an increased risk of developing high grade serous ovarian cancer (HGSOC). The majority of HGSOC develops in the fallopian tubes and later spreads to the ovaries and peritoneal cavity. Therefore, *BRCA*-positive women may consider risk-reducing salpingo-oophorectomy (RRSO) to preventatively remove their ovaries and fallopian tubes. The Hereditary Gynecology Clinic (HGC) in Winnipeg specifically targets care to the unique needs of *BRCA*-positive women through an interdisciplinary team of gynecological oncologists, menopause specialists, and registered nurses. A mixed-methods study design was used to explore the decision-making processes of *BRCA*-positive women considering (or who completed) RRSO, and how this decision was influenced by experiences with healthcare providers at the HGC.

BRCA-positive women without a previous diagnosis of HGSOC and who had previously received genetic counselling were recruited from the HGC and the Shared Health Program of Genetics & Metabolism. Forty-three women completed a survey and 15 completed an interview about their experiences and decisions surrounding RRSO. Surveys were analyzed to compare scores on validated scales related to decision-making and cancer-related worry. Interviews were transcribed, coded, and analyzed using a generic qualitative research approach called interpretive description, which is a commonly used to explore clinical phenomena.

The results of this study demonstrated that *BRCA*-positive women face complex decisions that are intertwined with unique experiences. *BRCA*-positive women interpreted their HGSOC risk through a personalized "lens" of contextual factors that impacted perceptions about the practical and emotional implications of RRSO, and therefore the need for surgery. Mean scores on validated scales evaluating the HGC's impact on decisional outcomes and

preparedness for decision-making about RRSO were not significant, indicating that the HGC played a supportive role for *BRCA*-positive women rather than helping with decision-making itself. Strategies for improving support, decisional outcomes, and the overall experiences of *BRCA*-positive women attending the HGC are described.

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LIST OF ABBREVIATIONS

ADP: Adenosine diphosphate
BRCA: Breast cancer (susceptibility) gene
BRCT: *BRCA1* C-terminal
CA125: Cancer antigen 125
CWS: Cancer worry scale
DCS: Decisional conflict scale
DSB: Double-strand break
DTC: Direct-to-consumer
EOC: Epithelial ovarian cancer
GC: Genetic counsellor
GO: Gynecological oncologist
HBOC: Hereditary breast and ovarian cancer
HCC: Hereditary Cancer Clinic
HCP: Healthcare provider
HGC: Hereditary Gynecology Clinic
HGSOC: High grade serous ovarian cancer
HRR: Homologous recombination repair
HRT: Hormone replacement therapy
HSC: Health Sciences Centre
ISDO: Interval salpingectomy with delayed oophorectomy
MRI: Magnetic resonance imaging
N: No
N/A: Not applicable
NCCN: National Comprehensive Cancer Network
NHEJ: Non-homologous end joining
NMD: Nonsense-mediated mRNA decay
OB: Oligonucleotide binding
ODSF: Ottawa Decision Support Framework
P/LP: Pathogenic/likely pathogenic
PARP: Poly (ADP-ribose) polymerase
PeriMP: Peri-menopausal
PI: Principal investigator
PostMP: Post-menopausal
PreMP: Pre-menopausal
PrepDM: Preparation for decision-making scale
REDCap: Research electronic data capture
RING: Really interesting new gene
RRSO: Risk-reducing salpingo-oophorectomy
STIC: Serous tubal intraepithelial carcinoma

SWD: Satisfaction with decision scale
TAH: Total abdominal hysterectomy
TVU: Transvaginal ultrasound
VUS: Variant of uncertain significance
Y: Yes

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

There are many implications to consider and decisions to make as a result of being breast cancer (susceptibility) gene (*BRCA*)-positive (i.e. individuals with a heterozygous, germline pathogenic or likely pathogenic [P/LP] variant in the *BRCA1* or *BRCA2* genes). In addition to making surgical and screening decisions related to an increased risk of breast, ovarian, and other cancers, women with P/LP variants in *BRCA1/2* are forced to consider how these decisions may impact their physical and mental health, family members, and relationships, among other complex factors. This is further compounded by the differential weighing of factors considered to be more or less pertinent depending on a woman's stage of life as well as personal and family history that may inform their perceived cancer risk. Healthcare providers (HCP), such as genetic counsellors (GC) and gynecological oncologists (GO), are specially equipped to guide patients through this potentially overwhelming time by providing relevant information and emotional support. The unique needs of *BRCA*-positive women have previously been recognized and attempts have been made to tailor healthcare accordingly, such as by the advent of the Hereditary Gynecology Clinic (HGC) in Winnipeg that provides care and resources specific to women at an increased risk for gynecological cancers. GCs that provide women with positive *BRCA1* and/or *BRCA2* genetic test results refer *BRCA*-positive women to the HGC to learn more about their age-related ovarian cancer risk and discuss the option of risk-reducing salpingo-oophorectomy (RRSO).

1.1.1 Research questions

The primary goal of this study was to explore how and for what reasons *BRCA*-positive women make decisions about whether or not to pursue RRSO (i.e. the decision-making process).

Embedded within this main research question are sub-questions: Are the factors and processes involved in decision-making different between: 1) pre- and post-menopausal women; or, 2) those who consulted a GO/gynecologist about RRSO versus those who did not. In addition, this study explored the overall experiences of *BRCA*-positive women with their HCPs, including GCs and GOs within the HGC, and the resulting influence of these interactions (if any) on their decision-making process.

1.2 HEREDITARY BREAST AND OVARIAN CANCER

All cancer is genetic in the sense that it develops as a result of P/LP variants in certain genes that help to regulate cell homeostasis, including processes such as DNA repair and cell division. The majority of cancers are sporadic. Sporadic cancers can develop due to the accumulation of somatic, deleterious variants in a number of tumor suppressor and oncogenes over one's lifetime for multifactorial reasons, including age, environment, and lifestyle. Less commonly (approximately 10-15% of the time), cancer predisposition can be hereditary (National Comprehensive Cancer Network, 2020). Individuals with hereditary cancer are born with a germline P/LP variant in one copy of a highly penetrant gene known to be associated with an increased risk for developing certain types of cancer. These individuals are at an increased risk for developing cancer because they only require one additional somatic P/LP variant in the second copy of the gene to contribute to cancer development (National Comprehensive Cancer Network, 2020). There is a large amount of variability in expressivity among individuals with germline P/LP variants in genes known to be associated with hereditary cancer, with the risk of developing cancer being greater in those that have a significant family history (Hartmann & Lindor, 2016). Cumulative lifetime risk of cancer is also affected by age, with the lifetime risk

being initially higher in younger individuals but decreasing the longer someone lives cancer-free (Chen & Parmigiani, 2007; Hartmann & Lindor, 2016). Hereditary cancer often occurs earlier in life and is inherited in an autosomal dominant fashion, meaning there is a 50% chance of passing on a germline P/LP variant in a gene known to be associated with a hereditary cancer syndrome to offspring. Therefore, hereditary cancer has implications for the individual with the genetic predisposition, as well as their family members (National Comprehensive Cancer Network, 2020).

Hereditary breast and ovarian cancer (HBOC) is a hereditary cancer syndrome associated with germline P/LP variants in the *BRCA1* and *BRCA2* genes. HBOC is associated with an increased lifetime risk for both breast and ovarian cancer, both of which will be discussed in the following sections. However, a focus will be placed on data related to ovarian cancer for the purpose of this thesis. The National Comprehensive Cancer Network (NCCN) guideline estimates that individuals with a *BRCA1/2* P/LP variant have a lifetime risk for breast and ovarian cancer between 41-90% and 8-62%, respectively, depending on the study population (National Comprehensive Cancer Network, 2020). More specifically, other studies have shown that individuals with P/LP variants in *BRCA1* have about a 46-65% risk of developing breast cancer and a 20-50% risk of developing ovarian cancer in their lifetime (Berliner et al., 2013; Hirst et al., 2018). Individuals with germline P/LP variants in *BRCA2* are at a 43-45% and a 5-23% lifetime risk of developing breast and ovarian cancer, respectively (Berliner et al., 2013; Hirst et al., 2018). This is compared to the general population risk of breast cancer of about 12% (Petrucelli et al., 1993). Ovarian cancer is rarer in the general population with an incidence of about 1.5% (Petrucelli et al., 1993). The risk for developing a second primary breast cancer approaches 50% for women with *BRCA1* and *BRCA2* P/LP variants (Graeser et al., 2009). Other

cancers associated with P/LP variants in *BRCA1* and *BRCA2* are male breast cancer, prostate cancer, pancreatic cancer, and melanoma (National Comprehensive Cancer Network, 2020). Table 1.1 summarizes the increased cancer risks and current screening guidelines for individuals with a P/LP variant in *BRCA1* and/or *BRCA2*. Annual mammograms and breast magnetic resonance imaging (MRI) are recommended starting at 30 years of age. Breast MRIs with contrast may be considered as early as 25 years of age based on personal and family history of breast cancer (National Comprehensive Cancer Network, 2020). Mastectomy and chemoprevention options, such as tamoxifen, may also be considered to reduce breast cancer risk. There are currently no recommended surveillance or chemoprevention guidelines for women at an increased risk for developing ovarian cancer. Therefore, individuals with a P/LP variant in *BRCA1/2* are left to consider RRSO as the most effective and viable option to reduce the risk of developing ovarian cancer (National Comprehensive Cancer Network, 2020). Guidelines suggest that men with *BRCA1* and/or *BRCA2* P/LP variants have clinical breast exams annually starting at approximately 35 years of age, and prostate cancer screening starting at 40 years of age (National Comprehensive Cancer Network, 2020). Both men and women with *BRCA2* P/LP variants may consider completing annual skin exams to screen for melanoma. Until recently, there have been no clear screening guidelines for pancreatic cancer. Emerging data has demonstrated the efficacy of pancreatic cancer screening for detecting surgically resectable disease and improving mortality in individuals with P/LP germline variants in pancreatic cancer susceptibility genes. Updated screening recommendations for individuals with *BRCA1* and *BRCA2* P/LP variants suggest considering pancreatic screening beginning at 50 years of age (or 10 years younger than the earliest diagnosis of exocrine pancreatic cancer) if the individual has a family history of one or more first degree relatives with exocrine pancreatic cancer on the same

side of the family with (or presumed to have) the identified *BRCA1/2* variant (National Comprehensive Cancer Network, 2020).

Table 1.1: *BRCA1* and *BRCA2*-related cancer risks and corresponding screening and management guidelines.

Type of cancer	*BRCA1*-related lifetime risk (%)	*BRCA2*-related lifetime risk (%)	General population lifetime risk (%)	Increased surveillance	Chemoprevention	Preventative surgery
Breast cancer						
Breast (female)	46-65	43-45	12	• Breast awareness starting at 18 years of age • Clinical breast exam every 6-12 months starting at 25 years of age • Annual mammogram starting at 30 years of age • Annual breast MRI starting at 25-30 years of age	• Medications to lower cancer risk in unaffected individuals such as: Selective estrogen receptor modulator (SERM) (i.e. Tamoxifen or Raloxifene), Aromatase inhibitor	• Mastectomy
Second primary breast	50	50	0.5-1 per year	N/A	N/A	• Mastectomy
Breast (male)	0.2-2.8	3-12	0.1	• Clinical breast exams annually starting at 35 years of age	N/A	N/A
Ovarian cancer						
Ovarian*	20-50	5-23	1.5	• Semi-annual TVU and blood testing for CA125 beginning at 30 years of	• Prolonged oral contraceptive use (≥5 years) can reduce ovarian cancer risk by up to 60%	• RRSO may be considered at 35-40 and 40-45 years of age for

Type of cancer	*BRCA1*-related lifetime risk (%)	*BRCA2*-related lifetime risk (%)	General population lifetime risk (%)	Increased surveillance	Chemoprevention	Preventative surgery
				age (NOT recommended)		individuals with *BRCA1* and *BRCA2* P/LP variants, respectively
Other cancers						
Prostate	Elevated	30-40	17	• Blood testing for prostate-specific antigen (PSA) starting at 40 years of age	N/A	N/A
Pancreas	Possibly elevated	5	1.3	• Consider pancreatic cancer screening at 50 years of age (or 10 years younger than earliest diagnosis in family) if family history is present	N/A	N/A
Melanoma	Possibly elevated	3	1	• Annual skin exams	N/A	N/A

N/A: Not applicable; TVU: Transvaginal ultrasound; CA125: Cancer antigen 125. *All ovarian cancers, including HGSOC. Adapted from (Berliner et al., 2013; Hirst et al., 2018; Malcolmson, 2019; National Comprehensive Cancer Network, 2020).

Ovarian cancer can develop from epithelial, germ, epidermoid, stromal, and border cells (Hirst et al., 2018). Epithelial ovarian cancer (EOC) is the most common, comprising 90% of ovarian cancers (Navaneelan & Ellison, 2015). EOC can be divided into five histological subtypes: high grade serous, low grade serous, endometroid, clear cell, and mucinous (Hirst et al., 2018). High grade serous ovarian cancer (HGSOC) is the most common histological subtype of EOC. HGSOC represents ~70% of all EOC diagnoses (Köbel et al., 2010) and accounts for 70-80% of EOC deaths (Bowtell et al., 2015; Lakhani et al., 2004; Schrader et al., 2012; Song et al., 2014). Therefore, HGSOC will be used when referring to ovarian cancer for the remainder of this thesis. The precursor lesions for HGSOC largely originate in the fallopian tube distal secretory epithelial cells. These benign-appearing lesions have characteristic mutant p53 protein expression and subsequently progress to serous tubal intraepithelial carcinoma (STIC), followed by carcinoma *in situ* that can metastasize to the peritoneal cavity and ovary (Jones & Drapkin, 2013; Levanon et al., 2008). While a substantial proportion of HGSOC arises from the fallopian tube epithelium, recent research using mouse models suggests that HGSOC can also originate from the ovarian surface epithelium (Zhang et al., 2019). The cell of origin may define transcriptional and behavioural differences in HGSOC, with HGSOC originating from the fallopian tube epithelial cells showing greater propensity for metastasis and responsiveness to chemotherapy than HGSOC that arises from the ovarian surface epithelium (Zhang et al., 2019). HGSOC is characterized by high genomic instability caused by P/LP variants in genes involved in homologous recombination repair (HRR) pathways (Bowtell et al., 2015; Hirst et al., 2018; Kroeger & Drapkin, 2017). Studies have estimated the prevalence of *BRCA1* and *BRCA2* loss-of-function variants to be 11-25% in individuals with HGSOC (Jones & Drapkin, 2013; Schrader et al., 2012; Song et al., 2014). The prevalence of *BRCA1/2* P/LP variants has been reported as

even higher (~39%) in individuals with metachronous HGSOC and breast cancer (Chao et al., 2020). Other genomic alterations present in HGSOC include *BRCA1* promoter hypermethylation, gain-of-function *TP53* variants (present in >95% of HGSOC), and cyclin E1 (*CCNE1*) amplifications (Hirst et al., 2018; Kroeger & Drapkin, 2017).

The heterogeneity of HGSOC makes treatment with single molecularly-targeted therapies difficult. HGSOC is initially quite responsive to platinum-based chemotherapies in combination with a taxane; however, resistance eventually emerges in 80-90% of patients (Bowtell et al., 2015; Hirst et al., 2018). The most significant recent breakthrough in the treatment of HGSOC has been the utilization of poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitors. PARP is a protein involved in single-stranded DNA break repair through the base excision repair pathway (Hirst et al., 2018; Taylor & Eskander, 2018). PARP inhibitors prevent PARP from facilitating base excision repair. This leads to the development of DNA double-strand breaks (DSB) at the replication fork that cannot be repaired in cells with defective HRR, resulting in DNA damage and eventual apoptosis (Bryant et al., 2005; Farmer et al., 2005; Hirst et al., 2018; Taylor & Eskander, 2018). PARP inhibitors are therefore 1000-times more sensitive in tumor cells with *BRCA1* and *BRCA2* P/LP variants compared to wild-type tumor cells (Taylor & Eskander, 2018). The recent SOLO-1 clinical trial demonstrated that women with newly diagnosed HGSOC and P/LP *BRCA1* and *BRCA2* variants had a 70% reduced risk of disease progression or death when receiving the PARP inhibitor olaparib after initial chemotherapy treatment compared to those taking a placebo over a median follow-up of approximately 40 months (Moore et al., 2018; Norquist, 2019). PARP inhibitors are indicated for treatment and maintenance in individuals with germline *BRCA1* and *BRCA2* P/LP variants and a diagnosis of HGSOC, fallopian tube, or primary peritoneal carcinoma following primary chemotherapy

(Taylor & Eskander, 2018). Based on these clinical responses, it is clear how beneficial the identification of P/LP *BRCA1* and *BRCA2* variants through genetic testing is early on in the course of HGSOC treatment (Norquist, 2019). This is true in both the germline and somatic context. It is now common practice for germline *BRCA1/2* testing to be offered to all patients with HGSOC, fallopian tube, or primary peritoneal cancers regardless of family history (which may be absent in more than 40% of cases) (George et al., 2017). This is true across all Canadian provinces, where genetic testing is routinely offered to individuals with isolated, non-mucinous EOC, including HGSOC (McCuaig et al., 2018). Recent research has shown that while approximately 57% of *BRCA1* and *BRCA2* P/LP variants identified in patients with HGSOC turned out to be hereditary upon completion of germline testing, about 43% of patients had a somatic *BRCA1/2* P/LP variant present in the tumor only (n=51 patients with HGSOC and an initially identified tumor *BRCA1/2* P/LP variant; 44/51 underwent genetic predisposition testing; 25/44 with germline P/LP variant) (Vos et al., 2019). As a result, there is a recent push towards a universal tumor *BRCA1/BRCA2* testing workflow in order to identify patients with negative germline *BRCA1/2* testing who may still be eligible for PARP inhibitor therapy given their tumor test results (McCuaig et al., 2018; Vos et al., 2019).

1.3 *BRCA1* AND *BRCA2*

The *BRCA1* and *BRCA2* genes remain the most important known predisposition genes for HBOC. The chromosomal locations of *BRCA1* and *BRCA2* are 17q21.31 and 13q13.1, respectively (Petrucelli et al., 1993). *BRCA1* consists of 24 coding exons and *BRCA2* has 27 coding exons (Petrucelli et al., 1993). Putative functional domains in *BRCA1* include the 5' really interesting new gene (RING) domain (implicated in protein-protein interactions such as

with BARD1), a coiled coil domain (binding partner with PALB2), and the 3' *BRCA1* C-terminal (BRCT) domain (Rebbeck et al., 2015; Venkitaraman, 2001). Functional domains in *BRCA2* include a conserved, eight amino acid repeat unit termed the BRC repeat domain (mediates binding with RAD51), DNA-binding and tower domains, as well as oligonucleotide binding (OB) folds (associated with localization of *BRCA2* to the site of DSBs) (Rebbeck et al., 2015; Venkitaraman, 2001). The types of variants identified to date in *BRCA1* and *BRCA2* vary greatly, and can be anything from insertions and deletions to missense and nonsense variants (Anglian Breast Cancer Study Group, 2000; Rebbeck et al., 2015). The ClinVar database (https://www.ncbi.nlm.nih.gov/clinvar/) lists a total of 3,028 P/LP variants in *BRCA1* and 3,481 in *BRCA2*, the majority of which are deletions resulting in a frame shift and loss of protein function.

Variants in certain "cluster regions" in *BRCA1* and *BRCA2* have been identified and found to be associated with differential breast and HGSOC risks (Rebbeck et al., 2015). An observational study by Rebbeck et al. (2015) sampled 19, 581 women with *BRCA1* and 11, 900 women with *BRCA2* pathogenic variants from 55 centers worldwide between 1937 and 2011 (the ascertainment date reflects the earliest date at which the individual came to the attention of a HCP or researcher, even though their research participation, genetic testing, and research data collection may have occurred years later). Among *BRCA1* carriers, 9,052 women were diagnosed with breast cancer, 2,317 were diagnosed with ovarian cancer (including HGSOC) and 1,041 were diagnosed with both breast and ovarian cancer. For *BRCA2* carriers, 6,180 women were diagnosed with breast cancer, 682 with ovarian cancer (including HGSOC) and 272 with both breast and ovarian cancer (Rebbeck et al., 2015). In particular, the researchers identified an ovarian cancer cluster region within exon 11 of *BRCA1* (c.1380 to c.4062) associated with a

relatively increased risk for ovarian cancer (including HGSOC). Of the variants identified in this region, those leading to nonsense-mediated mRNA decay (NMD) and causing premature termination were associated with the greatest risk for and earlier onset of HGSOC, while missense variants, in-frame deletions and nonsense variants not leading to NMD were associated with lower HGSOC hazard ratios (Rebbeck et al., 2015). Similarly, two ovarian cancer cluster regions localized to exon 11 within *BRCA2* (c.3249 to c.5681 and c.6645 to c.7471) were identified, with those leading to nonsense mediated decay being associated with higher HGSOC risk (Rebbeck et al., 2015).

The frequency of *BRCA1* and *BRCA2* P/LP variants in the general population is approximately 1:400 to 1:500 (Petrucelli et al., 1993). Nonetheless, founder effects do exist in certain populations. Population "founders" are groups of individuals who, for a time, remained isolated and consequently had high rates of consanguinity. This resulted in a normally rare variant becoming more common in the founder population (Ferla et al., 2007). The most prevalent founder population in reference to HBOC and *BRCA1/2* P/LP variants is the Ashkenazi Jewish population, whose ancestors originated in eastern and central Europe (Struewing et al., 1997). The combined frequency of specific founder P/LP variants in *BRCA1* (185delAG and 5832insC) and *BRCA2* (6174delT) in the Ashkenazi Jewish population is just over 2% (Struewing et al., 1997). In Canada, other important founder effects to consider are those identified in French Canadian, Indigenous, and Icelandic populations. In the province of Quebec, particularly the southern regions of Lac St. Jean/Saguenay and the area surrounding the St. Lawrence River, eight founder P/LP variants in *BRCA1* and *BRCA2* have been identified. The most common are nonsense variants in *BRCA1* (C4446T) and *BRCA2* (8765delAG) (Tonin et al., 1998). Two separate families of Cree and Ojibwe ancestry from Sandy Lake in Saskatchewan

and Shoal Lake, Manitoba have been identified as having the same variant in exon 11 of *BRCA1* (1510insG and 1506A>G in close proximity on the same allele), suggesting the presence of a founder effect in the Indigenous population (Liede et al., 2002). Finally, Manitoba has a significant Icelandic population. The c.771_775del5 (also commonly referred to in the literature as 999del5) founder variant in *BRCA2* has a carrier frequency of approximately 0.4% in Icelandic individuals (Janavičius, 2010; Johannesdottir et al., 1996). The molecular consequence of all of these founder variants is ultimately the loss of functional BRCA1 and/or BRCA2.

BRCA1 and BRCA2 are involved in many cellular processes, including transcription regulation, cell-cycle checkpoint activation, and DNA repair (Prakash et al., 2015). The role of BRCA1 and BRCA2 in DNA repair is crucial in understanding HBOC. Specifically, BRCA1 and BRCA2 are tumor suppressors involved in DSB repair through HRR. BRCA1 and BRCA2 function to maintain the integrity of the genome by interacting with other factors, such as RAD51 and PALB2, to precisely repair DSBs by copying the sister chromatid template (Powell & Kachnic, 2003; Prakash et al., 2015). HRR is active during the G_2 and S phases of the cell cycle (Prakash et al., 2015). BRCA1 and BRCA2 are also involved in a second DSB repair mechanism called non-homologous end joining (NHEJ). NHEJ is active during all phases of the cell cycle but does not use the sister chromatid as a template to facilitate DNA repair. As a result, it is more prone to error. HRR competes with NHEJ as the preferred mechanism for DSB repair (Prakash et al., 2015). Therefore, homozygous variants in *BRCA1/2* causing complete loss of BRCA1 and/or BRCA2 results in defective DSB repair, loss of genomic integrity, and tumorigenesis (Powell & Kachnic, 2003; Prakash et al., 2015). In addition, moderate-risk genes involved in HRR may be associated with HBOC. Several other proteins interact with BRCA1 and BRCA2 during HRR. Some of the genes that encode these proteins include *ATM, MRE11,*

NBN, RINT1, BARD1, PALB2, BRIP1, and the *RAD51* paralogs (*RAD51B, RAD51C, RAD51D, XRCC2* and *XRCC3*) (Nielsen et al., 2016; Norquist, 2019). P/LP variants in genes involved in HRR, including *BRIP1, RAD51C,* and *RAD51D,* are present in 2.5-3% of EOC and are associated with a moderately increased lifetime risk for HGSOC (McCuaig et al., 2018). Some moderate-risk and established genes related to lifetime HGSOC risk are outlined in Table 1.2.

Table 1.2: Germline P/LP variants in emerging moderate-risk and established genes associated with HGSOC risk other than *BRCA1* and *BRCA2*.

Gene	Lifetime risk of ovarian cancer* (%)
Emerging	
ATM	Unknown
BARD1	Unknown
BRIP1	~6-8
CHEK2	No known association
DICER1	Elevated
EPCAM±	Elevated
MSH6±	6-8
NBN	Unknown
PALB2	Unknown
PMS2±	Unknown/potentially elevated
RAD50/RAD51B	No known association
RAD51C	~5.2-9
RAD51D	7-12
SMARCA4	Elevated
TP53	Elevated
XRCC2	Insufficient data
Established	
MLH1 (Lynch syndrome) ±	5-20
MSH2 (Lynch syndrome) ±	10-38
STK11 (Peutz-Jeghers syndrome)	13-18**

Elevated: Evidence of association, but penetrance/risk not well established; Unknown: possibly increased risk based on some studies, but not well described or widely accepted; No known association: literature either shows no associated risk or not addressed in literature; Insufficient data: studies are inadequate to assess risk. *All ovarian cancers, including HGSOC; **Gynecological cancers including HGSOC, cervical and uterine; ±Involved in DNA mismatch

repair (Invitae, 2019; McCuaig et al., 2018; National Comprehensive Cancer Network, 2018; Nielsen et al., 2016; Norquist, 2019; Tung et al., 2016).

1.4 GENETIC TESTING AND COUNSELLING

Individuals with a personal cancer diagnosis or strong family history of cancer may be eligible for genetic testing. Guidelines for genetic testing eligibility vary between institutions. In general, individuals are considered to be high risk for HBOC when there is a clustering of early-onset cancers (i.e. before 50 years of age), specific patterns of cancer diagnoses (i.e. breast cancer and HGSOC within the same family, or multiple primary cancers in the same individual), male breast cancer, evidence of autosomal dominant inheritance, or certain ethnic backgrounds at a higher *a priori* risk for carrying known founder variants in *BRCA1* and/or *BRCA2* (i.e. the Ashkenazi Jewish population) (Berliner et al., 2013). It is widely accepted that while established genetic testing criteria is used to determine genetic testing eligibility, HCPs must use their clinical judgement to decide on the appropriateness of genetic testing for each individual (Berliner et al., 2013). There is a large discrepancy between individuals who meet NCCN eligibility criteria for genetic testing and those who actually receive genetic testing. Currently, there are an estimated 1.2 to 1.3 million women in the United States meeting select NCCN criteria that have never received genetic testing for HBOC (Childers et al., 2017). This includes ~400,000 women with ovarian cancer (including HGSOC), a large proportion of whom never discussed the option of genetic testing with a HCP (Childers et al., 2017). In a nationally representative sample of patients from the United States (N=47,218), 0.4% had a history of ovarian cancer (including HGSOC), of which 15.1% discussed, 13.1% were advised to undergo, and 10.5% actually underwent genetic testing (Childers et al., 2017). Similar findings are true to

Canada, with data from Ontario indicating that the referral rate for genetic counselling and testing for individuals with HGSOC is less than 25% (Demsky et al., 2013; McCuaig et al., 2018; McGee et al., 2017; Metcalfe et al., 2009). This may be partially due to the unmet need for GCs across North America, correspondingly long wait times for genetic testing and pre-test counselling (up to 2 years in Canada), as well as a lack of HCP awareness and knowledge of genetic testing (Childers et al., 2017; McCuaig et al., 2018). A randomized controlled trial called MAGENTA (Making Genetic Testing Accessible) aimed to address the gap in individuals requiring and accessing genetics services by evaluating the efficacy of alternative genetic counselling delivery models, such as online education and/or telephone counselling. (Rayes et al., 2019). Initial results from this study demonstrated that patients experienced similar levels of distress after receiving genetic test results, whether they received electronic genetic education and the release of genetic test results without genetic counselling or traditional pre- and post-test genetic counselling (E. M. Swisher et al., 2020). Indeed, the mode of results delivery at the Hereditary Cancer Clinic (HCC) within the Winnipeg Shared Health Program of Genetics & Metabolism switched from in-person to primarily telephone counselling in Autumn 2017 in an attempt to increase clinic and counsellor efficiency, as well as patient load. Finally, genetic testing is not obligatory, and patient preference plays a role when deciding whether or not to undergo genetic testing.

GCs are involved in helping patients make informed decisions about genetic testing. A GC is a trained professional who specializes in discussing hereditary cancer, why genetic testing is being offered, as well as the risks and benefits of genetic testing with patients (Berliner et al., 2013). This includes but is not limited to knowing about increased cancer risks, changes to cancer screening and management, eligibility for specific treatment (i.e. PARP inhibitors for

individuals with *BRCA1/2* P/LP variants), anxiety and worry related to genetic test results, implications for family members, and concerns about genetic discrimination (Berliner et al., 2013). The National Society of Genetic Counsellors (NSGC) Code of Ethics statement states that GCs must "seek out and acquire balanced, accurate and relevant information required for a given situation," and "enable their clients to make informed decisions, free of coercion, by providing or illuminating the necessary facts, and clarifying the alternatives and anticipated consequences" (Veach et al., 2018). GCs therefore take an active, "non-directive" approach to counselling that promotes patient autonomy and informed decision-making (Weil, 2000). Specifically, GCs are guided by the reciprocal engagement model of genetic counselling, wherein genetic-specific information, patient attributes (i.e. autonomy, resilience, and emotions) and the counsellor-counselee relationship are integral to positive genetic counselling outcomes (including effective decision-making, management, and adaptation) (Veach et al., 2007). It is the GC's hope that through the effective implementation of this model during pre- and post-test counselling, the patient is able to choose the course of action most appropriate to them (Weil, 2000).

As discussed previously in section 1.3, *BRCA1* and *BRCA2* are the genes most commonly implicated in HBOC, but there are also a number of moderate-risk genes that may be associated with increased breast cancer and HGSOC risk (Table 1.2). For this reason, unless a familial variant has already been identified, institutions largely offer genetic testing for HBOC in the form of multi-gene panels, which include *BRCA1* and *BRCA2* as well as other genes known to be associated with an increased risk of breast cancer and HGSOC (Berliner et al., 2013). In Winnipeg, the HCC offers genetic testing in the form of a 6 gene panel to eligible patients. The genes included on the panel are: *BRCA1, BRCA2, PTEN, CDH1, TP53* and *PALB2* (WRHA Program of Genetics & Metabolism, 2019). This panel was recently (as of October 2019)

revised to include 10 genes: *BRCA1, BRCA2, PTEN, STK11, TP53, PALB2, MLH1, MSH2, MSH6,* and *EPCAM* deletions. These genes are associated with an increased risk for HBOC-related cancers (i.e. breast cancer and HGSOC), as well as additional cancer types. For example, P/LP variants in *PTEN* are associated with Cowden syndrome, a hereditary condition linked to an increased risk for breast, thyroid, uterine, kidney and colon cancers (WRHA Program of Genetics & Metabolism, 2019). GCs at the HCC ensure patients undergo extensive pre-test counselling before providing a blood sample for genetic testing. If a patient provides informed consent for genetic testing, the GC explains the results of the genetic test to the patient in detail at a second appointment, either in-person or over the phone.

Results of a genetic test may be negative, uncertain, or positive. It is also possible to receive more than one of these results since a variant may be identified in more than one gene, or multiple variants may be identified within the same gene. For example, it was previously described in sections 1.2 and 1.3 how germline heterozygous P/LP variants in *BRCA1/2* result in an increased risk for HBOC-related cancers. However, inheritance of homozygous P/LP variants in *BRCA2* results in Fanconi Anemia, an autosomal recessive cancer susceptibility disorder characterized by bone marrow failure and congenital abnormalities (Howlett et al., 2002). Inheritance of homozygous P/LP variants in *BRCA1* are thought to be incompatible with life, although two patients with biallelic *BRCA1* variants have been reported and exhibited an increased risk for HBOC-related cancers (similar to those with a heterozygous *BRCA1* P/LP variant) in the absence of bone marrow failure (Sawyer et al., 2015). Individuals with a P/LP variant in both *BRCA1* and *BRCA2* have HBOC-related cancer risks that resemble those with a single heterozygous *BRCA1* or *BRCA2* P/LP variant (Rebbeck et al., 2016).

A negative genetic test result implies that an individual does not have a P/LP variant in any of the genes that were tested. Risk assessment and screening recommendations would therefore be based on personal or family history of cancer, and not based on a hereditary cancer predisposition syndrome like HBOC. An uncertain result is termed a variant of uncertain significance (VUS). In the case of a VUS, a variant has been identified in one or more of the genes that were tested: however, it is unclear whether this variant is benign/likely benign or P/LP. A patient with a VUS should be managed based on personal and family history of cancer, similar to a negative result. Patients with VUS results are encouraged to re-contact the genetics clinic every ~2-3 years to see if the VUS has been reclassified to either benign/likely benign or P/LP as research and knowledge in the field progresses. Finally, a positive genetic test result means that the patient has a P/LP variant in one or more of the genes that were tested, indicating the presence of a hereditary cancer predisposition syndrome. For example, a patient may be positive for a pathogenic variant in *BRCA1*. In this case, the patient has HBOC and is at an increased risk for HBOC-related cancers, such as breast cancer and HGSOC. The GC will initiate a discussion about implications for the patient and their family. This may include options for increased cancer screening and prevention (i.e. increased frequency of mammograms and breast MRIs, or risk-reducing surgery options; Table 1.1), as well as targeted, "cascade," genetic testing that can be offered to family members.

1.5 RISK-REDUCING SALPINGO-OOPHORECTOMY

RRSO is the removal of both the left and right fallopian tubes and ovaries to reduce one's risk of developing HGSOC. As previously described in section 1.2, the fallopian tubes have been identified as a site of origin for HGSOC (Jones & Drapkin, 2013). HGSOC is extremely

aggressive, and fewer than 25% of cases are detected at an early stage (stages 1 and 2), contributing to high mortality rates (Levanon et al., 2008). This is in part because, unlike mammograms and breast MRI to detect early-stage breast cancer, there are currently no recommended screening methods to detect HGSOC. Two methods that have been evaluated for their efficacy as a screening tool for HGSOC are TVU and the serum tumor marker CA125. CA125 is a glycoprotein that can be elevated in 80% of EOC overall, but only 50% of early stage EOC (Doubeni et al., 2016). While both of these methods have relatively high specificity and negative predictive value, the sensitivity and positive predicative value are inadequate for accurately detecting early stage HGSOC (Bast et al., 2005; Olivier et al., 2006). False positives are common due to alternate non-malignant reasons for elevated CA125 or abnormal TVU, such as menstruation and benign ovarian cysts (Bast et al., 2005; Olivier et al., 2006). RRSO is a strongly recommended strategy for reducing HGSOC risk since: 1) effective screening methods are currently unavailable; 2) HGSOC has been shown to originate in the fallopian tube epithelium; and, 3) there is an increased frequency of *BRCA1/2* P/LP variants in HGSOC (previously described in section 1.2). As outlined in Table 1.1, guidelines recommend that RRSO be considered in women with P/LP *BRCA1/2* variants after childbearing years, around 35-40 years of age for women with *BRCA1* P/LP variants and around 40-45 years of age for women with *BRCA2* P/LP variants (National Comprehensive Cancer Network, 2020). Multiple studies have shown that RRSO results in a significant reduction (approximately 80%; mean follow-up times range from ~2-10 years) in the risk for all ovarian cancer histotypes among *BRCA1* and *BRCA2* carriers compared to those who did not have RRSO (Hartmann & Lindor, 2016; McCuaig et al., 2018). There is also data to suggest a lowered breast cancer risk associated with RRSO performed pre-menopause due to a reduction in hormonal exposure following removal of

the ovaries (Hartmann & Lindor, 2016; National Comprehensive Cancer Network, 2020). A study conducted by Kauff et al. (2002) followed *BRCA*-positive women who elected for either RRSO (n=98) or surveillance in the form of gynecological examinations and TVU (n=72) over a mean follow-up period of approximately 24 months (Kauff et al., 2002). The primary outcome was time to cancer. Using a statistical model to predict the primary outcome, the researchers determined the 5-year cancer-free rate for both breast and gynecological (ovary and peritoneal) cancers to be 94% in the RRSO group compared to 64% of women electing for surveillance (Kauff et al., 2002). Recently, it has been proposed that RRSO be considered in women with P/LP variants in some moderate-risk genes associated with increased HGSOC risk (Table 1.2). In December 2019, the NCCN released an update to their genetic/familial high-risk assessment guidelines for breast cancer and HGSOC with recommendations that RRSO should be considered at 45-50 years of age in individuals with a P/LP germline variant in *BRIP1* (National Comprehensive Cancer Network, 2020). The age at which to consider surgery is not always specified for other moderate risk genes and more research is necessary to obtain evidence of HGSOC risk and management implications (Tung et al., 2016).

Although RRSO has proven to be effective for reducing HGSOC risk in *BRCA*-positive women, there are some important items to consider about the procedure. There may be tissue remaining post-RRSO and consequently, a residual risk of developing a primary peritoneal cancer (National Comprehensive Cancer Network, 2020). Surgical removal of the ovaries by RRSO ultimately induces premature menopause (i.e. “induced menopause”) (Shuster et al., 2010). Removal of the ovaries renders young women unable to become pregnant and will have an effect on family-planning and reproductive decisions. Induced menopause may also result in long-term health issues including an increased risk of cardiovascular disease, neurologic

impairment, anxiety and depression, impaired sexual function, and osteoporosis (Shuster et al., 2010). An ongoing clinical trial in the United States called the Women Choosing Surgical Prevention (WISP) study aims to determine whether interval salpingectomy with delayed oophorectomy (ISDO) can improve sexual functioning and menopausal symptoms compared to standard RRSO while still effectively reducing HGSOC risk (https://wisp.mdanderson.org/; ClinicalTrials.gov identifier: NCT02760849). A similar study (TUBA study) is currently being conducted in the Netherlands evaluating the effect of ISDO versus standard RRSO on menopause-related quality of life in pre-menopausal *BRCA*-positive women (Harmsen et al., 2015).

The majority of adverse health outcomes are associated with loss of estrogen post-RRSO in pre-menopausal women and can therefore be improved by hormone replacement therapy (HRT) (Richardson et al., 2017; Shuster et al., 2010). HRT may be combination (estrogen and progesterone) or estrogen-only. Estrogen-only HRT is only recommended for women who previously or concurrently underwent total abdominal hysterectomy (TAH), since progesterone is essential for preventing the development of endometrial cancer (Birrer et al., 2018). A systematic review of the literature (albeit based on limited data) supports that HRT is considered a safe and acceptable option for *BRCA*-positive women post-RRSO as it has not been found to have a significant impact on breast cancer risk (Birrer et al., 2018). However, HRT is often not recommended for women with a previous diagnosis of breast cancer since it has been shown to increase the risk to develop a new or recurrent breast cancer diagnosis (Holmberg et al., 2004). HRT has been shown to mitigate menopausal symptoms in women with P/LP variants in *BRCA1/2* who have undergone RRSO (Birrer et al., 2018). In addition, it has been shown to have beneficial effects on bone mineral density, mood, and reducing the risk of coronary artery

disease and total mortality by 24% and 30% before 60 years of age, respectively (Richardson et al., 2017). HRT is not without its own set of symptoms, and can trigger hot flashes and sweats, muscle and joint pain, vaginal dryness, and mood swings (Richardson et al., 2017). Women with *BRCA1* and *BRCA2* P/LP variants must ultimately weigh the risks and benefits of RRSO and HRT when deciding for or against surgery.

1.6 THE HEREDITARY GYNECOLOGY CLINIC MODEL

The HGC in Winnipeg, Manitoba was established in February 2018 to offer guidance and care specifically to *BRCA*-positive women considering RRSO. Patients are referred to the HGC by a GC at the HCC after receiving a positive genetic test result indicating they carry a P/LP variant in *BRCA1/2*. The HGC is modelled based on the Familial Ovarian Cancer Clinic at Women's College Hospital in Toronto (Women's College Hospital, https://www.womenscollegehospital.ca/programs-and-services/gynecology/familial-ovarian-cancer-clinic). Both clinics provide specialized care through an interdisciplinary team of GOs, menopause specialists, and registered nurses. The Familial Ovarian Cancer Clinic has a GC on site, while the Winnipeg HGC does not. In a single visit to the HGC, a patient is able to be seen by all 3 HCPs. The clinical nurse educator starts with patient intake and employs counselling skills to assess the patient's wellbeing, help with decision-making, and address any initial questions or concerns the patient may have. The GO speaks to the patient in depth about RRSO, including the risks and benefits of the procedure. The Menopause specialist speaks to the implications of RRSO related directly to induced menopause in currently pre-menopausal women. The patient is then able to synthesize all the information they have been provided during their appointment to make an informed decision about whether or not they wish to pursue RRSO.

The patient may make the decision to pursue surgery immediately, or go home and take time to consider their options before deciding before or against RRSO.

In addition to caring for *BRCA*-positive women, the clinic also provides support to women with Lynch syndrome. Lynch syndrome is a hereditary cancer syndrome caused by P/LP variants in *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM* and is associated with an increased risk primarily for colon, prostate and endometrial cancer (National Comprehensive Cancer Network, 2018). P/LP variants in *MLH1* and *MSH2* are also associated with an increased risk for HGSOC (Table 1.2) (National Comprehensive Cancer Network, 2018). Therefore, women with Lynch syndrome may also benefit from risk-reducing gynecological surgeries. The conversation differs from the one had with *BRCA*-positive women, however, as the risk for endometrial cancer associated with Lynch syndrome prompts a discussion about the option of TAH in addition to RRSO. TAH in combination with RRSO is a larger surgery with different implications than RRSO alone, and is beyond the scope of this discussion.

To date, the HGC and the Familial Ovarian Cancer Clinic at Women's College Hospital are the only two clinics of their kind in Canada and there is no published research evaluating the efficacy of the HGC clinic model. A similar "*BRCA* carrier clinic" exists at the Royal Marsden Hospital/Institute of Cancer Research in London, United Kingdom, that provides ongoing support and surgical prevention options to *BRCA*-positive individuals and their families (Ardern-Jones & Eeles, 2004). The model differs slightly from the HGC in that discussions are not limited to gynecological cancer risks (i.e. HGSOC), but also include clinical management options related to breast cancer risk reduction (i.e. mastectomy) (Ardern-Jones & Eeles, 2004). The clinic follows approximately 200 patients and provides the unique service of a "virtual" clinic where patients have the option of contacting nurses trained in oncology and genetics over

the telephone for ease of regular follow-up and support (Ardern-Jones & Eeles, 2004). A similar clinic model exists at the Davidoff Cancer Center, a division of the Rabin Medical Center in Israel. The clinic has followed 318 *BRCA*-positive women since its inception in 2001 through a team of medical oncologists, breast surgeons, gynecologists, plastic surgeons, and psycho-oncologists (Yerushalmi et al., 2016). Services offered include RRSO and mastectomy, annual breast imaging, gynecological exams, and psychosocial support (Yerushalmi et al., 2016). This clinic reports high rates of RRSO in pre-menopausal women, with ~87% of women > 40 years of age opting for RRSO (Yerushalmi et al., 2016). A similar evaluation of performance and patients' experiences at the HGC may be helpful in optimizing provision of care and decisional support to *BRCA*-positive women.

1.7 IMPACT OF RRSO

A large body of literature (conducted internationally, but primarily within in the United States) focuses on the impact of RRSO on high-risk HBOC women (either because of a *BRCA* P/LP variant or family history suggestive of HBOC), including post-operative symptoms related to induced menopause and HRT, the impact of RRSO on sexuality and quality of life, and how information on RRSO impact may have been useful to inform decision-making (Miller et al., 2010). While it is clear that the majority of women are overwhelmingly satisfied with their decision to pursue RRSO (~86-97% across multiple studies) (Miller et al., 2010; Westin et al., 2011), some report unexpected negative symptoms and lack of information on side effects related to induced menopause and HRT (Babb et al., 2002; Brotto et al., 2012; Campfield Bonadies et al., 2011; Cherry et al., 2013; Hallowell et al., 2004, 2012; Kim et al., 2014; Meiser et al., 2000; E. M. Swisher et al., 2001). Common post-operative symptoms experienced by

women who had RRSO include vaginal dryness, hot flashes, sexual side effects (including changes to libido and sex life), sleep disturbances, and emotional changes (Campfield Bonadies et al., 2011; Hallowell et al., 2004, 2012). While the more common symptoms of induced menopause, such as vaginal dryness and hot flashes, were discussed with women by their HCP pre-surgery, a large proportion of women reported having limited knowledge of the spectrum and severity of menopausal symptoms (Hallowell et al., 2004; Kim et al., 2014), or received little or no information related to the impact RRSO may have on their sex life (Brotto et al., 2012; Campfield Bonadies et al., 2011; Cherry et al., 2013; E. M. Swisher et al., 2001). In a web-based survey conducted by Kim, Skrzynia, & Mersereau (2014) including 151 high-risk women (41 of which were *BRCA*-positive), 29% of *BRCA*-positive women reported that they did not discuss the clinical impact and reproductive consequences of RRSO with their HCP (Kim et al., 2014). Another survey-based study by Campfield, Moyer, & Matloff (2011) including 98 *BRCA*-positive women known to have pursued RRSO showed that 60-80% of women never discussed the impact of RRSO on their body image and sex life, as well as the availability of sex counselling with their HCP (Campfield Bonadies et al., 2011). Study participants who responded to open-ended questions indicated that they wished they had known more about the impact of RRSO on their sex life and libido, they would have appreciated the option of having sex counselling and the opportunity to speak to their partner about the sexual impact of surgery, and finally that HCPs should provide as much information about menopausal, emotional, and sexual changes related to RRSO as possible (Campfield Bonadies et al., 2011). Interestingly, a study conducted by Westin et al. (2011) presented contradictory data suggesting that menopausal status was not a significant predictor of women's satisfaction with their choice of preventative strategy (i.e. RRSO versus surveillance) (Westin et al., 2011). This study also reported that women with

BRCA P/LP variants were more likely to be satisfied with their choice (whether it be RRSO or surveillance) compared to high-risk women without a *BRCA* P/LP variant (Westin et al., 2011). Women also reported wanting more information on RRSO in general (i.e. how it is performed, recovery time, etc.) (Babb et al., 2002) and the implications of HRT, specifically the long-term effects related to breast cancer risk and cardiovascular health (Babb et al., 2002; Brotto et al., 2012; Cherry et al., 2013; Hallowell et al., 2012; Meiser et al., 2000). This lack of information and knowledge on the impact of RRSO correlated with feeling unprepared for surgery (Brotto et al., 2012).

Studies have also explored the impact of RRSO on quality of life (Finch et al., 2013; Madalinska et al., 2005; Robson et al., 2003). Survey-based studies using validated scales (such as the Impact of Events Scale and Cancer Worry Scale) to measure the effect of RRSO have shown no significant impact on generic quality of life, however a significant decrease in cancer worry and anxiety has been seen (Finch et al., 2013; Madalinska et al., 2005; Robson et al., 2003). Finch et al. (2013) conducted a study based in Canada that found no significant difference in psychological distress or general health-related quality of life in 96 *BRCA*-positive women before and after RRSO. However, there was a clear decrease in HGSOC-related worry post-RRSO, with 34.3% of women reporting moderate to severe HGSOC-related worry pre-RRSO compared to 18.6% after RRSO (Finch et al., 2013). A similar pattern was seen previously by Madalinska et al. (2005) in the Netherlands when comparing high-risk HBOC women choosing RRSO (n=369) versus those undergoing surveillance (n=477) in the form of gynecological screening (i.e. pelvic exam, CA125, and/or TVU) for HGSOC (Madalinska et al., 2005). No significant difference was seen in generic quality of life between groups. However, there was a significant difference in condition-specific quality of life including less cancer worry (including

HGSOC and breast cancer worry for self, as well as family members) in the RRSO group compared to the surveillance group (Madalinska et al., 2005).

1.8 DECISION-MAKING AND RRSO

1.8.1 Factors influencing decision-making

Multiple studies present data supporting that the decision whether or not to pursue RRSO is complex and involves the consideration of many medical, psychological and social factors (Babb et al., 2002; Cherry et al., 2013; Hallowell et al., 2001, 2004; Hesse-Biber, 2014; Howard et al., 2009; Mahat-Shamir & Possick, 2017; Meiser et al., 2000; Miller et al., 1999, 2010; Ray et al., 2005; E. M. Swisher et al., 2001; Tong et al., 2015). Age and parity are predicters of RRSO uptake: older women with greater parity are more likely to pursue RRSO, logically because younger women may not be done with childbearing and wish to keep their ovaries for the time being (Miller et al., 2010). Knowledge of having a *BRCA* P/LP variant facilitates decision-making, in that women who are *BRCA*-positive are more likely to have RRSO (Hallowell et al., 2001; Hesse-Biber, 2014; Howard et al., 2009; Mahat-Shamir & Possick, 2017). However, having a P/LP variant in *BRCA*1/2 is not the sole driver of this decision and in some cases is over-ridden by personal and family history of cancer. In many cases, having a personal or family history of breast cancer and/or HGSOC is associated with greater uptake of RRSO, presumably because it is associated with a greater perceived risk of developing cancer in the future (Babb et al., 2002; Cherry et al., 2013; Hallowell et al., 2001; Hesse-Biber, 2014; Howard et al., 2009; Miller et al., 1999, 2010; E. M. Swisher et al., 2001). Hallowell et al. (2001) conducted interviews with pre-menopausal women from high-risk HBOC families in the United Kingdom (the majority had not had genetic test for *BRCA1/2*) who underwent either RRSO (n=23) or

surveillance (n=24) for HGSOC (Hallowell et al., 2001). The interviews revealed that witnessing a first degree relative, particularly a mother or sister, die or struggle with HGSOC heavily influenced the decision to pursue RRSO, with 87% of the surgery group versus 41% of the screening group having a first degree relative die from HGSOC (Hallowell et al., 2001). Interviews with 64 *BRCA*-positive women conducted by Hesse-Biber (2014) in the United States also support the notion that perceived cancer risk based on family history, and not just objective cancer risk related to being *BRCA*-positive, is associated with increased uptake of risk-reducing surgery, including RRSO (Hesse-Biber, 2014). Of 49 out of 64 women choosing risk-reducing surgery (i.e. RRSO, mastectomy and TAH) over cancer surveillance, 89% had a first degree relative diagnosed with cancer and 50% had a mother who died of cancer. This is in comparison to the 14 women who chose surveillance who had no family history of cancer or more distant relatives who were diagnosed with cancer (Hesse-Biber, 2014). Women in the surgery group also used the age at which their relatives were diagnosed to inform when they should pursue risk-reducing surgery (Hesse-Biber, 2014).

Studies have suggested that pursuing risk-reducing surgery is a means by which individuals can feel empowered and take control over their perceived cancer risk and vulnerability (Babb et al., 2002; Hallowell et al., 2004; Hesse-Biber, 2014; Mahat-Shamir & Possick, 2017; Meiser et al., 2000; Miller et al., 1999). For instance, qualitative interviews with *BRCA*-positive women revealed that deciding to pursue RRSO is viewed as a way to re-gain control over one's life by "eliminating" the impending threat of a cancer diagnosis (Hesse-Biber, 2014; Mahat-Shamir & Possick, 2017). Other women, particularly those who were found to be *BRCA*-positive without a significant family history of cancer, described their decision to pursue RRSO in a more negative light, stating that it felt like less of a choice and more of a necessity for

survival (Hesse-Biber, 2014; Mahat-Shamir & Possick, 2017). Along similar lines, those with greater feelings of anxiety and cancer worry are more likely to pursue RRSO as a means of taking control over and reducing one's anxiety and cancer-related distress (Hallowell et al., 2001; Howard et al., 2009; Miller et al., 1999). Another psychosocial aspect of decision-making to consider is the role of femininity and self-image. In some instances, RRSO impacts a woman's self-image since having ovaries may be perceived as being connected with the constructs of "femaleness" and motherhood (Mahat-Shamir & Possick, 2017). However, there are women who do not report RRSO as having an impact on their femininity, especially when compared to mastectomy, since it is not something that you can "see" (Meiser et al., 2000).

Finally, there is research suggesting that women consider social and familial obligations when making decisions about RRSO (Cherry et al., 2013; Hallowell et al., 2001, 2004; Hesse-Biber, 2014; Howard et al., 2009). An article by Howard, Balneaves, & Bottorff (2009) reviewing 43 publications (mostly from the United States, Australia, and the Netherlands) on the factors and contexts that influence decision-making related to cancer risk reduction strategies (i.e. RRSO and/or mastectomy) in high-risk HBOC women revealed that social context factors play an important role (Howard et al., 2009). Specifically, certain women decided to pursue risk-reducing surgery because they felt an obligation to stay alive for their families (Hallowell et al., 2001, 2004; Hesse-Biber, 2014; Howard et al., 2009). Conversely, some women decided to avoid risk-reducing surgery because it would impair their ability to work, take care of, and provide for their families, particularly their children (Hallowell et al., 2001, 2004; Howard et al., 2009). The decision to have RRSO was also described by women as a way to protect their families from witnessing them suffer or having to care for them because of a cancer diagnosis (Hallowell et al., 2001, 2004). Others thought that hospitalization and recovery following risk-reducing surgery

would actually be too emotional for their families and therefore opted for surveillance instead (Hallowell et al., 2001). In regards to other social obligations, Hesse-Biber (2014) revealed that some *BRCA*-positive women opted for cancer surveillance over risk-reducing surgery (i.e. RRSO and/or mastectomy) because it provided them with the opportunity to accomplish other life goals, such as starting a new career or completing a family, before committing to a high-impact surgery such as RRSO (Hesse-Biber, 2014). Indeed, pre-menopausal *BRCA*-positive women echoed these concerns in qualitative interviews conducted by Cherry et al. (2013) by stating that they were worried about the timing of surgery because they were not done having children (Cherry et al., 2013).

1.8.2 Decision-making styles and processes

The factors involved in decision-making can be differentiated from individuals' decision-making styles. A decision-making style is defined as "the learned, habitual response pattern exhibited by an individual when confronted with a decision situation" (Scott & Bruce, 1995). Decision-making styles that have previously been described include those who are: 1) rational; 2) intuitive; 3) dependent; 4) avoidant; and, 5) spontaneous (Scott & Bruce, 1995). Rational decision-makers use evidence and logic to assess alternative options, while intuitive decision-makers rely heavily on their feelings and emotions to guide their decision-making process. Those who are dependent often rely on advice and direction from others in order to make a decision. Dependent styles may overlap with avoidance, in that these individuals may employ tactics to delay decision-making altogether. Finally, spontaneous decision-makers have a sense of urgency and desire to make decisions as quickly as possible (Scott & Bruce, 1995). A qualitative study conducted by Howard et al. (2011) involving interviews with 22 *BRCA*-positive women revealed that they engaged in multiple decision-making styles and approaches to HBOC risk reduction

consistent with those outlined above. For example, the snap decision making style (i.e. spontaneous) was used by women who made decisions about risk-reducing surgery quickly and confidently, describing it as a "no brainer" (Howard et al., 2011). In contrast, the researchers described women who were avoidant and deliberative. These individuals deferred their decisions about risk-reducing surgery by going "back and forth" about the decision over an extended period of time, effectively "putting it off" until a later, unspecified date (Howard et al., 2011). Deliberative decision-makers also continuously incorporated new information (i.e. on statistics and percentages) from HCPs that impacted their decisions over time. Women who were intuitive relied on their instincts and emotions. They often looked inward in order to visualize how their decisions would impact their beliefs and identify (Howard et al., 2011). Finally, the authors described women who use rational logic as "if-then" decision-makers because they were able to weigh the pros and cons of hypothetical decisions and the resulting implications (Howard et al., 2011).

HCPs are hopeful that patients are rational decision-makers when it comes to their health and will adhere to their advice and recommendations. However, research suggests that patients rely on both logic and their intuition to make important health-related decisions, employing a more holistic rather than rational approach to decision-making (Dean & Rauscher, 2017; Howard et al., 2011). Dean and Rauscher (2017) held semi-structured interviews with 20 *BRCA*-positive women in committed relationships who were in the process of family-planning and considering risk-reducing surgery. They identified two clear types of decision making: logical and emotional, although the two were not mutually exclusive. Logical decision-makers considered the timeline for risk-reducing surgeries and the recommendations of their HCPs, prioritizing decreasing their HBOC risk over their emotional desire for motherhood. On the other hand, emotional decision-

makers prioritized their desire for children and were influenced by the guilt associated with passing on their *BRCA1/2* variant as well as hope for scientific advancements for treating and preventing cancer in the future (Dean & Rauscher, 2017). Ultimately, although these decision-making styles place differing weight on logic and emotions, both are synthesized and considered in complex healthcare decisions such as whether or not to pursue risk-reducing surgeries like RRSO, proving that decision-making about one's health is not entirely based on rational logic (i.e. cancer risk statistics and HCP's recommendations).

1.9 GAPS IN KNOWLEDGE AND RATIONALE FOR CURRENT STUDY

While the studies summarized in the preceding sections explore aspects of decision-making and the impact of RRSO, there are multiple limitations to consider. First, many studies that are purely quantitative focus solely on the impact of RRSO (i.e. on quality of life, physical and mental health), not specifically on the factors and processes women go through when making a decision about the surgery. Quantitative studies that survey high-risk women about these factors lack the advantage of in-depth exploration of topics normally provided by a qualitative research design. Qualitative studies exist but most are limited to patients' attitudes and perceptions post-RRSO and therefore lack an in-depth exploration of the factors involved in decision-making pre-surgery. These studies also include variability in their patient populations, with some women having a positive, negative, or unknown *BRCA1/2* variant status, previous HGSOC and/or breast cancer diagnosis, differences in the timing of when they had their surgery, as well as a family history of cancer or lack thereof. The studies discussed in section 1.8 mostly include patients from the United States and elsewhere outside of North America, and may not accurately reflect the experiences of Canadian women. In addition, some qualitative studies do

not ask about menopausal status. All of these patient characteristics are extremely important factors to consider when determining differences in how and why women make decisions about RRSO. Also, the majority of qualitative studies do not focus solely on RRSO, but "risk-reducing surgery" in general, which includes RRSO as well as mastectomy and sometimes TAH. The type of risk-reducing surgery is important to distinguish since a review of the literature has revealed that the decision-making process and impact of mastectomy differs from RRSO. For instance, women who had a mastectomy reported that removal of their breast tissue had a larger negative effect on body image and their perception of "femaleness" than removal of the ovaries (Mahat-Shamir & Possick, 2017; Meiser et al., 2000). Also, mastectomy does not impact the ability to have children, nor affect family-planning in the same way as RRSO (Meiser et al., 2000). Finally, there are established screening recommendations for breast cancer such as mammograms and breast MRIs. Therefore, surgery is not the only option to effectively mitigate breast cancer risk, whereas there is currently no recommended screening for HGSOC and women are left to consider the sole option of RRSO.

There is a need for updated data in the context of currently accepted guidelines for HGSOC genetic testing and risk reduction within Canada. Genetic testing for germline P/LP variants in *BRCA1/2* and other moderate-risk genes in women with HGSOC without a significant family history has become more frequent in recent years with the evolution of new research and changes to genetic testing eligibility criteria across Canada (McCuaig et al., 2018). This may subsequently increase the number of healthy women identified to harbour P/LP *BRCA1/2* variants through cascade testing that is initiated as a result of their affected relatives, ultimately leading to more *BRCA*-positive women considering RRSO. HCPs also have increased knowledge and clearer, updated guidelines on what to include in discussions about hereditary cancer and

options for HGSOC risk-reduction in the current medical landscape. This may influence what information women report being provided to them both before and after RRSO, and consequently impact their decisions and feelings about RRSO. Finally, there are no quantitative or qualitative studies that evaluate decisional support and decision-making processes in the context of the HGC model. Given that the HGC was established to specifically target the needs of *BRCA*-positive women considering RRSO, it is imperative to determine if it provides appropriate and effective care to this patient population by exploring patients' experiences within the HGC model.

This study used a mixed-methods design, with the aim of identifying themes related specifically to RRSO decision-making strictly in *BRCA*-positive women who have never been diagnosed with HGSOC. It also aimed to evaluate overall patient experience with HCPs (i.e. GOs and GCs) and the resulting effect on the RRSO decision-making process. It is novel because it explored *BRCA*-positive women's decision-making regarding RRSO both post- and pre-surgery, as well as in the context of an innovative clinic model (i.e. the HGC) and differences in menopausal status (i.e. pre- and peri/post-menopausal). In addition, this study explored patients' decision-making processes and overall experiences within the HGC compared to patients who did not follow a referral to the HGC and instead sought consultation with a gynecologist elsewhere, or those who did not seek a consultation at all. Identifying and qualitatively exploring the different factors involved in decision-making for RRSO may change the manner in which information related to HGSOC risk and the impact of RRSO is communicated to patients by GOs and GCs. It may also help guide how clinics that tailor care to women at an increased risk for gynecological cancers due to a hereditary cancer predisposition syndrome are modelled across Canada in the future. Understanding these factors will aid HCPs in tailoring appointments to

patients' specific informational needs and emotional concerns, ultimately leading to a more valuable and satisfactory patient experience.

CHAPTER 2: METHODOLOGY

2.1 OVERVIEW OF RESEARCH DESIGN

This study contained both a quantitative and qualitative research component, in the form of a survey and an interview, which will be described in detail in the following sections. It followed a convergent mixed-methods study design whereby quantitative and qualitative data collection and analysis were completed separately, and then merged and compared in order to obtain a more complete understanding of the research questions as well as validate one set of findings with the other (Creswell & Plano Clark, 2018). Eligible patients included *BRCA*-positive women (i.e. with a heterozygous germline P/LP variant in *BRCA1* and/or *BRCA2*) between the ages of 18 and 70 years of age who were able to read and speak English. Patients were excluded from the study if they had their ovaries and fallopian tubes removed before learning they were *BRCA*-positive, or if they had ever been diagnosed with HGSOC. Eligible patients were asked to complete: 1) a survey; 2) an interview; or, 3) a survey and an interview. Eligible patients were recruited from two sites, the HGC and the HCC, to ensure all potentially eligible patients were invited to participate (i.e. those who did not follow a referral to the HGC after their results appointment at the HCC; Figure 2.1). Recruitment from each site was both retrospective and prospective. For retrospective recruitment, eligible patients who had an appointment at the HGC beginning in February 2018 were identified from the clinic's electronic medical records system. At the HCC, eligible patients were identified from the patient databases SHIRE and Accuro. Eligible patients were identified from SHIRE between January 2013 to October 2018 (when the patient database system switched to Accuro). Eligible patients were identified from Accuro between October 2018 and August 2019. The student principal investigator (PI) remained blinded to potential study participants.

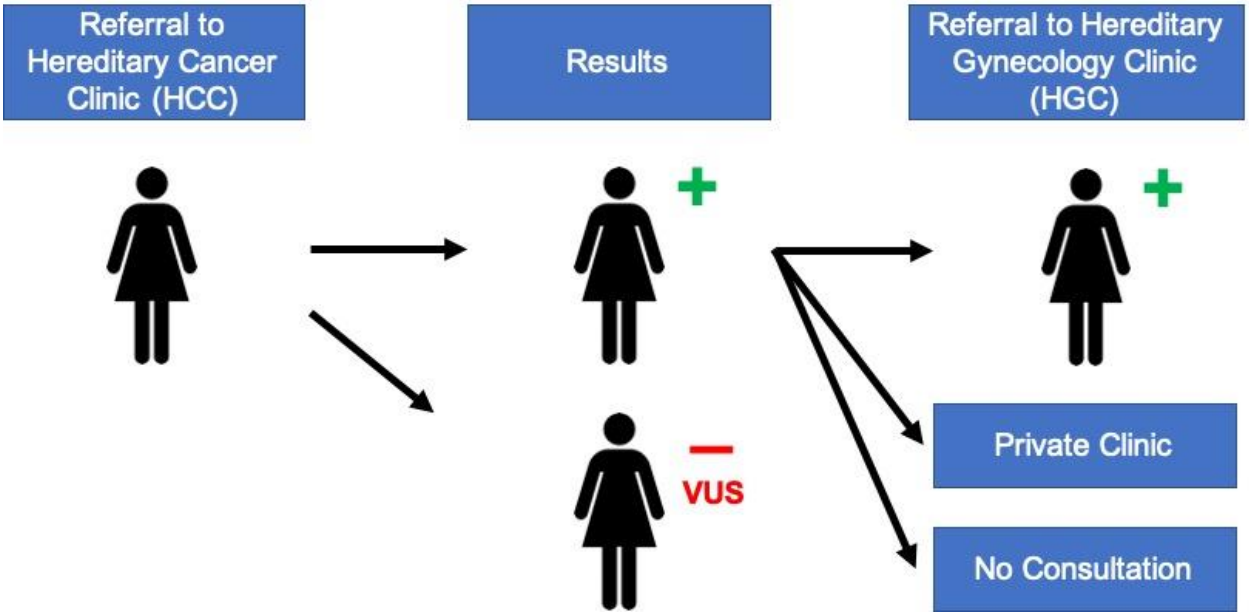

Figure 2.1: The patient "pipeline"

Patients are referred to a GC at the HCC for pre-test counselling about their hereditary cancer risk. Patients who are eligible and decide to have genetic testing receive their results from the GC over the phone or in-person at the HCC. Patients who are found to have a P/LP variant in *BRCA1* and/or *BRCA2* (i.e. are *BRCA*-positive) are referred to the HGC to discuss the option of RRSO. Some patients may forgo the referral to the HGC for consultation with a gynecologist at a private clinic, or may opt not to pursue a consultation altogether.

Kim Serfas (GC and a member of the student advisory committee) cross-referenced the list of eligible patients from the HCC with those identified from the HGC to ensure that no patients were recruited twice. Eligible patients were mailed a recruitment package in September 2019 containing a study invitation letter (Appendix A.1), survey (Appendix A.2), and interview consent form (Appendix A.3). A reminder recruitment package was mailed in November 2019 in an attempt to increase response rate. For prospective recruitment, eligible patients were identified and introduced to the study by a GO during their appointment at the HGC or by a GC during their genetic test result appointment/phone call at the HCC. Interested patients were given a recruitment package and/or asked to fill out a contact form (or asked permission by the HCP to fill out a contact form on their behalf if the discussion was over the phone), giving the student PI permission to contact them directly about the study.

This study was approved by the Research Ethics Board at the University of Manitoba (approval number HS22893/H2019:224), the Health Sciences Centre Research Impact Committee (approval number RI2019:055), as well as the CancerCare Manitoba Research Resource Impact Committee (approval number RRIC2019-15). This study has also been shared with and received support from the Manitoba Metis Federation and the Health Information Research Governance Committee of the First Nations Health and Social Secretariat of Manitoba.

2.2 SURVEY

The quantitative component of the study was an exploratory survey (Appendix A.2). The primary outcomes of the survey were to obtain: 1) a baseline description of the study population; 2) an overview of the factors patients considered when making decisions regarding RRSO; and, 3) an understanding of patients' comfort level and satisfaction with their decision as well as the

care they received from their HCPs. The survey was provided to study participants in both paper and online format. For the online survey, data was collected and managed using the REDCap (Research Electronic Data Capture) tool hosted at the University of Manitoba (Harris et al., 2009, 2019). REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and, 4) procedures for data integration and interoperability with external sources. By completing the survey, the participant consented to participate in this part of the study. A combination of previously validated scales were used to develop the survey questions, including the Satisfaction with Decision (SWD) scale (Holmes-Rovner et al., 1996), Preparation for Decision Making (PrepDM) scale (Bennett et al., 2010), Decisional Conflict Scale (DCS) (O'Connor, 1995), and Cancer Worry Scale (CWS) revised for breast cancer genetic counselling (Caruso et al., 2018). The questions in the survey corresponding to each of the validated scales are listed in Appendix A.4. The SWD scale was designed to measure patients' satisfaction with healthcare decisions, as well as the attributes of an effective decision (i.e. one that is informed, consistent with personal values, and behaviourally implemented). The SWD scale also differentiates satisfaction with the decision from satisfaction with other aspects of the healthcare experiences (i.e. care from a specific HCP) (Holmes-Rovner et al., 1996). The PrepDM scale was developed to assess how effective a decisional support intervention (in this particular case, consultation with a GO at the HGC) is at preparing a patient to communicate with their HCP and make a healthcare decision (Bennett et al., 2010). The DCS was designed to assess the level of decisional conflict experienced by patients when making a healthcare-related decision. Decisional conflict is defined as "a state of

uncertainty about the course of action to take" and may be elicited by potentially high-risk outcomes, the need for value trade-offs when making a decision, and/or anticipated regret over one's choice (O'Connor, 1995). The DCS evaluates uncertainty when making a decision, factors contributing to this uncertainty, and individuals' perceptions of effective decision-making (O'Connor, 1995). The CWS was designed and validated specifically in the context of cancer genetic counselling to measure cancer worry (i.e. worry of getting breast cancer, the impact of worry on mood and daily activities) and risk perception of being *BRCA*-positive (Caruso et al., 2018). Survey responses to statements on validated SWD, PrepDM, DCS, and CWS measures were scored on a 5-point Likert scale. For example, the SWD scale contained 6 statements scored from 1 (strongly disagree) to 5 (strongly agree), allowing for a possible score ranging from 6 to 30. The survey also included questions pertaining to demographic information, menopausal status, and personal/family history of cancer.

The paper survey was electronically distributed to the Ovarian Cancer Survivor group in Winnipeg, Manitoba for piloting and general feedback. This group was chosen to pilot the survey because they were a relevant patient population who have been diagnosed with HGSOC, and therefore were not eligible to participate in the study. Feedback was elicited on comprehensibility and the amount of time it took to complete the survey. Three individuals responded and completed the survey. Comments on the survey were limited to lack of applicability to the three individuals and therefore were not concerning. Two individuals spent 15 minutes completing the survey, and one individual spent 7 minutes competing the survey (this person indicated that they stopped at question number 17 since the rest of the survey questions did not apply to them). The online version of the survey was piloted by a small group of colleagues at the University of Manitoba to assess usability and the amount of time it took to

complete the survey. The final version of the survey was conservatively quoted to study participants as taking 15 to 20 minutes to complete. Data collection occurred from August 2019 to January 2020.

2.3 INTERVIEW

The qualitative portion of the study involved a semi-structured interview. Qualitative interviews are an extremely useful data collection method for gaining insight into individuals' lived experiences, particularly how they make sense of reality in relation to a phenomenon (i.e. the plethora of implications associated with being *BRCA*-positive, including consideration of RRSO) (Ravitch & Mittenfelner Carl, 2016). The interview explored in-depth: 1) the factors influencing patients' decision-making processes about RRSO; 2) the specific impact (if any) of the HGC on the decision-making process; and, 3) patients' overall experiences at the HGC and with their HCPs in general (i.e. GOs, GCs, menopause specialist, etc.). The target number of interviews was approximately 15 based on previous research indicating that a sample size of 15 is sufficient to reach thematic saturation, at which point no new themes are expected to emerge from the interviews (Guest et al., 2006). Participants who volunteered to complete an interview were purposively sampled in order to ensure that there was variability in patient demographics and experiences, as well as explore new themes as they emerged from the data.

Informed consent was obtained by the student PI before commencing the interview using the interview consent form (Appendix A.3). Interviews were conducted either in-person at the University of Manitoba or by phone depending on the participant's preference. Interviews were conducted by the student PI using a semi-structured interview guide (Appendix A.5) that was iteratively amended to address emerging themes as more interviews were completed. The student

PI met with Dr. Sharon Bruce, a professor at the University of Manitoba with qualitative research expertise and a member of the student advisory committee, to discuss proper interviewing techniques before conducting any interviews with participants. Interviews were audio recorded and transcribed intelligent-verbatim by either the student PI or a hired transcriptionist from the company TranscriptHeroes, who signed a confidentiality agreement before any data was shared. Participants who completed both the interview and survey were given a $20 gift card as a thank you for their participation.

2.4 THEORETICAL FRAMEWORK

The research questions, aims, and design of the study were guided by interpretive description and the Ottawa Decision Support Framework (ODSF; Figure 2.2). Interpretive description is a generic qualitative research approach based on the constructivist epistemological assumption that knowledge is formed through subjective experiences (Kahlke, 2014; Thorne et al., 2004). It is used primarily in the healthcare setting to understand clinical phenomena and is not strictly bound by an established qualitative methodology such as phenomenology or grounded theory to allow for more flexibility in data collection and analysis (Kahlke, 2014; Thorne et al., 2004). For example, an individual's experiences with disease, HCPs, and the healthcare system are integrated to shape their knowledge about the world as well as their place within it, which in turn influences how they make healthcare-related decisions (Kahlke, 2014; Thorne et al., 2004).

1. Assess client and practitioner determinants of decisions	**2. Provide decision support** **a. Prepare practitioner and client for decision-making** **b. Structure follow-up interaction**	**3a. Evaluate quality of decision and decision-making process**	**3b. Evaluate client outcomes of decision**
Sociodemographic and clinical characteristics	Tailor to participants' characteristics	Satisfaction with decision support and decision-making process	Improved health-related quality of life
Perception of the decision Knowledge Expectations Values Decisional conflict	Provide access to information Clarify/modify expectations Clarify values Tailor support to factors contributing to the decisional conflict	Improved knowledge Realistic expectations Improved clarity of values and value congruence with decision Reduced decisional conflict Reduced decision delay Satisfaction with decision	Reduced distress from consequences Reduced regret Appropriate persistence with decision
Perception of important others Norms Pressure Support Decision participation roles	Clarify/modify perceived norms Clarify pressure; facilitate self-help skills handling pressure Facilitate access to support Tailor support to decision participation preferences	Realistic perception of norms and pressure Satisfaction with decision support	Appropriate persistence with decision
Resources to make and implement decision Personal resources Experience Self-efficacy Skills Motivation Other resources External resources	Enhance self-help skills preparing for, making, and implementing decisions and coping with consequences Facilitate access to external resources	Improved self-efficacy Improved decision-making skills Decision implementation Improved knowledge of appropriate resources	Reduced distress from consequences Appropriate persistence with decision Appropriate and efficient use of resources Satisfaction with care

Figure 2.2: The Ottawa Decision Support Framework

The determinants of an individual's decision include: 1) their sociodemographic characteristics (i.e. age, gender, education, occupation, ethnicity, and health status); 2) their own perceptions of the decision (i.e. knowledge of alternatives, perceived risks and benefits, personal importance/value of risks versus benefits, and decisional conflict); 3) the perceptions of important others regarding the decision (i.e. societal norms, social pressures, support systems, and the individual's preference for level of participation in decision-making); and, 4) the resources available to make the decision (i.e. personal experiences/motivations/skills as well as external sources of information such as social networks, HCPs, and the internet). Decisional support is ideally provided by addressing the modifiable and suboptimal determinants of decisions (i.e. lack of knowledge, unrealistic expectations, or inadequate supports/resources) by actions such as giving tailored information, clarifying patients' values, as well as promoting patient self-help skills and autonomy. Finally, the quality of decision-making and decision outcomes are evaluated by assessing if the decision was informed, consistent with values, and acted upon with satisfaction. Realistic expectations and low decisional conflict are also indicators of high quality decision making. Reproduced from (O'Connor et al., 1998) with permission from Elsevier.

The ODSF commonly guides research about shared decision-making, a "process whereby decisions are shared by patients and doctors, informed by the best evidence available, and weighted in light of patients' individual characteristics and values" (Légaré et al., 2006). The ODSF takes into account key elements of patients' clinical decision-making including decisional conflict, needs, preferences, interventions, and quality (Légaré et al., 2006; Underhill & Crotser, 2014). It was originally developed as a framework for supporting health decisions that: 1) are stimulated by new circumstances or diagnoses (i.e. learning one is *BRCA*-positive); 2) require careful deliberation because of the uncertainty and value-sensitive nature of the implications; and, 3) require more effort during the deliberation (i.e. deciding about RRSO) versus implementation (i.e. completing RRSO) phase of the decision (O'Connor et al., 1998). The ODSF is organized and guided by the determinants of an individual's decision, interventions that may address these determinants and improve the quality of the decision-making process (i.e. the HGC), and finally assessing the success of the decisional support intervention on decisional outcomes (O'Connor et al., 1998).

Mixed-methods research inherently takes on some positivist assumptions in line with the quantitative aspects of the study. The ontological and epistemological assumptions of positivism are that there is an unchanging, single universal truth or reality that can explain individual's experiences and social phenomena (Ravitch & Mittenfelner Carl, 2016). Quantitative data collection (i.e. in the form of objective survey responses) is a means of systematically defining the underlying principles or "truths" that cause certain events to occur (Ravitch & Mittenfelner Carl, 2016), such as a patient's decision to pursue (or not to pursue) RRSO. Combining positivist and constructivist paradigms (such as interpretive description) through mixed-methods research allows for triangulation of data in order to strengthen the validity of results and obtain a more

complete understanding of the research problem (Creswell & Plano Clark, 2018; Ravitch & Mittenfelner Carl, 2016).

Finally, continuous dialogic engagement with community groups such as HGSOC survivors and women with known *BRCA1/2* P/LP variants informed the PI's understanding of these women's experiences, challenges, and decisions, which in turn helped to shape the content of the survey and semi-structured interview guide.

2.5 DATA ANALYSIS

2.5.1 Quantitative data analysis

Survey responses from REDCap and paper surveys were entered into a data tracking log by the student PI using Microsoft Excel. Quantitative statistical analysis was performed by Pascal Lambert, a health outcomes analyst at CancerCare Manitoba, using R software, version 3.6.2 (R Core Team, 2019). Survey responses were analyzed using the Wilcoxon signed-rank test to rank and compare mean scores on validated scales between pre- and post-menopausal women, as well as between women who sought consultation with the HGC versus those who consulted a gynecologist outside of HSC or did not have a consultation with a GO/gynecologist. The Wilcoxon signed-rank test is a non-parametric statistical method that can be used in place of a paired t-test to compare groups when the differences are non-normally distributed (Rey & Neuhäuser, 2011). Participants' mean scores on each of the validated scales were ranked based on value for each group (i.e. pre- and post-menopausal). The difference between the sum of the ranks for each group was calculated to generate a *p*-value. Additional comparisons that were made included differences in mean scores on validated scales between women of different ages, parity, cancer history (personal and family), and decision status (i.e. decided versus undecided

about RRSO). Cramer's V, a correlation for categorial data, was used to calculate the strength of association between menopausal status (pre- or post-menopausal) and age (< 50 or ≥ 50 years of age). Cramer's V can equal a value between 0 and 1, where 0 indicates no association and 1 means a perfect correlation. Any value > 0.25 is indicative of a very strong relationship (Akoglu, 2018). Descriptive statistics were used to report participant demographics. The Bonferroni calculation to correct for type 1 statistical error was not applied because all methods for adjusting *p*-values were too conservative. Based on a *p*-value of 0.05, one can expect 5% or 1 out of 20 analyses to be randomly significant. Therefore, based on the number of analyses performed in the present study, approximately one *p*-value is expected to be randomly significant. The weakest relationships are the most likely to be randomly significant.

2.5.2 Qualitative data analysis

Interview transcripts were analyzed by the student PI using a generic qualitative analysis approach characteristic of interpretative description that allowed for identifying, analyzing, and reporting patterns or themes within data without being bound by a pre-existing theoretical framework (Braun & Clarke, 2006; Thorne et al., 2004). However, analysis did draw upon aspects of grounded theory commonly used in interpretive description, including constant comparison and an iterative analysis process. Memos and post-interview reflections were used throughout the process of data collection and analysis, which helped in identifying preliminary themes and/or differences and similarities within and between interviews.

Qualitative analysis was performed by the student PI using Dedoose software, version 8.2.17 (Dedoose, 2019). Prior to reading transcripts, an initial list of codes was developed deductively based on the prepared interview guide and initial literature review. The first three transcripts were read and coded using the deductive codes. In addition, new codes were

inductively derived from the data. This first round of coding was descriptive and allowed for indexing of the data into broad thematic categories (Miles et al., 2014). Dr. Sharon Bruce also performed an initial pass through the first three transcripts. Common themes as well as potential codes were discussed. The initial code list was modified accordingly and used to code subsequent transcripts. The code list was modified iteratively as transcripts were analyzed and new topics began to emerge from the interviews. The coding of earlier transcripts was updated to be consistent with the finalized codebook. The final list of codes along with their definitions can be found in Appendix A.6. To ensure trustworthiness and rigor of analysis, two transcripts were co-coded by Dr. Sharon Bruce and the student PI to ensure the data was appropriately and consistently coded. Discrepancies between codes and potential themes were resolved through discussion. Constant comparison, memo writing, and continued dialogic engagement were used to look for similarities and differences between participants' experiences and decision-making processes (Charmaz, 1996). Data saturation was achieved at 16 interviews, at which point no new themes were emerging from the data (Guest et al., 2006). In line with a convergent mixed-methods study design, the results of the qualitative analysis were synthesized and compared with the quantitative results in order to present a more complete picture of the data set (Creswell & Plano Clark, 2018).

CHAPTER 3: RESULTS

3.1 SURVEY RESULTS

A total of 156 eligible patients from the HGC and the HCC were identified, of which 153 were identified retrospectively and 3 were identified and contacted prospectively (1 from the HGC and 2 from the HCC). Of the 153 retrospective recruitment packages mailed to participants, 6 were return to sender. Of the remaining individuals who received a recruitment package, 43 responded to the survey (Figure 3.1), yielding a response rate of approximately 29% (43/147). The demographics of survey respondents are outlined in Table 3.1.

The majority of survey respondents were less than 50 years of age (31/43, 72%), university educated (21/43, 49%), white/European (36/43, 84%), married (29/43, 67%), and had a household income of $80,000 or more (26/43, 60%). Most had one or more children (31/43, 72%). Nineteen (44%) respondents indicated that they still got their menstrual periods and 24 (56%) indicated that they no longer got their menstrual periods, either because of natural or surgically-induced menopause. The majority of participants already had RRSO or decided they would get RRSO in the future (28/43, 65%), while 13 (30%) were undecided and 2 (5%) were firmly decided against RRSO. Thirty-two (74%) respondents consulted a GO at the HGC about their RRSO decision, 2 (5%) consulted a gynecologist outside of the Winnipeg Health Sciences Centre (HSC), and 9 (21%) did not consult a GO at the HGC or a gynecologist outside of the Winnipeg HSC. Only 3 (7%) respondents did not meet with a GC to discuss their HGSOC risk and option of RRSO. Of the 17 (40%) respondents who indicated they had been diagnosed with breast cancer, 11 (26% of all respondents) had a mastectomy. Family cancer history was predominantly composed of breast cancer (39/43, 91%), with about half (22/43, 51%) of

participants indicating they had a family history of HGSOC. Finally, 26 (60%) individuals stated that they knew a family member who underwent RRSO.

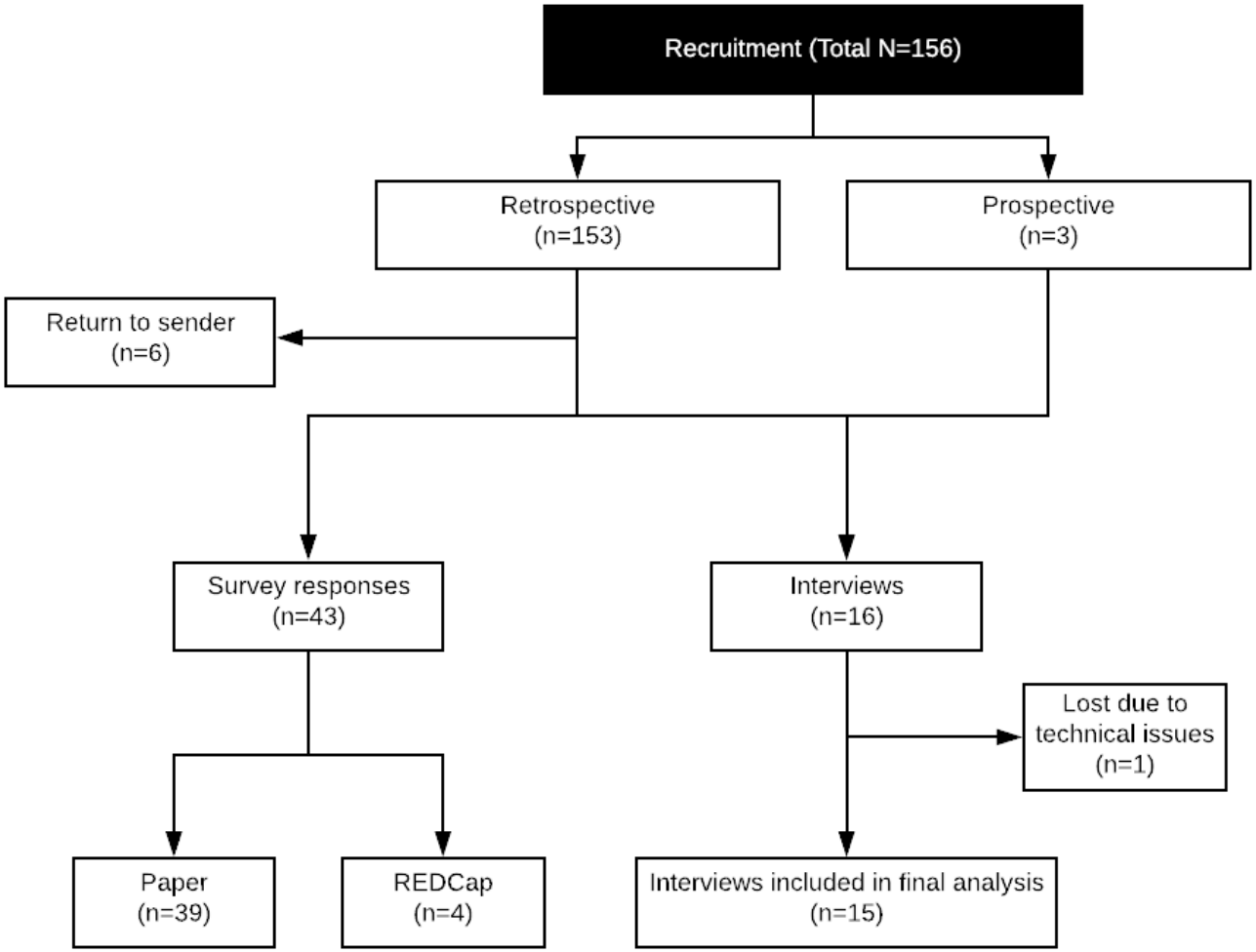

Figure 3.1: Flow diagram of survey and interview recruitment.

Table 3.1: Survey respondent demographics.

Variable	Number of survey respondents, n (%)*
Total survey respondents	43 (100)
Age	
< 50 years	31 (72)
≥ 50 years	12 (28)
Education	
High school/College/Trade/Technical school	21 (49)
Bachelor's degree or more	21 (49)
Prefer not to answer	1 (2)
Total family income	
< $79,000	13 (31)
≥ $80,000	26 (60)
Prefer not to answer	4 (9)
Race/ethnicity	
White/European	36 (84)
Non-white/European	1 (2)
Mixed heritage	5 (12)
Unknown**	1 (2)
Relationship status	
Single	6 (14)
Married	29 (67)
Other	8 (19)
Number of children	
0	12 (28)
1	8 (19)
2	17 (40)
≥ 3	6 (14)
Menstrual period status	
Pre-menopausal	19 (44)
Post-menopausal	24 (56)
Breast cancer	
Yes	17 (40)
No	22 (51)
Unknown**	4 (9)
Mastectomy	
Yes	11 (26)
No/Not applicable	32 (74)
Family history	
Breast cancer	39 (91)
HGSOC	22 (51)
RRSO	26 (60)
Spoke to GC	
Yes	40 (93)
No	3 (7)
Consultation	
HGC	32 (74)
Gynecologist outside HSC	2 (5)

Variable	Number of survey respondents, n (%)*
None	9 (21)
RRSO decision	
Decided for	28 (65)
Decided against	2 (5)
Undecided	13 (30)

*Rounding may cause some percentages not to add up to 100; ** Unknown refers to survey responses left blank by participants.

The differences in mean scores on each validated scale are listed as *p*-values for each group being compared in Table 3.2. The median of the means for each category are also listed in Table 3.2. Statistically significant differences in mean scale values between relevant groups are displayed as box plots in Figure 3.2. The box plots displaying data for groups not found to be statistically significant across validated scales can be viewed in Appendix A.7. Differences in mean scores on the CWS, DCS, and SWD scales between pre- and post-menopausal women were statistically significant, with pre-menopausal women demonstrating increased levels of cancer worry ($p < 0.001$) and decisional conflict ($p = 0.001$), as well as less satisfaction with their RRSO decision ($p < 0.001$) compared to post-menopausal women (Figure 3.2A). Pre- and post-menopausal women did not significantly differ in regards to how prepared their consultation with a GO/gynecologist made they feel to make a decision about RRSO based on PrepDM scores ($p = 0.439$; Table 3.2). Coinciding with menstrual status, women younger than 50 years of age felt more decisional conflict ($p = 0.032$) and less satisfaction with their RRSO decision ($p = 0.009$) than women 50 years of age or older (Figure 3.2B). Women < 50 years of age exhibited more cancer-related worry than women ≥ 50 years of age; however, this was not deemed to be significant ($p = 0.097$; Table 3.2). Differences in mean PrepDM scores based on age were not significant ($p = 0.557$; Table 3.2). Cramer's V correlation coefficient was calculated for menopausal status (pre- or post-menopausal) and age (<50 or ≥ 50 years of age). The correlation

was equal to 0.55, indicating a very strong relationship between menopausal status and age (Akoglu, 2018).

Table 3.2: Comparisons of scores on validated scales between groups.

Survey scales	**Median of mean values**		***P*-value***
	Menstrual status		
	"I have menstrual periods"	*"My menstrual periods have stopped"*	
CWS	2.50	0.50	< 0.001**
DCS	2.70	1.80	0.001**
SWD	0.00	4.60	< 0.001**
PrepDM	2.70	3.20	0.439
	Age		
	< 50	*≥ 50*	
CWS	2.00	0.50	0.097
DCS	2.00	1.50	0.032**
SWD	4.00	4.70	0.009**
PrepDM	3.20	2.40	0.577
	Children		
	No	*Yes*	
CWS	1.63	2.00	0.257
DCS	2.00	1.90	0.408
SWD	3.90	4.20	0.825
PrepDM	2.15	3.20	0.369
	Breast cancer		
	No	*Yes*	
CWS	2.50	0.50	0.004**
DCS	2.15	1.90	0.418
SWD	4.10	4.60	0.070
PrepDM	2.90	3.40	0.341
	Family history of HGSOC		
	No	*Yes*	
CWS	1.50	2.25	0.120
DCS	2.30	1.95	0.149
SWD	4.00	4.40	0.449
PrepDM	2.70	3.10	0.647
	Consultation (HGC or outside Winnipeg HSC)		
	No	*Yes*	
CWS	1.50	1.88	0.474
DCS	2.20	1.90	0.580
SWD	4.20	4.20	0.891
	***Decided about RRSO*±**		
	No	*Yes*	
CWS	2.25	1.38	0.016**
DCS	2.80	1.85	0.002**
PrepDM	2.40	3.25	0.188

**P*-values determined using Wilcoxon signed-rank test. Participants' mean scores on each of the validated scales were ranked based on value for each group. The median of the mean values for each scale and group are shown. The difference between the sum of the ranks for each group was calculated to generate a *p*-value; **statistically significant; ±Includes those who decided to have RRSO and those who decided not to have RRSO, compared to those who were undecided.

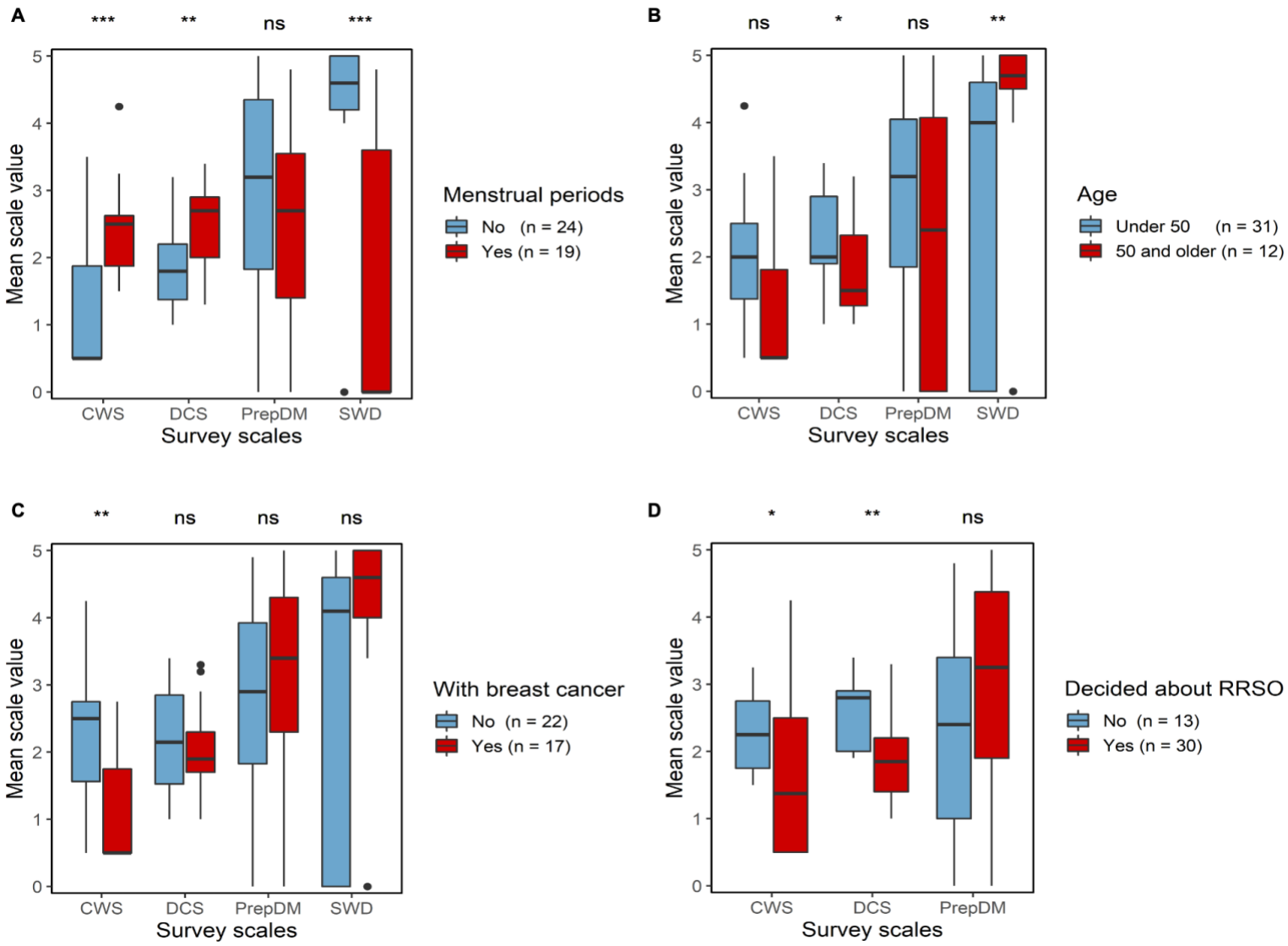

Figure 3.2: Differences in mean scale values between relevant groups.

The median of the mean scale values (listed in Table 3.2) are represented by the horizontal black lines within each bar. Outliers are represented by black dots. A; Differences in scores on the CWS ($p < 0.001$), DCS ($p = 0.001$), and SWD scale ($p < 0.001$) were statistically significant between women with and without their menstrual periods (i.e. pre- and post-menopausal), where pre-menopausal women experienced greater HGSOC-related worry and decisional conflict, as well as less satisfaction with their RRSO decision than post-menopausal women. B; Differences in scores on the DCS ($p = 0.032$) and SWD scale ($p = 0.009$) were statistically significant between women < 50 and ≥ 50 years of age, where women < 50 years of age experienced greater decisional conflict and less satisfaction with their RRSO decision than women ≥ 50 years of age. C; Differences in scores on the CWS ($p = 0.004$) were statistically significant between women with and without a personal history of breast cancer, where those with a previous breast cancer diagnosis experienced less HGSOC-related worry than those without a previous diagnosis of breast cancer. D; Differences in scores on the CWS ($p = 0.016$) and DCS ($p = 0.002$) were statistically significant between women who were decided versus undecided about RRSO, where women who were firmly decided for or against RRSO experienced less HGSOC-related worry and decisional conflict than those who were undecided about RRSO. ns, non-significant; *$p < 0.05$; **$p < 0.01$; *** $p < 0.001$.

Women with a previous diagnosis of breast cancer had significantly less cancer-related worry than women without a previous diagnosis of breast cancer ($p = 0.004$). A diagnosis of breast cancer did not significantly impact differences in mean scores between DCS, SWD, and PrepDM scales (Table 3.2; Figure 3.2C).

Women who were decided about RRSO (i.e. made a firm decision for or against surgery) had significantly less cancer worry ($p = 0.016$) and decisional conflict ($p = 0.002$) than women who were undecided about RRSO (Table 3.2; Figure 3.2D). There was a trend towards women who were undecided about RRSO feeling less prepared to make a decision than women who were decided about RRSO; however, the difference between mean PrepDM scores was not statistically significant ($p = 0.188$; Table 3.2). A comparison of SWD scale scores was not made for these groups because women who were undecided about RRSO were not asked to complete SWD questions because they had not yet made a firm decision about RRSO.

Differences in mean scores on the CWS, DCS, SWD scale, and PrepDM scale were not statistically significant between women with versus without children or women with versus without a family history of HGSOC (Appendix A.7). Differences in mean scores on the CWS, DCS, and SWD scale for women who consulted a GO/gynecologist were also statistically insignificant compared to those who did not consult a GO/gynecologist (Appendix A.7). The largest difference in the median of mean values for women with versus without children was seen for the PrepDM scale (difference in median mean values = 1.05; Table 3.2), suggesting that those with one or more children may feel more prepared to make a decision about RRSO after their consultation with a GO/gynecologist than those without children ($p = 0.369$; Table 3.2). For a family history of HGSOC, the largest difference in scores was seen for the CWS (difference in median mean values = 0.75; $p = 0.120$; Table 3.2). Therefore, those with a family history of

HGSOC may be more worried about their own HGSOC risk than those without a family history of HGSOC. Finally, scale scores based on consultation with a GO/gynecologist did not differ greatly. Differences in scores on the CWS (difference in median mean values = 0.38) and DCS (difference in median mean values = 0.30) between these groups suggests that women who consulted a GO/gynecologist regarding RRSO may have felt less decisional conflict ($p = 0.580$), but increased cancer worry ($p = 0.474$) compared to those who did not consult a GO/gynecologist (Table 3.2). There was no difference in the median of mean SWD scale scores, suggesting that women in this group are equally as satisfied with their RRSO decision regardless of if they consulted a GO/gynecologist or not ($p = 0.891$; Table 3.2). PrepDM scores were not compared as women who did not consult a GO/gynecologist were not asked to complete survey questions pertaining to how their consultation prepared them to make a decision.

3.2 INTERVIEW RESULTS

There was an overwhelming interest from survey participants in completing the interview portion of the study, with a total of 29 contact forms received. As mentioned previously, interview participants were purposively sampled in order to represent participants from a variety of demographic and social parameters (i.e. age, relationship status, parity, menopausal status, family and personal history of cancer, etc.). A total of 16 interviews were conducted, one of which was lost due to technical issues, leaving a total of 15 interviews completed and analyzed to reach thematic saturation (Figure 3.1). Interviews lasted an average of 36 minutes and 56 seconds (ranging from 00:23:00 to 00:55:41). Interview participant demographics are outlined in Table 3.3. The majority of interview participants were < 50 years of age (9/15, 60%), with the mean age of interview participants being approximately 44 years of age. The majority of participants were university educated (8/15, 53%), white/European (14/15, 93%), married (10/15, 67%), and had one or more children (10/15, 67%). Ten (67%) of the interview participants had not had RRSO and 8/15 (53%) were pre-menopausal at the time of the interview. Notably, 5/6 interview participants ≥ 50 years of age had completed RRSO (one participant, P013, had the surgery tentatively scheduled but had not completed it yet), while no interview participants < 50 years of age had completed RRSO at the time of the interview (Table 3.4).

Table 3.3: Interview participant demographics.

Variable	Number of interview participants, n (%)*
Total interview participants	15 (100)
Age	
< 50 years	9 (60)
≥ 50 years	6 (40)
Education	
High school/College/Trade/Technical school	7 (47)
Bachelor's degree or more	8 (53)
Race/ethnicity	
White/European	14 (93)
Non-White/European	1 (7)
Relationship status	
Single	3 (20)
Married	10 (67)
Other	2 (13)
Number of children	
0	5 (33)
≥ 1	10 (67)
Menstrual period status	
Pre-menopausal	8 (53)
Post-menopausal	6 (40)
Peri-menopausal/Unsure	1 (7)
RRSO completed	
Yes	5 (33)
No	10 (67)

*Rounding may cause some percentages not to add up to 100.

Table 3.4: Specific interview participant information.

Participant ID	Age range (years)	RRSO completed
P001	30-39	N
P002	60-69	Y
P004	60-69	Y
P005	30-39	N
P006	50-59	Y
P007	20-29	N
P008	30-39	N
P009	40-49	N
P010	30-39	N
P011	50-59	Y
P012	40-49	N
P013	50-59	N*
P014	30-39	N
P015	30-39	N
P016	50-59	Y

N, No; Y, Yes. *Participant's RRSO scheduled but not yet completed.

The thematic framework derived from an in-depth qualitative analysis of the interview transcripts is outlined in Figure 3.3. To summarize, women first learn that they are at an increased risk for HGSOC when they are told they are *BRCA*-positive (usually by a GC). These *BRCA*-positive women then perceive their HGSOC risk through a personalized "lens" that is defined by contextual factors, such as their age, family history of cancer, beliefs, values, and previous experiences with the healthcare system. The lens through which women perceive their HGSOC risk also contributes to how the practical and emotional implications of being *BRCA*-positive, as well as the need for RRSO, are interpreted. They attempt to cope with these implications in a manner deemed suitable to them, mainly through gathering information (i.e. from their healthcare providers or external sources) and sharing information with others (i.e. through support groups or blogs). They also utilize their support networks (i.e. family members, other *BRCA*-positive women) as a coping mechanism. Ultimately, the decision whether or not to pursue RRSO depends on what each individual believes provides them with the most control over their perceived cancer risk and associated implications, which is informed by the unique context of their own lives (i.e. contextual factors). Finally, decision-making is cyclical and fluid in that the RRSO decision may be revisited as contextual factors, and therefore perceived risk, implications, and information needs, change over the course of one's life.

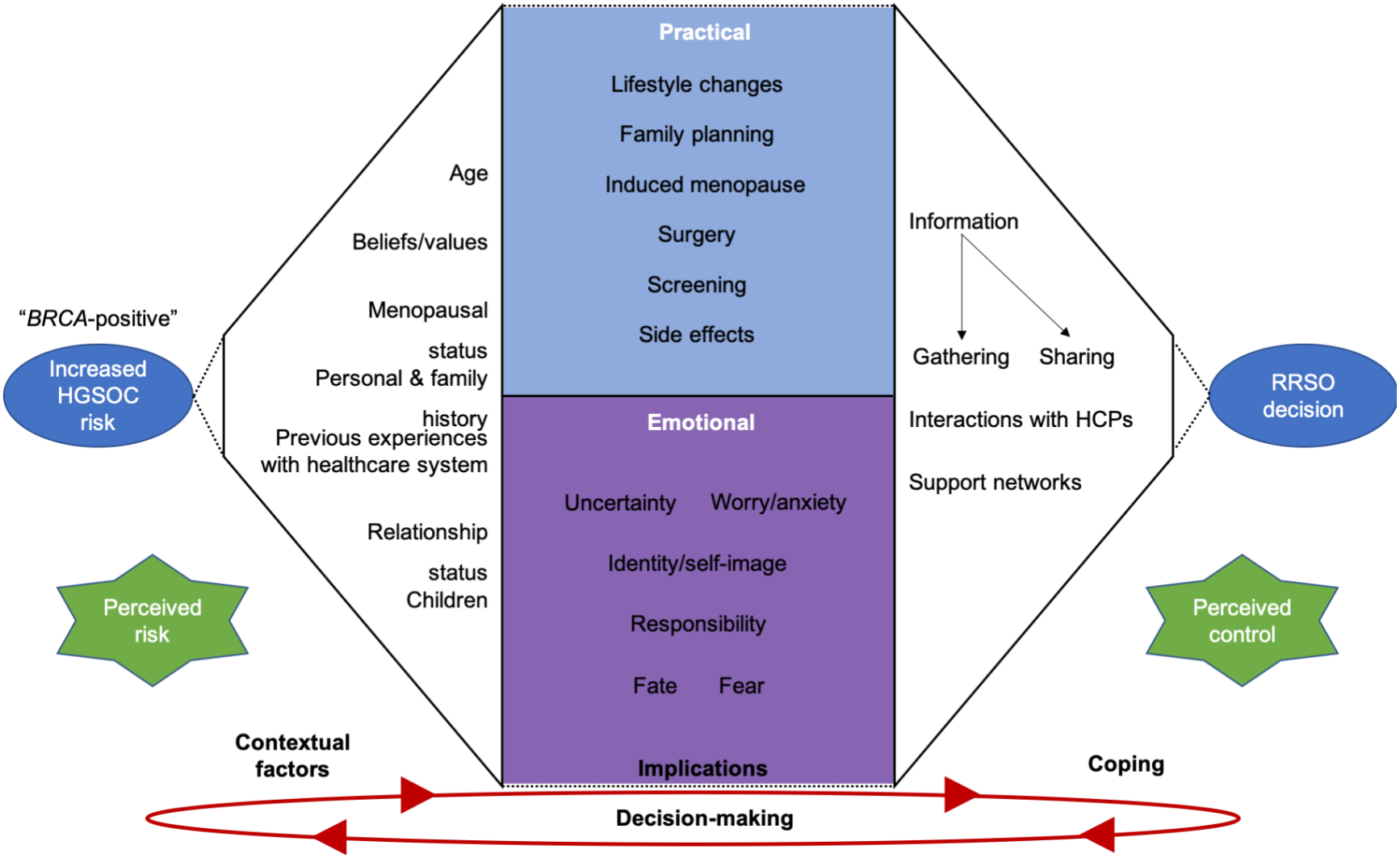

Figure 3.3: Qualitative thematic framework.

Patients are told they are *BRCA*-positive and therefore have an increased risk for HGSOC. Patients perceive their risk through a personalized "lens" that is defined by contextual factors. The lens through which a patient perceives their HGSOC risk also contributes to how the practical and emotional implications of being *BRCA*-positive, as well as the need for RRSO, are interpreted. Patients attempt to cope with these implications by gathering and sharing information, interacting with HCPs, and utilizing their support networks. Ultimately, the decision whether or not to pursue RRSO depends on what the patient believes provides them with the most control over their perceived cancer risk and associated implications, which is informed by the unique context of their own lives (i.e. contextual factors). Decision-making is fluid and cyclical in that the RRSO decision may be revisited as contextual factors, and therefore perceived risk, implications, and information needs, change over the course of one's life.

3.2.1 Contextual factors and implications

Contextual factors that help to define a woman's stage of life, such as their age and menopausal status, have an impact on how they view multiple practical implications of being *BRCA*-positive. For example, younger (and often pre-menopausal) women perceived the impact of surgery differently than older, often post-menopausal women, placing different emphasis on issues such as family planning and induced menopause in reference to RRSO:

> *"At this point my husband and I are wanting to have children so having surgery to remove ovaries and breasts isn't really in the picture. It's not an option." – P009 (Age: 40-49; RRSO: N)*

> *"I've been in menopause for eight years, I have zero desire for children… So [my ovaries are] like an old pair of shoes. It sounds bad - But you know, they were a nice pair of shoes, they were great, they looked good on me, and now they're not in fashion anymore." – P013 (Age: 50-59; RRSO: N)*

> *"It wasn't ideal to go through menopause super young and it was also a decision that could be made after any decisions around family had been finalized. At that point I didn't feel like I was in any rush because I've heard from different medical professionals that people will often wait or it's not necessarily done super young." – P001 (Age: 30-39; RRSO: N)*

Those with children expressed a degree of responsibility towards them, indicating that they decided to pursue risk-reducing surgery for the benefit and wellbeing of their children. One participant (P008) expressed this feeling in regards to her mastectomy, but noted that the "ideas remain pretty firm with the oophorectomy as well":

> *"With young children too, like the decision was also based on the fact that I didn't want them to see me sick, I wanted them to see me approach the decision with strength and then be okay on the other end." – P008 (Age: 30-39; RRSO: N)*

> *"I kind of weighed the pros and cons, and my daughter was at the top of the list. Like if I drew a web, a word web and put her name in the middle like the little sticks would be sticking out, like what happens if her dad passes away and I'm already gone, what happens if he's alive but not doing well and I'm sick and she's 17 and have to look after us kind of thing… So that's why I made those decisions, like it was basically because of… yeah it was because of her. I wasn't worried about my husband, I wasn't worried about*

> *my dad, I wasn't worried about my sisters or my brother or anything like that or my nieces or nephews, it was my daughter." – P016 (Age: 50-59; RRSO: Y)*

Women of different ages and menopausal status were generally reflective and self-aware that their decisions and opinions may differ had they been in a different stage of their lives. This supports the notion that decision-making regarding RRSO may be revisited over the course of one's life as circumstances fluctuate. For instance, some women may decide that RRSO is not ideal for them to complete before having a family, and therefore they may re-evaluate this decision once they are past childbearing age:

> *"It made it so much easier after menopause, you know, childbearing and everything. I think it would be a different story had I been younger." – P004 (Age: 60-69; RRSO: Y)*

> *"Because of my age, the ovaries and reproductive are no longer working, so it's absolutely irrelevant. If I was in my twenties, this would be really devastating, because of course, I had children, I wanted them, and I think I would have believed that I became an invalid woman… If I had to do it in my twenties and I didn't have my children, because I know that at that time – I don't know where I got the idea from, but if I wasn't married and had children before the age of twenty six, that would be a woman failure, that I wasn't succeeding as a potential wife and mother." – P013 (Age: 50-59; RRSO: N)*

> *"Maybe in some cases for other women, maybe they're younger, maybe they're not sure if they want to have kids, or they're still of childbearing years or something, or maybe they don't have the history that I have, and it might be a lot harder to make that choice, but it really wasn't hard for me." – P011 (Age: 50-59; RRSO: Y)*

Some of the younger interview participants who were not currently in a long-term relationship commented on how being *BRCA*-positive impacted their approach to romantic relationships and communication with potential partners, making it more difficult:

> "*I would love to have kids but if I didn't have my ovaries then I couldn't. Would that change your partner's decision to wanting to get together with you because you couldn't have kids and that was really important to them?" – P014 (Age: 30-39; RRSO: N)*

> *"I'm single and what if I meet someone and he's like, 'No, don't do that' or he really wants to have kids. And then you're like, well, sorry. I can't do that for you. You know? It's more of the social aspect of it… I know that I should do it because I don't want to have cancer again but socially it's tough… I do one day maybe want to find a husband*

maybe and so in that way it's sort of tough to be like, do I make a decision now or do I wait?"– P007 (Age: 20-29; RRSO: N)

Multiple women made comments pertaining to how they weighed the potential side effects and implications of RRSO against their risk of HGSOC. They acknowledged how the decision is not as "black and white" as it may seem and that there are factors to consider in addition to an increased risk of HGSOC, such as hormonal side effects and an increased risk for other health conditions like cardiovascular disease associated with RRSO and induced menopause:

"Am I making weird anecdotal decisions, when it's 'so what' if you're a little bit weird or hot flashy, when you don't get ovarian cancer. So I feel like I might have poor temperature regulation and this will happen to me for at least, you know, until I get tapered to proper hormone levels. Like I know that this thing will happen that's fairly minor, as compared to something terrible like ovarian cancer. But it might happen. You know what I mean? It's weird that you weigh them the way that you do." – P010 (Age: 30-39; RRSO: N)

"I just saw a doctor and I'm going to see a gynecological oncologist in a couple of weeks and she already said, 'no, I think you can wait until 35 or 38. Having an oophorectomy so young puts you at an increased risk for heart disease in your 40's and 50's.' So I don't know, there's so many options of the pros and cons that you have to really decide what's more important. Do I not want to not have heart disease but then have ovarian cancer or do I stick it out with the heart disease? It's just so many 'what ifs.'" – P007 (Age: 20-29; RRSO: N)

The complexity of the decision contributed to uncertainty, particularly pertaining to the side effects of RRSO, induced menopause, and HRT. For instance, the uncertain impact on mood, identity, and breast cancer risk:

"I still don't know what it's going to look like on the other side. So a lot of my questions come from, well how is this going to affect my daily life afterwards, being in forced menopause, and what is that going to be like? Am I going to notice these hormonal changes? And of course no one can give me that answer." – P008 (Age: 30-39; RRSO: N)

"Like the thing is, if you were to go through menopause, I know there's hormones that people can get put on but, at the same time, do those cause cancer? Could that increase my risk of getting breast cancer?" – P014 (Age: 30-39; RRSO: N)

> *"Who will I be after? Just like what if it changes you somehow? I realize that the point is the hormone replacement will just replace what you had. A question I always wondered was, like, do women's hormone levels differ and does anyone measure what someone's like pre-levels were?" – P010 (Age: 30-39; RRSO: N)*

Personal and family history of cancer, as well as previous experiences with the healthcare system, were also important contextual factors that contributed to the perceived emotional and practical implications of being *BRCA*-positive and the RRSO decision-making process. For example, women with a previous diagnosis of breast cancer stated that their past experience with cancer was a huge factor in how they perceived their HGSOC risk and decision about RRSO, where having a previous cancer diagnosis increased their perceived risk and need for RRSO:

> *"This one there was no wiggle room, like there was no other decision to make for me. I wouldn't risk going through chemo again… There was no ifs, ands and buts about it, it wasn't a well, let's wait and see and wait 'till I get cancer and do something about it. No, it was like if there's something I can do I'm going to do it." – P002 (Age: 60-69; RRSO: Y)*

> *"It freaks me out because I'm a statistical outlier. My girlfriend is a [scientist] so she's like you're a total outlier. Every symptom, everything happens to you. So having breast cancer at 31, I was diagnosed, and then all of sudden I have this higher rate of getting ovarian cancer and ovarian cancer we all know is the silent killer, you don't see symptoms or anything. So I'm like okay well I have to wait 'till I'm 35? So it kind of freaks me out but it's one of these things that you just shove in the back of your head." – P005 (Age: 30-39; RRSO: N)*

A handful of women who were interviewed had a mastectomy in the past, either as a direct result of a breast cancer diagnosis or as a risk-reducing measure after discovering they were *BRCA*-positive. Past experience undergoing a preventative surgery either positively or negatively influenced women's feelings about undergoing RRSO. Those who had a positive experience with mastectomy seemed to express less concern about RRSO compared to those who had a past negative experience with their mastectomy:

> *"I think that it would be something that I would consider doing. It's obviously a big decision to make. But I mean I did the preventative surgery for the breast cancer so I wouldn't be opposed to doing the other surgery." – P014 (Age: 30-39; RRSO: N)*

> *"I also thought of it as a very traumatic thing, again, to make this decision to remove my organs, when I had already regretted removing my breasts. So I found that to be maybe triggering some traumatic experience from that." – P012 (Age: 40-49; RRSO: N)*

Additionally, one woman in particular expressed concerns about having to deal with a cancer diagnosis in addition to a number of other emotionally and physically demanding health concerns, and used this as reasoning in support of risk-reducing surgery:

> *"I have depression and anxiety. I think that's enough to live with, and fibromyalgia. Why would I want to increase the size of my party? I need to do things to minimize what causes me trauma. And this does that… I worry lots, and I do not need another guest." – P013 (Age: 50-59; RRSO: N)*

In addition to personal experiences with cancer, family history of cancer also played a role in how women perceived their HGSOC risk and made decisions about RRSO. Some women used their relative's experiences as a reference point when assessing their own cancer risk and the appropriate time to pursue RRSO (if at all). For instance, women may decide what age they should be worried about being diagnosed with HGSOC, or what age to pursue surgery, based on when their family members were diagnosed or how old they were when they had RRSO:

> *"I mean within my family a little bit we talk about it because there are people in my family who are* BRCA-*positive who have had surgery and who haven't. For example, I mentioned I had one aunt who had both her breasts and ovaries removed, I have another aunt who is positive, she's had breast cancer twice and has survived and has chosen not to do any of the surgeries. And then my sister is also* BRCA-*positive and just close in age to myself so we both are kind of talking about these decisions a little bit together…. Our experiences are different. She has a family, I don't and also the care that we receive in different provinces is different as well I've noticed…. But in terms of ovary removal we're both like I guess still not ready to go through menopause." – P001 (Age: 30-39; RRSO: N)*

> *"I think it doesn't matter if you're a male or a female, I mean you still have a 50 percent chance that you're a carrier, and it doesn't even matter. It doesn't necessarily mean you're going to get cancer, because if you look at my older sister, she's never had any cancer and she's 65. And my other sister is six years older than me and she got breast*

> *cancer, but my older sister didn't get anything, but she's still opting to do all of these surgeries because that doesn't mean it won't come later on. I mean it's a choice that you have to make." – P011 (Age: 50-59; RRSO: Y)*

> *"It is based on the fact that ovarian cancer is so hard to detect. And knowing that my grandmother passed away from it, it was – like she was older when she was diagnosed, I think she was 70, so in my head I feel like I've got time but I also don't want to take advantage of that." – P008 (Age: 30-39; RRSO: N)*

Personal and family history also contributed to emotional implications such as cancer-related worry, anxiety, and fear. For example, having a personal or family history of cancer may numb an individual's fear of being diagnosed themselves or conversely, increase their cancer-related worry and anxiety:

> *"I stopped fearing cancer after I watched my mom pass away... With all the cancer that's been in my family it's basically I'm going to get it no matter what. This is just prevention from this type of cancer." – P016 (Age: 50-59; RRSO: Y)*

> *"I had an oncologist say, 'well we would probably with your family history maybe recommend the prophylactic surgery a little bit earlier than say for example what your sister could have.' And so that freaked me out." – P007 (Age: 20-29; RRSO: N)*

> *"Fear kicks in and goes, oh, just get the damn ovaries out so you stop worrying about this. And then another voice kicks in and says, really, because when you took your breasts off, did it actually prevent you from worrying about getting cancer again? No, no, it didn't. So just because you remove your ovaries, does that mean you're not going to get cancer again? No, it doesn't, it doesn't mean that. You know, I still have a liver, I have lungs and skin. What are they going to do? Like, strip me? Like, let's get real here, you can't just remove people's body parts." – P012 (Age: 40-49; RRSO: N)*

Emotions like worry, anxiety, and fear also surfaced as a direct result of learning one was *BRCA*-positive, unrelated to previous personal health experiences or family history. Women commented on how the knowledge they were at an increased risk for breast cancer and HGSOC affected them (or not) on a daily basis:

> *"It's also something I realized that I don't need to be thinking about on a daily basis, you know. I could stress over these types of decisions if I really wanted to all the time but I've learned that I have to compartmentalize that decision and not face that decision every day, just revisit it every once in a while. Because I don't need it to like hang over my life every single day but it is still there in the background." – P001 (Age: 30-39; RRSO: N)*

> *"I call it cancer hypochondria… you don't feel good or something is happening and you're like, 'oh my gosh, what is that.'" – P005 (Age: 30-39; RRSO: N)*

> *"The other day I felt like a huge lump right above my breast and I was just like, 'Oh my goodness. I have stage four breast cancer' because I also had a headache so I obviously have metastasis to the brain… I was just freaking out and so I ran on over to CancerCare Urgent Care and they get me in and then they're like, 'we think that's hormonal,' and then the next day I got my period. And so obviously it was. So I was just a wreck and I'm not always like that but it's there a bit more when you're doing breast exams or when you're feeling some abdominal discomfort, you're well, 'well is that it? Is that the cancer?' You know? And so it is a worry." – P007 (Age: 20-29; RRSO: N)*

HGSOC-related worry seemed in some cases to be a direct result of how women interpreted the effectiveness of screening versus RRSO. Women who felt comfortable with screening expressed feeling less cancer-related worry while those who acknowledged the lack of effective screening methods felt increased worry about HGSOC as a "silent killer":

> *"I also still don't feel a rush because if I'm getting screened so regularly and they're noticing things before they become an issue, like I'm not fearful about this killing me or anything, any time soon, like I don't live in fear. I know that I'm getting regular tests and I feel like I'm on top of it so I feel safer now and I feel like I have time to make these decisions." – P001 (Age: 30-39; RRSO: N)*

> *"Most of the cancer starts in your fallopian tubes and moves to your ovaries, and usually they don't find it 'till late third, fourth stage, which is really way behind the A-ball, so let's get rid of it before it can sneak up and be a real, real problem. And I agree with that, because it's something hidden, and why would you want to wait 'till stage three or four to find something out?" – P013 (Age: 50-59; RRSO: N)*

Some women also expressed fear about the surgery itself. However, this was never sufficient enough of a reason to decide against RRSO altogether. Others did not have concerns about the surgical procedure:

> *"I had never had a surgery in my life other than giving birth to my children. So again, I was concerned with the anesthetic, I was concerned with the side effects, concerned with recovery time, things like that." – P006 (Age: 50-59; RRSO: Y)*

> *"I'm not scared of surgery. I've had knee surgery before. The double mastectomy was a big one. I'm okay with that." – P014 (Age: 30-39; RRSO: N)*

Participants' beliefs and values played a substantial role in shaping their attitudes and feelings about being *BRCA*-positive, as well as the practical steps they took in response to their increased HGSOC risk. A consistent theme that arose was how women viewed their fate after learning they were *BRCA*-positive, interpreting their cancer risk as either something they were able to alter or something that was beyond their control:

> *"I'm more of a realist when it comes to things. I'm not an optimist where I'm like, I'm going to live and everything is going to be rainbows and sunshine. I'm a realist. I have a higher rate of getting cancer in my ovaries." – P005 (Age: 30-39; RRSO: N)*

> *"You feel mortal I guess… It makes you sort of just want to do the best that you can to, you know, stay healthy and prevent things that you can prevent. Obviously, you can't stop death or stop illness but the nice thing about knowing that you're positive is that you can sort of do something about it." – P015 (Age: 30-39; RRSO: N)*

> *"It's genetics. They're yours but you don't have any control over what's in them and whether you have this or that." – P010 (Age: 30-39; RRSO: N)*

Based on how women interpreted their fate, in conjunction with other emotional and practical implications of being *BRCA*-positive, they were able to make decisions about lifestyle changes and/or RRSO based on what provided them with the greatest amount of perceived control over their HGSOC risk. A couple of participants summarized the control that RRSO gave them over their HGSOC risk, saying:

> *"When you receive that diagnosis you're like on a conveyor belt, you have to go, go, go. At least there is some control in this method in that you can decide when it happens, and you can be healthy when it happens." – P008 (Age: 30-39; RRSO: N)*

> *"I've just decided that I want to reduce that risk. I have an 80 percent chance of [breast cancer] happening again, and so I want to reduce that risk down to 10, and the only way I can do that is by removing my breasts. And that's also why I removed my ovaries and my fallopian tubes." – P011 (Age: 50-59; RRSO: Y)*

Others were confident in the lifestyle changes they had made in order to mitigate their HGSOC risk and were comfortable not having RRSO:

> *"I'm doing everything I can in my power… So that includes eating really healthy, cutting out meat and dairy and eggs and also I've cut out alcohol… I'm exercising and I'm eating well and getting lots of greens. And I'm monitoring my health with my family doctor." – P009 (Age: 40-49; RRSO: N)*

> *"I believe that if I remove [my ovaries], my health starts deteriorating… My whole goal here was not to focus on cancer, but to focus on becoming healthy to my core, finding out if I really was living the life where I can feel light and not heavy and depressed and frustrated, you know. Because I think when you're living in that state, you're in that homeostasis and disease can't exist. So the focus was, let's not focus on avoiding cancer, let's not give cancer attention, let's give health your attention, let's give healing your attention." – P012 (Age: 40-49; RRSO: N)*

Finally, multiple women discussed the impact that RRSO would have on their female identity and self-image. Some felt as though removing their ovaries made them feel like less of a woman, while others did not feel it had an impact on their perceptions of "femaleness." In addition, some women recognized how this impact may differ between mastectomy and RRSO since the breasts are an external, visible organ while the ovaries are internal:

> "*Your ovaries and fallopian tubes and your uterus, that's a very important part of you as a lady. It's annoying sometimes but it is an important part of you. And so I think for them they can be like, 'well if it's going to give you cancer get rid of it.' Or your breasts, that's a huge part of you to just say, 'it's got to go.'" – P007 (Age: 20-29; RRSO: N)*

> *"I think what happens psychologically a lot of times, if you're going to remove a woman's breasts and you're going to remove a woman's ovaries, you're making them a man… So this, to me, is going against what a woman is all about. So when you remove estrogen from a woman's body, you turn them into a masculine figure, and I think the body is super sad about that." – P012 (Age: 40-49; RRSO: N)*

> *"Ovaries are internal. So if you remove ovaries, no one will be able to see a physical difference. I'm looking at my body on a daily basis. So in my mind, if I remove my ovaries, of course there'll be surgery but it won't be as… I know it sounds a little counter-intuitive, but it's not as invasive. I know it's internal surgery – but removing ovaries is very clean in a sense of, you go in, you remove them and that's all you do. And then I'm sure that there's symptoms and recovery from that and your body goes through changes and all of that. But, at the same time, it's not external and it's not noticeable so once it's done, it's like getting your appendix removed or getting your tubes tied if you wanted to not have kids anymore. Do you know what I mean?" – P009 (Age: 40-49; RRSO: N)*

In summary, *BRCA*-positive women differ in the contextual factors that define them, including but not limited to their age, menopausal status, parity, relationship status, personal and family history of cancer, as well as personal beliefs and values. This section outlines how these contextual factors influence the perceived practical and emotional implications of RRSO, such as induced menopause, family planning, uncertainty, fear, and HGSOC-related worry.

3.2.2 Coping

Women in this study largely focused on either gathering or sharing information as a means of coping with the emotional and practical implications of being *BRCA*-positive and having an increased risk of HGSOC. The majority of women gathered information related to their cancer risk and risk-reducing surgeries through a variety of different sources, including their HCPs, emerging research and relevant literature, as well as other *BRCA*-positive women. Women mainly sought information from GCs and GOs/gynecologists; however, other HCPs women used included primary care physicians, surgeons, nurse practitioners, and those located within specialty clinics such as the Breast Health Centre in Winnipeg. HCPs were able to address some of the practical implications of being *BRCA*-positive and/or RRSO by putting women's cancer risks into context and comparing these risks to the general population:

> *"[The gynecological oncologist] showed me the piece of paper of the percentage at which I'm at. He's like, 'you're higher than normal but you're still within a normal range at my age. But once you're hitting these ages your risk goes up significantly.' And he's like, 'this is why we wait until this point.' So that was good to have that." – P005 (Age: 30-39; RRSO: N)*

> *"I honestly can't say that there was anything that was the most helpful other than discussing the risks, and the long term [cancer] risks… I'm not a big numbers person. It doesn't affect all my decisions. But I think because it was a higher number than the average female, then that affected my decision for sure." – P006 (Age: 50-59; RRSO: Y)*

> *"I think it was probably the medical genetics people, they have these super old flip books… And it just talks about* BRCA1 *versus* BRCA2 *and where the risk lies for breast cancer versus ovarian cancer over time. Again – you could never get it, you could get it*

> *early, you could get it at the age that everyone in the population would get it. But I liked that because all of sudden, you know, like your risk of breast cancer is 80 percent, but it's like, okay, 35 is the danger zone. Ovaries, 45 is the danger zone. Right? I kind of liked that, and then* BRCA1 *and* BRCA2 *don't carry the same risks. It flip-flops between breast and ovarian... I guess like a risk assessment with my information compared to what the literature says." – P010 (Age: 30-39; RRSO: N)*

Some women also commented on the ability of their HCPs to address some of the emotional implications that came with being *BRCA*-positive, and therefore ease their cancer-related worry, fear, and uncertainty:

> *"They [HCPs at the HGC] listened a bit more to what I had to say, so I felt the fit was better and I felt better after talking to them." – P012 (Age: 40-49; RRSO: N)*

> *"I think the genetic counselling was really helpful. It's definitely something I appreciated that it was available because then you don't have to do all the research yourself and you have someone who can kind of tell you a little bit of what you expect. And I think she at the time had told me about like support groups and things like that, which I might take advantage of in the future. So I found the whole experience, it was daunting but it was really helpful. And then I also thought that the surgeon was just really helpful as well. He was just an open and accepting kind of guy and he didn't make you feel weird and was able to address some of fears or concerns really well. So I feel like overall like doctors have been really good about it." – P015 (Age: 30-39; RRSO: N)*

While women's experiences with their HCPs were overwhelmingly helpful, some commented on the quantity and quality of information that they received. Some women felt that they lacked an appropriate amount of information to make a decision about RRSO and needed to seek out more, or that the information they received from their HCPs was not sufficient enough for them to make an informed or confident decision:

> *"They had talked to me about a salpingo-oophorectomy or whatever, versus taking out the uterus. And I didn't really get what, like pros and cons around that. I know if you leave the uterus, you need estrogen and progesterone as your home replacement therapy, but if you don't have the uterus, you can just do estrogen, or whatever it is. But then I don't know what all the pieces are. Why people choose to leave it, or why people choose to take it. I feel like it was just kind of glossed over." – P010 (Age: 30-39; RRSO: N)*

> *"I am aware that these medical teams are super-educated, they have stuff behind their things. But you know what, statistics aren't everything, because you know what, those statistics they give you on those papers, they have no idea the emotional status of that*

woman, they have no idea if she had depression, they have no idea if she has food intolerances, they have no idea if she felt inner anger." – P012 (Age: 40-49; RRSO: N)

"[the ovarian surgery] is something I'd definitely consider. The little that I've talked to doctors about it they've sort of suggested that I wait till the age of [menopause] but I don't know if that's entirely necessary or not. So that's another reason to talk to a specialist about it." – P015 (Age: 30-39; RRSO: N)

"I did go see [a gynecological oncologist] and he was like not really helpful at all. So I didn't really get any answers. I kind of left thinking, I don't know what to do right now and he couldn't tell me anything." – P014 (Age: 30-39; RRSO: N)

Conversely, some women mentioned receiving an overwhelming amount of information that wasn't necessarily helpful for their decision-making process at the time of the appointment:

"I think they give you so much information because… it's good because everybody takes away something different. You hear what they're saying but you're not always listening if that makes sense." – P005 (Age: 30-39; RRSO: N)

"I felt a bit overwhelmed at that appointment. It felt very like, 'you should go for surgery, you should go for surgery.'" – P010 (Age: 30-39; RRSO: N)

"I feel like in that [genetic counselling] appointment, they just tell you everything where you can't really process it. I think it would have been great if they could have another appointment after. Like you get your results and then it's like, okay you've had time to think about it, let's talk about it. Rather than having to make all those decisions right away. Like yeah, I do want to see that doctor and sure you can… It was just a lot when you're already kind of overwhelmed by hearing the results, to like process it." – P014 (Age: 30-39; RRSO: N)

Multiple women appreciated that the information they received from their HCPs was largely based on recent and relevant research. As well, some women decided to do their own research as a means of gathering information:

"They walked through the procedure. It was very based on current research, and the reason I can tell that is because I had some questions and the doctor said, 'I'm going to get back to you,' and within a few hours of the appointment she called back with essentially proof – research that had been done – which supported her assumption, or her idea that I should be waiting until I was 40. So I felt it was very research-based." – P008 (Age: 30-39; RRSO: N)

"I went in thinking 'I'm going to have my ovaries removed…' Whereas it's like, 'no you don't have to. We can if you really want, but we don't recommend it based off these numbers and this research.' And I like the research part of it because I think that it's

> *valuable to education and getting people to understand where they're at." – P005 (Age: 30-39; RRSO: N)*

> *"I've done research with myself, just doing research and finding doctors and studies that focus on whole food, plant-based lifestyle as preventative measures and there's lots of information about that… I feel really confident in my decision because I've done a lot of research." – P009 (Age: 40-49; RRSO: N)*

> *"I thought, 'what if I don't get these surgeries, what will happen? What are the rates again? Tell me my percentages of getting breast cancer, tell me my percentages of getting ovarian cancer. What if I have this kind of a lifestyle, does it still affect the percentages?' So then I started more research, more proactive finding out more information about the* BRCA *gene." – P006 (Age: 50-59; RRSO: Y)*

Other *BRCA*-positive women undergoing similar challenges and experiences were also considered valuable sources of information. Some women had already communicated with other *BRCA*-positive women and found it to be helpful, while others had not yet had the chance to reach out to others but saw the value in speaking to women with similar experiences (i.e. through participating in support groups):

> *"I process by talking. I process by learning what other people have done and what works for them and trying to visualize that working for me as well. I was actually following a young girl on YouTube." – P006 (Age: 50-59; RRSO: Y)*

> *"I would totally love to be, like talk to people that are my age, that did this… To be like, what happened?" – P010 (Age: 30-39; RRSO: N)*

> *"I don't know what it will be like to have the hysterectomy done... I've had conversations with other women in the past that have had it done, but it was with a different ear… I wasn't listening for self-learning, I was listening to hear, not to respond or to own. So now I need to listen to hear, to accept and come to my own conclusions." – P013 (Age: 50-59; RRSO: N)*

In addition to information gathering, women engaged in information sharing through multiple modalities as a means of coping with the emotional and practical implications of being *BRCA*-positive and the difficult decisions that come along with it. For instance, interviewees talked about the helpfulness of writing public blog posts and participating in community outreach:

> *"The second major healing thing I did was write… So I started a blog, where I wrote 'Who am I', and that was the very first blog post. And the second blog post was my release – the start of releasing my decision to remove my breasts, releasing that trauma from me. And I did that through writing. It just came naturally, it just flowed out of my head and I couldn't write fast enough. It just came pouring out of me, and the second thing was to put it out there for the world to read, so communication. And then not fearing what people thought of me and not fearing to hide behind my experiences, and letting people know. Because you can't help people unless you let people know – so you can go through these things and keep it hidden, because you're so scared about what other people are going to think about you, but you have to get beyond that, beyond that fear of just pressing that button, like, send, you know. And then I remember biting my nails, and I remember crying while I wrote it, and then feeling the release after. Like, oh thank god, I don't have to hold that in anymore." – P012 (Age: 40-49; RRSO: N)*

> *"Where I live we have this huge cancer fundraiser coming up and they're like, 'well can you speak for it?' At first I was like, 'no way. Find a better speaker.' But at the same time, it's okay because I can probably say something and even if I just reach one person to say to get checked, you've made a difference right? So I can use this crappy situation and be super grumpy all the time but I could also be like, 'no, I'm going to help people with it.'" – P007 (Age: 20-29; RRSO: N)*

The majority of women also sought support through their loved ones (i.e. partner, children, parents, friends, etc.), who stood by them through their decision-making process, provided advice and encouragement, as well as listened to their concerns and stories. Others mentioned they were hesitant to share with those who were close to them for fear that they would be unable to empathize with their unique situation:

> *"I think [my partner and I] have an understanding that this is totally my decision and he's very supportive of that… He respects me and my decision and all that stuff. I feel like my family's supportive too. The* BRCA *comes from my mom's side but my dad is always passing us any piece of research that he sees online, he's emailing us and looking out for us so that's kind of cool." – P001 (Age: 30-39; RRSO: N)*

> *"My super close friends, we do talk about it sometimes but you don't always want to be weighing down a conversation with cancer because it's kind of depressing… So we do talk about it but it's tough because I don't think they understand… We're supposed to be going travelling all the time and drinking wine all the time. Bringing up this cancer thing is kind of a damper." – P007 (Age: 20-29; RRSO: N)*

Finally, women talked about their HCPs being a part of their support network. In reference to the HGC in particular, one participant emphasized how the clinic made her feel "special" and understood the unique challenges she faced as a *BRCA*-positive woman:

> *"I remember a nurse handing me a card if I ever had any concerns or issues or needed to visit them or be admitted or something, there was contact information. That made me feel like I was special maybe as a* BRCA-*positive person that I would get – it would be understood, the position that I'm in or something." – P001 (Age: 30-39; RRSO: N)*

Ultimately, women's interactions with their HCPs and support networks allowed them to both gather and share information as a means of coping with the complex emotions and practical considerations that result from being *BRCA*-positive. Information related to RRSO surgery and side effects, cancer screening, and induced menopause (among other important topics) is gathered through appointments with HCPs, personal research, and speaking to others. It is then synthesized in order to make a decision regarding RRSO. Concurrently, the gathering and sharing of information through interactions with HCPs and support networks aids in easing emotions such as worry, anxiety, fear, and uncertainty. Taken together, *BRCA*-positive women are able to make a decision about RRSO based on their unique needs.

3.3 SYNTHESIS OF RESULTS

The most significant factor identified in this study influencing the decision-making process and feelings towards the RRSO decision was menopausal status. This was evident based on both the quantitative and qualitative results. The most significant differences ($p < 0.001$) between pre- and post-menopausal women were seen on the CWS and SWD scale (Table 3.2; Figure 3.2A). Decisional conflict measured using the DCS was also significantly less for post-menopausal versus pre-menopausal women ($p = 0.001$). Similar quantitative findings were found related to age (< 50 or ≥ 50 years of age). This is understandable since age was found to have a very strong relationship with menopausal status (indicated by a Cramer's V of 0.55), where older women were more likely to be post-menopausal at the time of their RRSO decision. In line with these quantitative findings, women who were post-menopausal at the time of their RRSO decision commented, "it made it so much easier after menopause" (P004; Age: 60-69; RRSO: Y). Women who felt the decision was easier to make because they were past menopause, and therefore past childbearing age, showed less decisional conflict related to the RRSO decision. Having fewer factors to consider when a woman is older (i.e. concerns about family planning and induced menopause are absent) may also explain the higher levels of satisfaction (measured by SWD scale scores; Figure 3.2A-B) with their decision. Women ≥ 50 years of age commented that they were "not planning on having kids anyways so it didn't matter" (P011; Age: 50-59; RRSO: Y), and referred to their ovaries as "absolutely irrelevant" (P013; Age: 50-59; RRSO: N). In contrast, younger women experienced more decisional conflict and were less satisfied with their decisions regarding RRSO, possibly because of the increased complexity of the associated emotional and practical implications, including concerns about family planning and induced menopause. Women < 50 years of age stated, "it wasn't ideal to go through menopause super

young" (P001; Age: 30-39; RRSO: N). Others said, "at this point my husband and I are wanting to have children so having surgery to remove ovaries and breasts isn't really in the picture" (P009; Age: 40-49; RRSO: N) and that they "can't really do anything about it immediately if you want children. So it's kind of like a waiting game" (P015; Age: 30-39; RRSO: N). The variation in responses on the SWD scale were quite large, perhaps as a result of the heterogeneity of contextual factors between participants of the same age within the sample. For example, having (or wanting) children or not, being in a relationship or single, personal and family history of cancer, as well as beliefs and values differ amongst participants. Variations amidst these contextual factors, even amongst women of similar ages, may alter how one perceives the emotional and practical implications of RRSO, as well as how one copes with their RRSO decision. This may result in differing levels of satisfaction about RRSO-related decisions, and therefore the large distribution of mean SWD scores in women < 50 years of age.

HGSOC-related worry was significantly greater for pre- versus post-menopausal women (Figure 3.2A). This is consistent with younger women who felt fearful and worried about their cancer risk, consistent with higher scores (although not significant) on the CWS compared to women ≥ 50 years of age (Figure 3.2B). These women said that they had "cancer hypochondria" (P005; Age: 30-39; RRSO: N) and, "it is a worry. It's sort of always there" (P007; Age: 20-29; RRSO: N). On the other hand, a few women < 50 years of age did not seem to allow the fear of getting cancer consume their lives, and therefore were not as worried about their HGSOC risk. They commented that they "don't need to be thinking about it on a daily basis" (P001; Age: 30-39; RRSO: N) and, "don't think on a regular basis I feel scared about it" (P014; Age: 30-39; RRSO: N).

Quantitative analysis revealed that having a previous diagnosis of breast cancer did not have a significant impact on decisional conflict (measured by the DCS) compared to those without a previous diagnosis of breast cancer (Table 3.2; Figure 3.2C). This is in contrast to qualitative findings that suggested having a personal history of breast cancer reinforced one's decision to pursue RRSO because "if someone's gone through chemo once they don't want to go again" (P002; Age: 60-69; RRSO: Y). Another woman seemed to have little decisional conflict about her decision to pursue RRSO, stating, "as soon as I found out I had [breast] cancer, and I know that they're related… I just said, 'I want them out'" (P011; Age: 50-59; RRSO: Y). Interestingly, HGSOC-related worry (measured by the CWS) was significantly lower for women who had previously been diagnosed with breast cancer versus those who had not. This may be because there were a greater number of women ≥ 50 years of age in this group, and the likelihood of being diagnosed with breast cancer increases with age. Furthermore, older women are more likely to have already had RRSO, significantly reducing their risk of developing HGSOC and as a result, their HGSOC-related worry.

Individuals who were decided about RRSO (either firmly for or against) had significantly less HGSOC-related worry and decisional conflict than those who were undecided about RRSO (Figure 3.2D). In the qualitative interviews, women who had made a firm decision about RRSO did so because it provided them with greater perceived control over their HGSOC risk. Feeling an increased level of control over their situation, whether through surgery or other means, may contribute to lower levels of HGSOC-related worry:

> *"It's very hard to detect ovarian cancer, and usually when you have it, it's almost at a point where it's too late to treat. And I thought I'm not screwing around with this, I don't need them, let's get them gone… It's all it was, that's the only reason, otherwise I had no reason to remove them." – P011 (Age: 50-59; RRSO: Y)*

> *"What do you need to do to not let [cancer] happen again? You know, that put a huge responsibility on myself to heal, huge, because I was not going to allow them to cut me open and remove me anymore." – P012 (Age: 40-49; RRSO: N)*

The above examples exhibiting motivation to reduce and take control over one's HGSOC risk are also consistent with and exemplary of reduced decisional conflict. One woman was very clear that she was motivated to reduce her cancer risk and had little decisional conflict about RRSO, stating, "I wouldn't have hesitated, I would have definitely had the surgery… There would be absolutely no question in my mind, I would not take the risk of having ovarian or uterine cancer" (P002; Age: 60-69; RRSO: Y). Of note, this woman was also ≥ 50 years of age and post-menopausal, which may additionally be contributing to her reduced decisional conflict.

A handful of women who were decided against RRSO exhibited decreased cancer worry as a product of their trust in their HCPs and the feeling of reassurance related to the healthcare they were receiving as a result of being *BRCA*-positive:

> *"I'm not super worried. And I think part of the reason I'm not worried is I've received very good care, like I've received very good surveillance. People are very interested in investigating, like I'm sent for tests. Any time that I have any sort of cramping or issues my doctor has sent me for ultrasounds, pelvic ultrasounds. So I've actually had like probably one a year over the last five or six years. So I feel like I'm getting a lot of positive attention and positive healthcare without actually being sick yet. So, you know, I know that the resources are there for me when I need them. If I have any concerns the doctors will take them seriously because they know that I am high risk." – P001 (Age: 30-39; RRSO: N)*

Quantitative results comparing those with and without children showed that there were no significant differences between groups for any of the validated scales (Table 3.2; Appendix A.7). Those without children scored slightly lower on the PrepDM scale, suggesting that they may feel less prepared to make a decision about RRSO after their consultation with a GO/gynecologist than those with children. Results from the qualitative interviews suggest that children and family planning may have a greater impact on how prepared a woman feels to make a decision, as well

as her decisional conflict about RRSO, than expected from the survey results. For example, not yet having children was often quoted as one of the largest barriers to pursuing surgery:

> *"Maybe because I don't have kids, my two sisters who were tested and got the results, each of them had three kids by the time that they were told that. And so maybe the push is a little bit different. I sort of just have that constantly in the back of my mind but I also just don't want to be married and having kids right now." – P007 (Age: 20-29; RRSO: N)*

> *"If I had children already, if I had a family already, I wouldn't be so hung up on keeping my ovaries especially, and my breasts, but for different reasons. I still need them to have a family. I mean if I had a family, I don't know what my position would be because I wouldn't be worried about starting a family. So maybe I would do the ovaries and just not worry about it." – P009 (Age: 40-49; RRSO: N)*

Other survey results that were inconsistent with the interview findings were that scores on the validated scales did not significantly differ for those who had a family history of HGSOC versus those who did not (Table 3.2; Appendix A.7). The interviews revealed that women took their family history of HGSOC into account when making a decision about RRSO. Having a close relative diagnosed with or die from HGSOC informed a participant's risk perception and seemingly increased the motivation to pursue RRSO. This is consistent with survey results showing a trend towards reduced decisional conflict as well as increased cancer worry, preparation for, and satisfaction with decision-making for women with a family history of HGSOC compared to those without, however these findings were insignificant. Women opted to pursue surgery because of their fear of developing HGSOC, stating things like, "that's what my mother and grandmother died from" (P011; Age: 50-59; RRSO: Y). When "the history is there" (P006; Age: 50-59; RRSO: Y), it reinforced the decision and reduced decisional conflict about pursuing RRSO:

> *"I saw what [my mother] went through and I would never have wanted to go through that… Like seeing someone go through chemo and radiation and all that, it takes a toll on your body. So if there's a way to prevent it, why not do it?" – P014 (Age: 30-39; RRSO: N)*

Perhaps the most surprising finding consistent between survey and interview results was the lack of significant impact consultation with a GO/gynecologist, whether at the HGC or not, had on HGSOC-related worry, decisional conflict, and satisfaction with RRSO decision (Table 3.2; Appendix A.7). It is also worth noting that PrepDM scores did not significantly differ between any groups compared during the analysis, suggesting that the GO at the HGC (or in a minority of cases, gynecologist outside of the HSC) did not have a significant impact on preparedness for RRSO decision-making between groups (Table 3.2). Interviews revealed that women had often made up their mind about RRSO before attending the HGC, and that they used these consultations more as a source of information and ongoing support, instead of for advice and help with RRSO decision-making or to reduce their decisional conflict:

> *"It didn't change my decisions, it just reinforced them. When she gave us the chart with the percentages and the risks I thought that was just valid information for me but it didn't change anything." – P002 (Age: 60-69; RRSO: Y)*

> *"It was more, well do we need to convince you to have this surgery? And I was like, look, I'm here to tell you I want the surgery, so it was more just them giving me information about the risks that were involved… And it didn't really matter, I had already made up my mind, this is what I want to do." – P011 (Age: 50-59; RRSO: Y)*

> *"They listened a bit more to what I had to say, so I felt the fit was better and I felt better after talking to them." – P012 (Age: 40-49; RRSO: N)*

These findings are in line with the model proposed in Figure 3.3, in which HCPs such as GOs at the HGC are utilized by patients more as a means of coping with the practical and emotional implications of being *BRCA*-positive through information gathering and specialized support, rather than to help them make a decision about RRSO.

CHAPTER 4: DISCUSSION

4.1 DISCUSSION OF RESULTS

4.1.1 Summary of findings

The primary goal of this study was to explore how and why *BRCA*-positive women make decisions about RRSO. Based on the results of this study, it is evident that the decision whether or not to pursue RRSO is complex and involves many interrelated factors and considerations. Some of the factors identified in this study to be involved in RRSO decision-making have previously been described (section 1.8.1), including responsibility for family members (Hallowell et al., 2001, 2004; Hesse-Biber, 2014; Howard et al., 2009), age, parity, family planning and timing of surgery (Cherry et al., 2013; Miller et al., 2010), family history of breast cancer and HGSOC (Hallowell et al., 2001; Hesse-Biber, 2014), as well as self-image (Mahat-Shamir & Possick, 2017; Meiser et al., 2000). While it is evident that menopausal status played a significant role in participants' decision-making processes, one's menopausal status is intertwined with age and stage of family planning, where pre-menopausal women are younger and earlier in the stages of their family planning (i.e. they may have less or no children). These are contextual factors that were identified as having an impact on *BRCA*-positive women's perceived emotional and practical implications of RRSO, and therefore their final decision about RRSO. Indeed, Cramer's V indicated a very strong correlation between age and menopausal status (0.55). Comparisons of scores on the CWS, DCS, and SWD scales supported that pre-menopausal, and therefore younger, women exhibited greater levels of HGSOC-related worry and decisional conflict, as well as decreased satisfaction with their RRSO decision compared to older, post-menopausal women. The implications related to building a family, side effects of induced menopause, impact on romantic relationships and self-image, as well as HGSOC-related

fear and anxiety are perceived as greater for pre-menopausal women. Therefore, pre-menopausal women may spend more time coping with and re-evaluating their situation over the course of their lives in order to make a decision about RRSO compared to post-menopausal women. The recommendation from HCPs to delay consideration of RRSO until after child-bearing is complete (i.e. 35-40 and 40-45 years of age for individuals with P/LP variants in *BRCA1* and *BRCA2*, respectively; Table 1.1) adds time for younger women to revisit the decision-making process over the course of their lives as contextual factors, and therefore perceived implications of RRSO, change. When women finally make a firm decision about RRSO (i.e. either for or against surgery), it is based on what provides them with the greatest perceived level of control over their HGSOC risk as well as what makes sense to them in the context of their lives at the present time. Making a firm decision about RRSO significantly reduces HGSOC-related worry and correlates with significantly reduced decisional conflict (Figure 3.2D). This notion is supported by previous studies (described in sections 1.7 and 1.8.1) that have identified reduced levels of HGSOC-related worry in women who chose RRSO (Finch et al., 2013; Madalinska et al., 2005; Robson et al., 2003), using RRSO as a means of gaining control over their perceived vulnerability, distress, and anxiety (Babb et al., 2002; Hallowell et al., 2004; Hesse-Biber, 2014; Mahat-Shamir & Possick, 2017; Meiser et al., 2000; Miller et al., 1999).

In this study, *BRCA*-positive women were identified as being decided or undecided about surgery. Although the focus of this study was on the factors involved in and experiences surrounding decision-making, rather than personality traits and decision-making styles, some similarities can be drawn from the study findings with the decision-making styles previously described in section 1.8.2. For example, *BRCA*-positive women who were undecided about RRSO exhibited a more avoidant or deliberative decision-making style (Howard et al., 2011;

Scott & Bruce, 1995), wherein they mulled over their decisions for an extended period of time and continuously incorporated new information as they received it from a variety of sources (i.e. HCPs, family, friends, support groups, the internet, etc.). In comparison, some women who were decided about RRSO seemed to demonstrate more "snap" or spontaneous decision-making styles (Howard et al., 2011; Scott & Bruce, 1995), where their decision about RRSO was firm and confident. As in the study by Howard et al. (2011), where "snap" decision-makers described their choices as "no brainers," an interviewee with a similar attitude in this study stated, "there was no ifs, ands, and buts" (P002; Age: 60-69; RRSO: Y) about her decision to pursue RRSO. Finally, the literature on decision-making styles described in section 1.8.2 suggests that individuals often incorporate multiple decision-making styles at once when making important decisions. As presented in this study, *BRCA*-positive women used both rational and emotional/intuitive decision-making styles (Dean & Rauscher, 2017; Howard et al., 2011) when deciding about RRSO. For example, they synthesized information about the relative risk for developing HGSOC over the course of their lives (rational, based on established statistics) with the desire for a family and responsibility felt towards their children (emotional and feelings-based).

This study identified that the HGC does not significantly impact *BRCA*-positive women's preparedness for decision-making about RRSO as much as previously assumed. This was exemplified by the lack of significant differences on PrepDM scale scores between groups (i.e. pre- and post-menopausal women, women < 50 and ≥ 50 years of age, women with and without children, as well as women with and without personal and/or family history of breast and/or HGSOC; Table 3.2). Previous literature (described in section 1.7) has suggested that uncertainty or lack of adequate information about side effects related to induced menopause and HRT, as

well as the impact of RRSO on sexuality and body image, may contribute to feeling less prepared to make a decision about RRSO (Babb et al., 2002; Brotto et al., 2012; Campfield Bonadies et al., 2011; Cherry et al., 2013; Hallowell et al., 2004, 2012; Kim et al., 2014; Meiser et al., 2000; E. M. Swisher et al., 2001). The results of this study suggest that the HGC is an accurate source of information related to the hormonal and sexual side effects of RRSO, but that emotional implications like worry, fear, and uncertainty related to surgery and HGSOC risk are interpreted through personal contextual factors that uniquely define each individual (Figure 3.3) and undoubtably impact feelings of preparedness to make a decision about RRSO. A potential framework for improving preparedness for RRSO decision-making will be described in section 4.1.2.

Those who consulted a GO/gynecologist did not have significantly greater levels of satisfaction with their RRSO decision, or significantly less HGSOC-related worry and decisional conflict than those who did not consult a GO/gynecologist. However, it was evident that the HGC remains essential through its role in the coping stage of the decision-making process. Based on the interview results, *BRCA*-positive women utilize the HGC and their HCPs as a source of information and support to rationalize and cope with their RRSO decision. For instance, the HGC provides information on HGSOC risk stratified by age. Learning this information may help a *BRCA*-positive woman justify her decision to wait until she is older to pursue RRSO, when her HGSOC risk is perceived as "high enough" to outweigh the other practical and emotional implications of surgery. In addition to gathering information on the practical implications of RRSO, such as induced menopause and HRT, HCPs within the HGC were used as an emotional support system for *BRCA*-positive women. The opportunity for scheduled follow-up appointments allows ample opportunity for continued support throughout

the course of one's life and decision-making process. Individuals also identified other *BRCA*-positive women, loved ones (i.e. friends, family, partners, etc.), and information sharing through community outreach (i.e. fundraisers) and electronic sources (i.e. internet blogs, YouTube) as means of coping throughout their decision-making process.

4.1.2 The HGC as a source of decisional support

O'Connor et al. (1998) defines an effective decisional support intervention as one which decreases an individual's decisional conflict as well as increases an individual's satisfaction with their final decision and decision-making process. The HGC may benefit from modifications to its framework that effectively improve these decisional outcomes. As discussed in section 2.4, identifying the determinants of a patient's decision is one of the first important aspects of facilitating informed, shared decision-making (Figure 2.2). The current HGC model does an excellent job of identifying patients' clinical information and demographics (i.e. medical and family history, age, menopausal status, etc.), as well as providing information on HGSOC risk and RRSO tailored to these characteristics. Other determinants of decisions include the patient's perception of the decision, as well as how they view the perception of others and their available personal and external resources (Figure 2.2) (O'Connor et al., 1998). The current HGC model effectively provides information on the RRSO procedure, alternatives, and implications (both benefits and risks) to patients in order to increase their knowledge and set realistic expectations regarding HGSOC risk. Educational resources, including informative websites and anatomical diagrams, are also presented to patients during their appointment. While knowledge and information are an important aspect of decision-making, exploring personal values, beliefs, support networks, social circumstances, preferences for involvement in decision-making, and past experiences is essential to fully understand the determinants of a patient's decision and

subsequently tailor support as well as the structure of patient-provider interactions (O'Connor et al., 1998). It is understandable that time constraints and high patient volumes may limit the ability of HCPs within the HGC to fully explore and attend to these aspects of decision-making. Decision aids have proven to be a cost-effective means of facilitating shared and informed decision-making (Légaré et al., 2006; O'Connor et al., 1998; Uhlmann et al., 2009). When used alongside traditional counselling, they have been shown to improve knowledge, lower decisional conflict, reduce indecisiveness, manage patient expectations, as well as improve agreement between patients' values and choices (Légaré et al., 2006; O'Connor et al., 1998; Uhlmann et al., 2009). Decision aids are standardized, evidence-based tools that can be administered by the physician or accessed by patients through multiple modalities (i.e. internet, audio, print, etc.) (Uhlmann et al., 2009). A physical or electronic self-administered decision aid may be distributed before the HGC appointment. The decision aid could provide basic information about HBOC and RRSO, tailored HGSOC risk information, as well as implications of RRSO and potential side effects. Providing this information before, rather than during, the appointment may help patients feel less overwhelmed and improve information retention. In order to explore patient "norms" and the experiences of others, it may also be helpful to include examples of previous patients' decisions and rationale for their diverging opinions and outcomes. Alternatively, the decision aid may direct individuals to external resources for further information or support (i.e. support groups for *BRCA*-positive women, or for women who have experienced surgically induced menopause). Finally, an exercise wherein women are presented with case examples and are to choose between potential outcomes may aid in clarifying patients' values surrounding the RRSO decision (O'Connor et al., 1998). Such an intervention may aid in

increasing patients' satisfaction with and preparedness for their RRSO decision, as well as reducing decisional conflict after a visit to the HGC.

4.1.3 The Role of GCs in the decision-making process

GCs are equipped with a unique skill set in order to facilitate informed decision-making as well as explore patients' values, concerns, and emotions. The reciprocal engagement model of genetic counselling emphasizes the importance of patient emotions, resiliency, and autonomy (Veach et al., 2007). A GC's skills in advanced empathy are especially useful for exploring and clarifying patients' values. For example, a GC may utilize techniques such as questioning, confrontation, modeling, and addressing complex emotions in order to facilitate decisions about termination in a prenatal context (Weil, 2000). Responding empathetically to patients allows them to feel understood and encourages self-empathy as well as recognition of the complexity of the choice at hand, which is central to the patient's ability to take action (Uhlmann et al., 2009). These skills, as well as the GC's practice-based competencies in communication, critical thinking, interpersonal skills and professional values, are extremely transferable to different contexts (Uhlmann et al., 2009). Therefore, a GC would be a beneficial addition to the HGC model. Specifically, a GC would be suited to address aspects of the ODSF related to empowering patients to recognize how their past experiences have prepared them with the skills necessary to make difficult decisions amidst times of uncertainty (O'Connor et al., 1998). Promoting patient autonomy and self-awareness in this way may help *BRCA*-positive women to solidify and increase confidence in their RRSO decision, resulting in greater preparedness for difficult decision-making (Uhlmann et al., 2009). It may also increase patient satisfaction with their RRSO decision and reduce their decisional conflict by helping patients recognize their own self-efficacy and ability to cope with the implications of their decision.

Contracting, the process by which a mutually agreed upon agenda is established with the patient, is also a skill unique to GCs (Uhlmann et al., 2009). In the context of the HGC, contracting would be an effective means of gathering information about the patient's initial concerns and feelings about RRSO as well as being *BRCA*-positive in general. Additionally, the GC's ability to elucidate patient preferences would be helpful for determining each patient's preferred participation role in decision-making (Figure 2.2). Subsequent interactions with the support nurse, menopause specialist, and GO could then be tailored to patients' specific concerns, which were initially elucidated by the GC. The GC's ability to promote self-efficacy would also be effective at encouraging active participation in decision-making. A stronger desire for involvement in decision-making has been shown to be associated with higher information helpfulness and lower decision difficulty (Uhlmann et al., 2009). Contracting is not a "one-off event." It must be continuously revisited in order to address the emerging needs and concerns of the patient (Uhlmann et al., 2009). Often, *BRCA*-positive women who are at an increased risk for developing HGSOC but are undecided about RRSO are followed by the HGC on an annual basis. Re-contracting with *BRCA*-positive women at each of their follow-up appointments at the HGC would be helpful in re-assessing how their contextual factors, as well as perceived emotional and practical implications of RRSO, have changed since their last appointment.

The vital counselling role of the GC cannot be over-stated when it comes to providing a supportive environment for patients to experience appropriate empathy, as well as the time to express their emotions and feel understood (Uhlmann et al., 2009). Specifically in the context of cancer, the GC is able to explore the patient's beliefs about HBOC and their risk of developing cancer, the meaning of cancer in their lives, their past personal and familial experiences with cancer, as well as any fears, emotions, and expectations that may influence their perception of

the disease and the choices to be made (Weil, 2000). Exploring and normalizing the patient's narrative in this way allows for them to express their emotions and experience the relief that this brings. Reducing emotional intensity helps to limit decisional avoidance and the impact of these feelings on the decision-making process by helping patients to more clearly consider their options and potential implications (Weil, 2000). The results of the present study demonstrated that the majority of *BRCA*-positive women referred to the HGC have already made a decision about RRSO, and are instead attending for decisional reassurance and support. GCs often provide support to patients whose decisions are firm by providing the necessary emotional support described above, as well as "social and professional legitimization" (Weil, 2000) of the conclusion reached by the patient. Finally, one interview participant in particular suggested that a GC within the HGC model would be helpful because they would act as a reference point for ongoing support, especially between follow-up appointments. She stated that a GC would provide a "person to go to" if a "question comes up," without "interrupting the doctor who I have to schedule an appointment with" (P005; Age: 30-39; RRSO: N). This is not an uncommon role of GCs within genetics clinics, who often field and respond to questions from patients over the phone and email as they arise after their initial appointment. GCs also occasionally follow-up with patients after their genetic counselling appointments to "check in" and provide additional support if needed. A GC's practice-based competencies in genetics expertise and education undoubtably qualifies them to address the questions and concerns of *BRCA*-positive women (Accreditation Council for Genetic Counselling (ACGC), 2019). Therefore, this is a realistic expectation for what the role of a GC within the HGC may entail.

4.1.4 The impact of the biomedical lens on patient perceptions, decision-making, and patient-provider relationships

A large body of research within the realms of sociology and medical anthropology attempt to critically analyze and deconstruct the assumption that the viewpoints taken by biomedicine are single, objective truths. Western medicine valorizes certain health behaviours and considers them the "norm," while any action, belief, or state divergent from this normative view prompts feelings of cognitive dissonance within the individual and is frowned upon by society (Lupton, 1995, 2003; Rhodes, 1996). Both HCPs and patients are socialized to accept the factual, objective assumptions of biomedicine as truth and see the world through a "biomedical lens" (Lupton, 1995, 2003; Rhodes, 1996), which ultimately impacts their perceptions of disease, healthcare-related decisions, and interactions with each other.

The thematic framework presented in Figure 3.3 suggests that patients perceive the practical and emotional implications of being *BRCA*-positive, as well as their HGSOC risk and need for RRSO, through a personalized lens composed of unique contextual factors. The perspective of social constructionism described above assumes there is a "common-sense" knowledge pervasive throughout the field of biomedicine (Rhodes, 1996). Additionally, it is often assumed by the biomedical community that patients follow a rational style of decision-making that is based on facts and statistics (Dean & Rauscher, 2017; Howard et al., 2011). Therefore, one can assume that socialized norms about the appropriate attitude to have or path to follow after learning one is *BRCA*-positive influences the perceptions and decisions of the women in the present study. Arguably, based on the prevailing attitudes and experiences of interviewees in this study as well as published guidelines (National Comprehensive Cancer Network, 2020), RRSO is considered the "gold standard" for *BRCA*-positive women looking to

significantly reduce their HGSOC risk. Indeed, HCPs overwhelmingly (and understandably) recommend and promote patient actions that align with current standards of care. One interview participant acknowledged this about her GO, stating "I feel like surgeons want to cut… That's their job. They do surgery. They want to do surgery" (P010; Age: 30-39; RRSO: N). When a patient's views align with their HCP's within the biomedical model, they are often accepted and the patient enjoys a smoother, more positive experience. However, issues arise when HCPs encounter patients whose views do not necessarily align with the biomedical lens. Often, patients with non-traditional perspectives are challenged by the views of their HCPs and report more negative experiences with the healthcare system. For instance, one interviewee who held a more holistic, non-Western view of her health and had decided against RRSO disagreed with her oncologist's approach to treatment that was based solely on "statistics based on bloodwork" and "chemotherapy, which is a drug" (P012; Age: 40-49; RRSO: N). This misalignment of personal views ultimately led to her feeling misunderstood and having a poor experience with her HCP. Another instance of patient care being negatively impacted by disagreements about normative beliefs and practices is exemplified through the experience of interviewee P014 (Age: 30-39; RRSO: N). She stated that her appointment with the GO was "not really helpful at all" because she did not fit the mould of the typical patient. Specifically, she was "not sexually active" and felt that some of her concerns were dismissed by her HCP. While HCPs are understandably bound by certain guidelines and standards of care, it is important to recognize and appreciate the diversity of patients' backgrounds, needs, beliefs, and perspectives in order to facilitate more positive patient experiences.

Reflexivity in practice requires an individual to look inward and sensitize themselves to "the manner in which ways of knowing are generally accepted as common-sense and taken-for-

granted" (Lupton, 1995). In order to combat the normative views of the biomedical lens, HCPs must critically appraise their actions and use of knowledge in order to understand what values they are portraying and ultimately projecting onto their patients (Lupton, 1995). In other words, it is important for HCPs to acknowledge that there are alternative truths and ways of seeing the world other than those portrayed through the biomedical lens, and to respect these views while remaining true to the medical principle of beneficence. Every patient is defined by unique contextual factors, including beliefs and values, which define how they perceive their health, including the need to pursue RRSO. Remaining open to different perspectives facilitates patient-centered discussions and ensures each *BRCA*-positive woman receives quality care that is tailored to their specific situational and emotional needs. Continuing to conduct research that integrates anthropological and sociological views into biomedicine will aid in raising awareness of and promoting provider reflexivity (Rhodes, 1996). Additionally, working within the ODSF (previously described in section 4.1.2; Figure 2.2) will allow HCPs within the HGC to practice reflexivity, as well as consistently recognize and explore the determinants of patients' RRSO decisions to facilitate shared decision-making and a satisfactory patient experience (O'Connor et al., 1998).

4.2 STUDY LIMITATIONS

There are multiple limitations of the present study to consider. First, certain survey elements could be improved to better capture participant information and contextual factors to make for easier interpretation of results. For instance, the survey did not ask participants to differentiate between natural and surgically induced menopause (i.e. menopause as a result of RRSO). This may have had an effect on quantitative results. For example, the mean scores on the CWS for pre-menopausal women was greater than post-menopausal women, while the mean

scores on the CWS were lower for women < 50 years of age versus those ≥ 50 years of age. One would expect that the majority of women < 50 years of age would also be pre-menopausal, and therefore CWS score should be consistent between these two groups. It is possible that these seemingly contradictory findings are related to survey design, where women < 50 years of age who had RRSO and experienced induced menopause before responding to the survey (i.e. specified that they were post-menopausal) may have also indicated that they had decreased HGSOC-related worry, since their risk of developing HGSOC after RRSO was dramatically reduced. This issue could be resolved by asking women to clarify whether they were pre- or post-menopausal at the time of surgery. In addition, the survey questions were largely aimed at evaluating decisional outcomes related to women's experiences at the HGC or with a GO/gynecologist. Based on interview results, it is clear that the GC plays a large role in decisions and experiences related to being *BRCA*-positive and RRSO. The addition of survey questions pertaining specifically to women's genetic counselling appointments (i.e. PrepDM scale questions related to genetic counselling versus the HGC appointment) may be helpful in obtaining a more holistic understanding of participants' experiences and the level of decisional support provided by the GC.

Second, some participants who were recruited retrospectively may have completed RRSO and attended their initial appointments at the HGC years prior to study participation, making them prone to recall bias. Both the survey and interview questions required participants to remember how and what they were feeling at the time of their initial appointments with GCs and GO/gynecologists. Therefore, it is possible that some recollections of past experiences and feelings became increasingly inaccurate over time, affecting survey and interview responses. Editing eligibility criteria to only include women who were recently (i.e. within the year) seen at

the HCC or HGC may help to eliminate recall bias. However, it would also reduce the sample size and power of quantitative results. Creating more stringent eligibility criteria to reduce recall bias may be a more effective strategy for a centre with a greater volume of patients, particularly in terms of prospective recruitment.

Third, the relatively small sample size was a limitation in terms of quantitative data analysis. It would have been desirable to determine how highly correlated certain variables, such as menopausal status and age, were to one another in order to assess how each were influencing decisional outcomes (i.e. decisional conflict, satisfaction with decision, etc.). However, the statistical models necessary to make these predictions (i.e. quantile regression models) require large cohorts in order to have the same power as the Wilcoxon signed-rank test used in the present study. Therefore, answering the question of whether or not variables are correlated is possible, but cohort size would be a limitation and the output produced would likely be unreliable.

In this study, strategies were implemented to ensure trustworthiness and rigor in data collection and analysis, including multiple coding and dialogic engagement (previously described in section 2.5.2). Nevertheless, within a qualitative research paradigm there is the potential for the researcher's subjective bias to influence results. For example, the unique positionality and experiences of the student PI (who conducted all of the interviews for this study) may have impacted the types of follow-up questions asked in interviews, or the way in which the interviewer reacted to interviewee responses. Similarly, the student PI's subjective bias may have influenced the themes that were derived from analysis of the interview transcripts, wherein another researcher with a separate knowledge base or set of experiences may have interpreted the data differently. To increase interpretive validity and reduce bias further, it would

have been ideal to have a member of the advisory committee co-code all of the interview transcripts with the student PI. Investigator triangulation (i.e. having multiple researchers involved in data analysis) encourages the production of more complex data due to generative exchange between researchers (Ravitch & Mittenfelner Carl, 2016). Unfortunately, this was not possible due to the time and resource constraints of this study. Having more than one interviewer and using a structured, rather than semi-structured, interview guide may also reduce bias and achieve greater uniformity across interviews. However, structured interview guides limit the use of follow-up questions and probes (Ravitch & Mittenfelner Carl, 2016), diminishing the complexity of discussions and personalization of interviews.

Finally, time constraints limited the ability to assess long-term decisional outcomes. A longitudinal study design would be ideal for measuring and comparing each woman's level of decisional conflict, satisfaction with decision, preparation for decision-making, and HGSOC-related worry at time points before and after their HGC appointment. This type of longitudinal study design would be the most ideal for evaluating the HGC's effectiveness as a resource for *BRCA*-positive women. It would also be interesting to re-evaluate decisional outcomes and conduct interviews with the same participant over time, to see if changing contextual factors indeed influence how they view the RRSO decision. A multiple interview design would also yield the potential to assess if women's experiences post-RRSO aligned with their perceived expectations before surgery.

4.3 FUTURE DIRECTIONS

While the present study provides interesting and valuable insight into the decision-making processes and experiences of *BRCA*-positive women, additional research is necessary to

further explore these topics. As previously mentioned in section 4.2, a longitudinal study design would be necessary and helpful in evaluating long-term decisional outcomes, such as decisional conflict and preparedness for decision-making, pre- and post-RRSO as well as after implementation of a decision aid at the HGC to facilitate informed, value-based decision-making. In addition to evaluating the HGC in Winnipeg, studies exploring the decisions and experiences of *BRCA*-positive patients within similar clinic models across the country would be an important step in situating the results of this study within the current landscape of healthcare across Canada. Having results from multiple centres would also allow researchers to compare clinical designs and strategies in order to determine the most supportive model for patients.

One of the primary focuses of this study was evaluation of the HGC model. However, it was previously mentioned in section 4.2 that this was also a study limitation since there was a lack of quantitative data evaluating the impact of the GC on decisional outcomes. Qualitative interviews revealed that discussions with GCs were in fact quite detailed and influential on patients' decisions and experiences. Future research may be aimed at assessing how interactions with GCs and other genetics professionals within genetics clinics impact decision-making about RRSO. For instance, exploring preparedness for decision making about RRSO in *BRCA*-positive women who consulted a GC versus those who did not. This is extremely applicable within the current era of increased availability to direct-to-consumer (DTC) testing, where individuals who privately access genetic testing for hereditary cancer predisposition syndromes may receive positive results without the ability to speak to a GC. In this case, it would be interesting to explore the experiences of women who discovered they were *BRCA*-positive through DTC testing compared to those who learned their results through a more traditional trajectory of care (i.e. through a referral to a genetics clinic and subsequent genetic counselling and testing).

In addition to increased access to DTC, the field of genomics and genetic medicine has grown over the years to include new genes associated with moderately increased lifetime risks for different types of cancer, including HGSOC (Table 1.2), on hereditary cancer gene panels. For instance, the *PALB2* gene is included on the 10 gene panel offered to eligible patients through the HCC (previously described in section 1.4). While P/LP variants in *PALB2* are known to be associated with an increased risk of breast cancer (National Comprehensive Cancer Network, 2020), research is insufficient to accurately estimate the increased lifetime risk of HGSOC and this remains unknown (Table 1.2). Another example of an emerging moderate risk gene is *BRIP1*, which is associated with a lifetime risk of HGSOC of approximately 6-8% (Table 1.2). As these and other moderate-risk genes continue to be researched and added to hereditary cancer gene panels, there is a greater chance that patients may receive genetic test results with uncertain implications for their future health. For instance, a patient may learn that they have a P/LP variant in a gene with only a moderately increased, or even unknown, risk for HGSOC. Women deciding whether or not to pursue RRSO in the context of a moderate or uncertain level of increased HGSOC risk may have different concerns and decision-making processes than *BRCA*-positive women with a substantially increased lifetime risk for developing HGSOC and established management guidelines (Table 1.1). Therefore, conducting exploratory interviews with women who have P/LP variants in genes associated with a moderately increased risk for HGSOC would be particularly helpful in understanding how their decisions and experiences may differ from that of *BRCA*-positive women and if so, how patient care can be modified to better suite their needs.

Finally, while it is not the current standard of care within the HGC, some interview participants mentioned asking about or researching the option of ISDO during the interviews. As

previously discussed in section 1.5, research is currently underway to assess the efficacy of ISDO for improving sexual functioning and menopausal symptoms compared to standard RRSO while still effectively reducing HGSOC risk. The potential to significantly reduce HGSOC risk while avoiding the symptoms of induced menopause by delaying oophorectomy is a huge benefit to pre-menopausal women considering risk-reducing surgery. ISDO may become a viable option for these women in the future, and possibly even the standard of care recommended by HCPs. If available, the option of ISDO would dramatically impact *BRCA*-positive women's decision-making processes by removing the practical implication of induced menopause, as well as the emotional implications associated with the uncertainty of menopausal side effects. Expanding the aims of the current study to encompass the decisions and experiences of *BRCA*-positive women considering ISDO would be necessary in order to capture how the factors involved in decision-making may differ from women considering RRSO. Additionally, a qualitative study design involving semi-structured interviews similar to those conducted in the present study would be an advantageous addition to research evaluating the long-term quality of life outcomes in *BRCA*-positive women having ISDO compared to RRSO.

CHAPTER 5: CONCLUDING REMARKS

In summary, *BRCA*-positive women considering (or who completed) RRSO were recruited through the HGC and HCC between August 2019 and January 2020 and asked to complete a survey and/or interview. As expected based on previous literature, survey and interview results revealed that pre-menopausal women take more factors into consideration when deciding about RRSO (i.e. family planning and symptoms associated with induced menopause), contributing to increased levels of HGSOC-related worry and decisional conflict, as well as decreased satisfaction with their RRSO decision compared to post-menopausal women. The HGC model, designed to provide support and information to *BRCA*-positive women through an interdisciplinary team of GOs, a menopause specialist, and a registered nurse navigator, did not significantly impact the decisional outcomes of *BRCA*-positive women. This result holds true for pre-menopausal women, who did not exhibit significantly different levels of preparedness for decision making compared to post-menopausal women. While informational needs were met, including information about HGSOC risk, RRSO, induced menopause, and HRT, pre-menopausal women still expressed uncertainty about some practical implications of RRSO in the context of their own lives, as well as emotions such as fear, worry, anxiety, and concerns about self-image. Strategies to improve decisional outcomes, specifically for pre-menopausal women contemplating RRSO, include incorporating a decision aid and/or GC into the HGC model. Both a decision aid and GC provide additional decisional support that is specifically aimed at helping *BRCA*-positive women recognize their ability to make difficult decisions (i.e. promote self-efficacy and autonomy), identify potential alternatives and implications, as well as recognize how each alternative aligns with their personal beliefs and values. GCs also have the advantage of possessing unique psychosocial skills that allow them to explore complex emotions,

empathetically respond to, and continuously re-contract with patients throughout the course of the decision-making process about RRSO.

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APPENDIX

A.1 Study invitation letter

Invitation to Participate in a Research Study

Name of study: Decisions surrounding risk-reducing bilateral salpingo-oophorectomy: Experiences of *BRCA*-positive women

Student Principal Investigator: Selina Casalino, Genetic Counselling Trainee (xxx-xxx-xxxx; xxx@xx.ca)

Student Supervisor: Dr. Mark Nachtigal (xxx-xxx-xxxx; xxx@xx.ca)

Dear potential participant,

You have been identified as eligible to participate in a research study about the decisions you made after receiving your genetic test result. Please read the following information carefully. Completing this study is voluntary and you do not have to participate if you don't want to. If you require more information before deciding whether or not to complete the study, you can contact the Student Principal Investigator, Selina Casalino, whose contact information is listed above.

This study is being conducted by Selina Casalino, a Genetic Counselling Trainee at the University of Manitoba, in partial fulfilment of a Masters of Science degree. Her supervisor for this study is Dr. Mark Nachtigal.

What is the study about?

Women with genetic changes (sometimes called mutations) in genes called *BRCA1* or *BRCA2* are considered to be "*BRCA*-positive" and have a higher risk of developing both breast and ovarian cancer. There are good screening options, such as regular mammograms, available to detect breast cancer at an early stage. Unfortunately, similar screening options do not exist for detecting ovarian cancer. Therefore, if a woman is found to have a mutation in *BRCA1* or *BRCA2*, they may discuss the option of risk-reducing surgery with their healthcare provider. A specific form of risk-reducing surgery for ovarian cancer, called bilateral salpingo-oophorectomy, involves removing the ovaries and fallopian tubes.

Deciding to remove ovaries and fallopian tubes is a difficult decision for many women because it may have consequences for their health, family planning, and quality of life. This research study will explore how and why *BRCA*-positive women make decisions for or against risk-reducing surgery (i.e. removal of ovaries and fallopian tubes). It will also explore if and how this decision is supported by the patient's healthcare team.

Why am I being asked to participate in this study?

You are being asked to participate in this study because you have previously been seen at the Hereditary Gynecology Clinic or Shared Health Program of Genetics & Metabolism and are between the ages of 18 to 70 years old with a genetic change (i.e. mutation) in a gene called *BRCA1* or *BRCA2*. The table below outlines the eligibility criteria for this study:

You are eligible to participate in this study if:	You are NOT eligible to participate in this study if:
- You have a mutation in the *BRCA1* and/or *BRCA2* genes that increases your risk of developing breast and ovarian cancer - You are a female - You are between the ages of 18 and 70 - You are able to speak and read English	- You removed your ovaries and fallopian tubes (i.e. bilateral salpingo-oophorectomy) before learning you had a mutation in *BRCA1* or *BRCA2* - You have ever been diagnosed with ovarian cancer

What will happen if I choose to participate in this study?

If you volunteer to participate in this study, you may choose to complete one of the following:

1. A survey
2. An interview
3. Both a survey AND an interview

If you choose to complete a survey: You will be asked to answer a series of questions that will take approximately 15-20 minutes to complete. You may fill out and return the survey included in this package to the Principal Investigator, Selina Casalino, by scanning and sending the completed document by email (xxx@xx.ca) OR by mailing it using the return envelope and postage provided. Alternatively, you may complete the survey online at the following website: **https://rsurvey.med.umanitoba.ca/redcap/surveys/?s=DLE7RE8DPY**. By filling out this survey, you are consenting to participate in the study. Your survey responses will be kept anonymous and you will not be asked to enter any personal information (i.e. name, birthdate, email, phone number) when completing the survey.

If you choose to complete an interview: You will participate in a one-on-one interview with Selina that will take approximately 45 minutes to complete. Before completing the interview, Selina will go through the consent form (included in this package) and obtain your verbal consent to participate in the interview. The verbal consent will take about 15 minutes to complete. During this interview, Selina will ask you a series of questions about your experiences and decisions regarding risk-reducing surgery. Examples of these questions may include "When did you learn you were *BRCA*-positive" or "How has this news affected your life." You can choose to complete this interview in person at the Winnipeg Health Sciences Centre or University of Manitoba, or over the phone. If you are interested in completing an interview, you may fill out and return the contact form included in this package to Selina by scanning and sending the completed document by email (xxx@xx.ca) OR by mailing it using the return envelope and postage provided. Selina will contact you about the interview upon receiving the contact form. Alternatively, you may contact Selina directly at the email address or phone number provided above to arrange an interview. Your responses to interview questions will be kept completely confidential.

If you choose to complete a survey AND an interview: If you are interested in completing an interview in addition to the survey, you may fill out and return the contact form included in this package along with your completed survey to Selina by scanning and sending the completed

documents by email (xxx@xx.ca) OR by mailing them using the return envelope and postage provided. Selina will contact you about the interview upon receiving the contact form and completed survey. Alternatively, you will be provided with Selina's contact information at the end of the online survey. You may contact Selina directly at the email or phone number provided to arrange a time to complete the interview. Selina will go through the consent form (included in this package) and obtain your verbal consent to participate before completing the interview. Your responses to interview questions will be kept completely confidential. It will take a total of approximately 75-80 minutes to complete the survey, verbal consent and interview. Participants who complete both a survey and interview will be given a $20 gift card as a thank you for their time.

Participating in this study is completely voluntary. You do not have to participate in this study. You can withdraw from the study at any time. You do not have to answer any questions during the survey or interview that you are uncomfortable with.

Are there any risks or benefits to participating in this study?

The risks of participating in this study are low. It is possible that some of the questions may be upsetting or cause psychological discomfort. You reserve the right to not answer any questions you feel uncomfortable with.

There is no direct benefit to participating in this study. However, your participation is important to us and your answers may contribute to improving how healthcare is delivered to *BRCA*-positive women.

Who can I contact for more information?

If you have any questions about the study please do not hesitate to contact either the Principal Investigator, Selina Casalino, or the Student Supervisor, Dr. Mark Nachtigal, at the email address or phone number provided above. This study and survey has been approved by the University of Manitoba Health Research Ethics Board.

Thank you for taking the time to consider participating in this study.

Sincerely,

Selina Casalino

Genetic Counselling Trainee
University of Manitoba
Email: xxx@xx.ca
Phone: xxx-xxx-xxxx

A.2 Survey

Survey

Name of study: Decisions surrounding risk-reducing bilateral salpingo-oophorectomy: Experiences of *BRCA*-positive women
Student Principal Investigator: Selina Casalino, Genetic Counselling Trainee (xxx-xxx-xxxx; xxx@xx.ca)
Student Supervisor: Dr. Mark Nachtigal (xxx-xxx-xxxx; xxx@xx.ca)

Please circle your response to the following questions. If you feel uncomfortable answering a question, please circle "Prefer not to answer."

Please send your completed survey to the Student Principal Investigator, Selina Casalino, either by mail using the enclosed return envelope and postage OR by scanning and emailing it to xxx@xx.ca. By completing and returning this survey, you are consenting to participate in the study.

Demographic and Background Information

1. What is your age?
   a) 18-29
   b) 30-39
   c) 40-49
   d) 50-59
   e) 60-69
   f) 70+
   g) Prefer not to answer

2. What is the highest level of education you have completed?
   a) Grade _____ (Please indicate highest grade completed)
   b) Completed high school
   c) Graduated college, trade/technical school
   d) Graduated Bachelor's degree (I.e. BA, BSc)
   e) Graduated Post graduate degree
   f) Prefer not to answer

3. What was your total family income (before taxes) last year?
   a) Less than $10,000
   b) $10,000-19,000
   c) $20,000-39,000
   d) $40,000-59,000
   e) $60,000-79,000
   f) $80,000 or more
   g) Prefer not to answer

4. Which of the following best describes your race/ethnicity?
   a) Indigenous (i.e. Inuit, First Nations, Métis)
   b) Asian – East (i.e. Chinese, Japanese)
   c) Asian – South (i.e. Indian, Sri Lankan, Indo-Caribbean)
   d) Asian – South East (i.e. Vietnamese, Filipino)
   e) Black – African (i.e. Ghanaian, Somalian)
   f) Black – North American
   g) Black – Caribbean Region (i.e. Jamaican, Trinidadian, Barbadian)
   h) Latin-American (i.e. Argentinian, Chilean, Cuban)
   i) Middle Eastern (i.e. Egyptian, Iranian, Israeli, Palestinian)
   j) White/European (i.e. English, Greek, Italian, Serbian)

k) Mixed heritage, please specify - _____

l) Other(s), please specify_____

m) Prefer not to answer

5. What is your relationship status?
   a) Single
   b) Married
   c) Common-law
   d) Divorced/Separated
   e) Widowed
   f) Other, please specify_____
   g) Prefer not to answer

6. How many pregnancies have you had?
   a) 0
   b) 1
   c) 2
   d) 3
   e) 4
   f) 5+
   g) Prefer not to answer

7. How many children do you have?
   a) 0
   b) 1
   c) 2
   d) 3
   e) 4
   f) 5+
   g) Prefer not to answer

8. Are you currently pregnant?
   a) Yes
   b) No
   c) Prefer not to answer

Health/Cancer History Questions

9. What is your current menstrual period status?
   a) I have menstrual periods
   b) My menstrual periods have stopped
   c) I am unsure whether or not my menstrual periods have stopped

10. Have you ever been diagnosed with breast cancer?
    a) Yes (Please answer 10a-b)
    b) No (Please proceed to question 11)

    10a) Are you currently undergoing treatment for breast cancer?
    a) Yes
    b) No

    10b) Have you ever had a risk-reducing mastectomy (unilateral or bilateral)?
    a) Yes
    b) No

11. Do you have any family members who have been diagnosed with breast cancer?

a) Yes
b) No
c) Unsure

12. Do you have any family members who have had a risk-reducing mastectomy (unilateral or bilateral)?
    a) Yes
    b) No
    c) Unsure

13. Do you have any family members who have been diagnosed with ovarian cancer?
    a) Yes
    b) No
    c) Unsure

14. Do you have any family members who have had risk-reducing gynecological surgery (i.e. have had their ovaries and fallopian tubes removed)?
    a) Yes
    b) No
    c) Unsure

15. Have you ever spoken to a genetic counsellor about your risk for developing ovarian cancer?
    a) Yes
    b) No
    c) Unsure

16. Are you worried about the possibility of getting ovarian cancer some day?
    1= Not at all (Please proceed to question 17)
    2= Slightly
    3= Moderately
    4= Very
    5= Extremely

    16a) Does this worry affect your mood?
    1= Not at all
    2= Slightly
    3= Moderately
    4= Very
    5= Extremely

    16b) Does this worry interfere with your ability to do your daily activities?
    1= Not at all
    2= Slightly
    3= Moderately
    4= Very
    5= Extremely

17. How likely do you believe it is that you will get ovarian cancer at some point in your life?
    1= Not at all
    2= Slightly
    3= Moderately
    4= Very
    5= Extremely

Decision-Making Questions

18. After learning I was *BRCA*-positive, I…
    a) Saw and/or consulted a gynecological oncologist at the Hereditary Gynecology Clinic located at the Winnipeg Health Sciences Centre
    b) Saw and/or consulted a gynecologist outside of the Winnipeg Health Sciences Centre (i.e. private clinic)
    c) Did not see and/or consult a gynecological oncologist or gynecologist

19. After learning I was *BRCA*-positive, I…
    a) Made the decision to remove my ovaries and fallopian tubes (i.e. risk-reducing surgery)
    b) Made the decision to keep my ovaries and fallopian tubes
    c) Am undecided about whether or not to remove my ovaries and fallopian tubes (i.e. risk-reducing surgery) (Please proceed to question 28)

Please answer the following questions about the decision whether or not to pursue risk-reducing gynecological surgery (i.e. removal of ovaries and fallopian tubes). Please indicate to what extent each statement is true for you AT THIS TIME.

20. I am satisfied that I am adequately informed about the issues important to my decision
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

21. The decision I made was the best decision possible for me personally
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

22. I am satisfied that my decision was consistent with my personal values
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

23. I expect to successfully carry out the decision I made
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

24. Did you consult with anyone in making your decision?
    a) Yes
    b) No (Please proceed to question 25)

    24a) Who did you consult in making your decision? (Circle all that apply)
    a) Family
    b) Friend

c) Other healthcare provider, please specify_____
d) Spiritual healer
e) Elder
f) Other, please specify_____

25. I am satisfied with my decision
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

26. This decision was hard for me to make
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

27. It was clear what choice was best for me
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

28. It was explained to me that surgically removing my ovaries and fallopian tubes is an option available to reduce my risk of developing ovarian cancer
a) Yes
b) No

29. I feel like I know the benefits of risk-reducing surgery
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

30. I feel like I know the risks and side effects of risk-reducing surgery
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

31. I feel like I need more advice and information about the choices
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

32. I know how important the benefits of risk-reducing surgery are to me in this decision
1= Strongly disagree
2= Disagree
3= Neither agree nor disagree
4= Agree
5= Strongly agree

33. I know how important the risks and side effects of risk-reducing surgery are to me in this decision
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

34. It is hard to decide if the benefits are more important to me than the risks, or if the risks are more important than the benefits
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

35. I feel/felt pressure from others in making this decision
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

36. I had the right amount of support from others in making this choice
    1= Strongly disagree
    2= Disagree
    3= Neither agree nor disagree
    4= Agree
    5= Strongly agree

Questions 37-46 are asking you about your consultation with the gynecological oncologist/gynecologist. Please ONLY respond to these questions if you answered a) or b) to question 18.

Did the care you received from the gynecological oncologist/gynecologist and their healthcare team….

37. Help you recognize that a decision needs to be made?
    1= Not at all
    2= A little
    3= Somewhat
    4= Quite a bit
    5= A great deal

38. Prepare you to make a better decision?
    1= Not at all
    2= A little
    3= Somewhat
    4= Quite a bit
    5= A great deal

39. Help you think about the pros and cons of each option?
    1= Not at all
    2= A little
    3= Somewhat
    4= Quite a bit
    5= A great deal

40. Help you think about which pros and cons are most important?
    1= Not at all
    2= A little

3= Somewhat
4= Quite a bit
5= A great deal

41. Help you know that the decision depends on what matters most to you?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

42. Help you organize your own thoughts about the decision?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

43. Help you think about how involved you want to be in this decision?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

44. Help you identify questions you want to ask your doctor?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

45. Prepare you to talk to your doctor about what matters most to you?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

46. Prepare you for a follow-up visit with your doctor?
1= Not at all
2= A little
3= Somewhat
4= Quite a bit
5= A great deal

Thank you for completing this survey.

A.3 Interview consent form

Consent to Participate in an Interview

Name of study: Decisions surrounding risk-reducing bilateral salpingo-oophorectomy: Experiences of *BRCA*-positive women

Student Principal Investigator: Selina Casalino, Genetic Counselling Trainee (xxx-xxx-xxxx; xxx@xx.ca)
Student Supervisor: Dr. Mark Nachtigal (xxx-xxx-xxxx; xxx@xx.ca)

Introduction

You are being asked to complete an individual interview as a part of a research study about the decisions you made after receiving your genetic test result. This consent form will be reviewed with you in detail with the Student Principal Investigator, Selina Casalino, either in person or over the phone. You will be provided with a copy of this consent form so you can follow along during the consent process, and so you have a copy for your records. If there is any part of this consent form you do not understand, please do not hesitate to ask the Student Principal Investigator to explain. After orally reviewing this consent form, you may provide your verbal consent to participate or not. Please do not verbally consent to participate until all of your questions have been answered to your satisfaction. Completing this study is voluntary and you do not have to participate if you don't want to. If you require more time to consider participating in the study or not, you may re-contact the Principal Investigator at a later date that is convenient for you.

The Student Principal Investigator is Selina Casalino, a Master's student in the Genetic Counselling Program at the University of Manitoba. The student supervisor is Dr. Mark Nachtigal, an Associate Professor in the Department of Biochemistry & Medical Genetics at the University of Manitoba.

What is the study about?

Women with genetic changes (sometimes called mutations) in genes called *BRCA1* or *BRCA2* are considered to be "*BRCA*-positive" and have a higher risk of developing both breast and ovarian cancer. There are good screening options, such as regular mammograms, available to detect breast cancer at an early stage. Unfortunately, similar screening options do not exist for detecting ovarian cancer. Therefore, if a woman is found to have a mutation in *BRCA1* or *BRCA2*, they may discuss the option of risk-reducing surgery with their healthcare provider. A specific form of risk-reducing surgery, called bilateral salpingo-oophorectomy, involves removing the ovaries and fallopian tubes to reduce the risk of developing ovarian cancer.

Deciding to remove their ovaries and fallopian tubes is a difficult decision for many women because it may have consequences for their health, family planning, and quality of life. This research study will explore how and why *BRCA*-positive women make decisions for or against risk-reducing surgery (i.e. removal of ovaries and fallopian tubes). It will also explore if and how this decision is supported by the patient's healthcare team.

Why am I being asked to participate in this study?

You are being asked to participate in this study because you have previously been seen at the Hereditary Gynecology Clinic or Shared Health Program of Genetics & Metabolism and are between the ages of 18 to 70 years old with a genetic change (i.e. mutation) in a gene called *BRCA1* or *BRCA2*. The table below outlines the eligibility criteria for this study:

You are eligible to participate in this study if:	You are NOT eligible to participate in this study if:
- You have a mutation in the *BRCA1* and/or *BRCA2* genes that increases your risk of developing breast and ovarian cancer - You are a female - You are between the ages of 18 and 70 - You are able to speak and read English	- You removed your ovaries and fallopian tubes (i.e. bilateral salpingo-oophorectomy) before learning you had a mutation in *BRCA1* or *BRCA2* - You have ever been diagnosed with ovarian cancer

What will happen if I choose to complete an interview for this study?

Before receiving this consent form, you would have spoken to the Student Principal Investigator, Selina Casalino, about participating in an interview for this study. During this phone call, you would have scheduled an agreed upon date and time to complete the verbal consent and interview either in-person at the Winnipeg Health Sciences Centre or University of Manitoba, or over the phone. You would have received a copy of the consent form in the study recruitment package. Please use this document to follow along during the consent process and review it as much as you need before consenting to participate. Selina can provide you with another copy of the consent form either in-person or over email if necessary.

On the date and time of the scheduled interview, Selina will call you at the phone number you provided on the contact form (if you decide to conduct the interview over the phone) OR you will meet Selina at the agreed upon location at the Health Sciences Centre or University of Manitoba (if you decide to conduct the interview in-person). The interview will take place in a private room. The interview will be between you and Selina only. Selina will complete the verbal consent to participate in the interview. This will take approximately 15 minutes to complete. She will answer any questions you have about the study or consent form before starting the interview. The interview will take approximately 45 minutes to complete. During this interview, Selina will ask you a series of questions about your experiences and decisions regarding risk-reducing surgery. Some of these questions may include "How did you feel when you learned you were *BRCA*-positive" or "Did you feel like you had the information necessary to make an informed decision about risk-reducing surgery." This interview will be recorded so that it can be transcribed later. You do not have to answer any questions you feel uncomfortable with and can choose to stop the interview at any time. We plan on asking 15 people to complete an interview for this study. The results of the interview may be published and presented in journal articles,

abstracts, conferences, or posters. No names or other personal identifying information will be included in journal articles, abstracts, conferences, posters, or presentations.

If you also completed a survey for this study, you will be given a $20 gift card as a thank you for your time after completing the interview.

Are there any risks to participating in this study?

The risks of participating in this study are low. It is possible that some of the questions may be upsetting or cause psychological discomfort. You reserve the right to not answer any questions you feel uncomfortable with and may stop the interview at any time. If you require psychological support, you may discuss your concerns with the support nurse at the Hereditary Gynecology Clinic or with your genetic counsellor. Alternatively, you may notify Selina who can connect you with the proper supports at the Hereditary Cancer Clinic, Hereditary Gynecology Clinic, or an external counselling service (For example, Klinic Community Health in Winnipeg).

Are there any benefits to participating in this study?

There is no direct benefit to participating in this study. However, your participation is important to us and your answers may contribute to advancements in research that may inform how healthcare is delivered to *BRCA*-positive women.

Will my information be kept confidential?

All information collected during this study will be kept completely confidential. Only the members of the study team and the Research Ethics Board of the University of Manitoba will have access to the information collected during this study. Both of these parties have a professional responsibility to protect your privacy. The only instance(s) where confidentiality must be broken as required by law are if you express intent to harm yourself or others, or tell us about inappropriate practice of a healthcare provider.

The interview will be audio recorded with your agreement. All interviews will be read and transcribed by the Student Principal Investigator, a member of the study team, or a hired professional transcriptionist from the company TranscriptHeroes. A confidentiality agreement will be signed with TranscriptHeros prior to sending them any audio files. This agreement ensures that the content of the interviews will not be discussed with anyone outside the study team. Any quotations from interviews that may be used in written or oral reports or presentations will remain anonymous. Participant identifiers will be removed from transcribed interviews. Each audio file and transcript will have a specific code that can only be linked back to the participant by a code key, which is kept in a secured location. Only the Student Principal Investigator and members of the study team will have the code key that can link the codes back to the participant's identifiers. The audio files and transcripts will be uploaded to an online folder accessible only to the student principal investigator, study team, and the transcription company. The online folder will be stored on a password protected computer located in Basic Medical Science Building room 310 at the University of Manitoba and is protected according to the Personal Health Information Protection Act. Contact forms containing your name and phone

number will be stored separately from consent forms and completed surveys in locked filing cabinets in the Basic Medical Science Building room 310 at the University of Manitoba. All study materials (i.e. audio files, transcripts, contact forms, consent forms) will be kept for one year after completion of the study, after which time they will be destroyed.

Are there any costs to participating in this study?

There will be no cost to you to participate in the study, other than the time it takes to conduct the interview. If you choose to complete an interview in-person, you may have to pay for transportation to and from the Winnipeg Health Sciences Centre or University of Manitoba. The cost of a regular bus fare on the Winnipeg Transit is $2.95. The cost of a senior fare is $2.45.

Do I have to participate in this study?

Participating in this study is completely voluntary. You do not have to participate in this study. If you agree to participate and then change your mind later, you may withdraw from the study at any time without judgement. Refusing to participate or withdrawing from the study will not affect any care you receive from the Winnipeg Regional Health Authority. If you decide to stop participating in the study we will ask you how you would like us to handle the data collected up to that point. This could include returning it to you, destroying it or using the data collected up to that point. Additionally, if you do not want to answer some of the questions you do not have to, but you can still be in the study.

Who can I contact for more information?

If you have any questions about the study please do not hesitate to contact either the Principal Investigator, Selina Casalino, or the Student Supervisor, Mark Nachtigal, at the email address or phone number listed below:

Selina Casalino
Phone: xxx-xxx-xxxx
Email: xxx@xx.ca

Mark Nachtigal
Phone: xxx-xxx-xxxx
Email: xxx@xx.ca

This study has been approved by the University of Manitoba Health Research Ethics Board. If you have questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at xxx-xxx-xxxx. If you wish to receive a short summary of the study results upon completion of the study, please let the Student Principal Investigator know of the best way to get this to you.

Consent statement

1. I have reviewed all 5 pages of this consent form with the Student Principal Investigator.
2. I understand what this study is about and have had the opportunity to ask questions, all of which have been answered to my satisfaction.
3. I understand that participating in this study is voluntary and I do not have to participate in this study.
4. I understand that any information collected about me during this study will be kept confidential.
5. I understand that any information about me collected during this study may be viewed by the Student Principal Investigator, Selina Casalino, or a member of the study team, as well as the University of Manitoba Research Ethics Board.
6. I understand that I have the right to not participate in this study, or withdraw from the study at any time.
7. I understand that giving my verbal consent to participate in this study does not waive any of my legal rights.
8. I understand that I will receive a copy of this consent form for my records.

Does the participant agree to participate in the study?

○ Yes (Document verbal consent below) ○ No

Name of Participant:

_____

Signature of Participant (ONLY if consent conducted in-person):

_____

Person Obtaining Consent

I have read this form to the participant. An explanation of the research was given and questions from the participant were solicited and answered to the participant's satisfaction. In my judgment, the participant has demonstrated comprehension of the information. The participant has provided oral consent to participate in this study.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date

A.4 Validated scales and survey questions

Scale	Survey questions*
Cancer Worry Scale (CWS)	Are you worried about the possibility of getting ovarian cancer some day?
	Does this worry affect your mood?
	Does this worry interfere with your ability to do your daily activities?
	How likely do you believe it is that you will get ovarian cancer at some point in your life?
Decisional Conflict Scale (DCS)	This decision was hard for me to make
	It was clear what choice was best for me
	I feel like I know the benefits of risk-reducing surgery
	I feel like I know the risks and side effects of risk-reducing surgery
	I feel like I need more advice and information about the choices
	I know how important the benefits of risk-reducing surgery are to me in this decision
	I know how important the risks and side effects of risk-reducing surgery are to me in this decision
	It is hard to decide if the benefits are more important to me than the risks, or if the risks are more important than the benefits
	I feel/felt pressure from others in making this decision
	I had the right amount of support from others in making this choice
Preparation for Decision-making (PrepDM)	Did the care you received from the gynecological oncologist/gynecologist and their healthcare team….
	Help you recognize that a decision needs to be made?
	Prepare you to make a better decision?
	Help you think about the pros and cons of each option?
	Help you think about which pros and cons are most important?
	Help you know that the decision depends on what matters most to you?
	Help you organize your own thoughts about the decision?
	Help you think about how involved you want to be in this decision?
	Help you identify questions you want to ask your doctor?
	Prepare you to talk to your doctor about what matters most to you?
	Prepare you for a follow-up visit with your doctor?
Satisfaction with Decision (SWD)	I am satisfied that I am adequately informed about the issues important to my decision

Scale	Survey questions*
	The decision I made was the best decision possible for me personally
	I am satisfied that my decision was consistent with my personal values
	I expect to successfully carry out the decision I made
	I am satisfied with my decision

*All question responses are based on a Likert scale of 1 to 5 where 1=Strongly disagree/Not at all and 5=Strongly agree/A great deal.

A.5 Semi-structured interview guide

Thank you for agreeing to participate in an interview for my study. Before we talk about your personal experiences, I have a few background questions I'd like to ask you. As a reminder, you do not have to answer any question you don't want to. In this case, please let me know and we can move on to the next question. Are you ready to begin?

Demographic/Background Questions

1. What is your current age?
2. What is the highest level of education you have completed?
3. What do you do for work?
4. What is your race or ethnicity?
5. What is your relationship status? *(Follow-up: For example, single, married, divorced, common-law, etc.)*
6. Do you have any children? *(Follow-up: How many? How old are they?)*

Health/Cancer History Questions

1. Do you still get menstrual periods? *(Follow-up: Have you gone through menopause? Are you currently undergoing menopause?)*

2. Have you ever been diagnosed with breast cancer?
    a. When were you diagnosed?
    b. Do you know what type of breast cancer you had?

3. Have you ever had a risk-reducing surgery? *(Follow-up: For example, a mastectomy or removal of ovaries or fallopian tubes)*
    a. What type of risk-reducing surgery did you have?
    b. When did you have risk-reducing surgery?
    c. How was this experience for you?

4. Do you know if anyone in your family has had breast cancer?
    a. Who in your family had breast cancer?
    b. How old were they when they were diagnosed with breast cancer?
    c. Did they have any genetic testing done?

5. Do you know if anyone in your family has had ovarian cancer?
    a. Who in your family had ovarian cancer?
    b. How old were they when they were diagnosed with ovarian cancer?
    c. Did they have any genetic testing done?

6. Do you know anyone in your family who has had risk-reducing surgery?
    a. For what reason did they have risk-reducing surgery?
    b. What type of risk-reducing surgery did they have?

Experiences and Decision-Making Questions

1. When did you learn that you were *BRCA*-positive?

   a. Can you tell me more about that experience? *(Probes: Who told you that you were BRCA-positive? What was your reaction to receiving this information? Did you have any immediate questions or concerns after receiving this information? What were the next steps you took after learning this information?)*

2. How has receiving this news affected your life? *(Probes: What did receiving this news make you think about (For example, your plans for the future)? Have you made any changes in your life as a result of receiving this news?*

3. There are many decisions to be made as a result of being *BRCA*-positive. Have you talked to anyone about this? *(Probes: Who have you talked to (for example, family, friends, healthcare providers, counsellors, etc.)? What did you talk to them about?)*
   a. Who have you found to be the most helpful? Why?
   b. Who have you found to be the least helpful? Why?

4. Have you talked to a genetic counsellor or gynecological oncologist at the Health Sciences Centre? *(Probes: If not, did you consult a different healthcare provider? Who? Where?)*
   a. Can you tell me more about what happened at that/those appointment(s)? *(Probes: What was your overall experience at the appointment? What information did they give you? Was there anything that was particularly helpful or unhelpful? Did you feel comfortable and supported during the appointment(s)?)*

5. Have you made a decision about risk-reducing bilateral-salpingo oophorectomy (i.e. removal of ovaries and fallopian tubes) yet?
   a. Can you walk me through the process you went through while making this decision? *(Probes: What factors were the most important to you in making this decision? Do you wish there was anything you would have known more about before making a decision? How do you feel about the decision you have made? Did the healthcare providers you've spoken to throughout this process impact your decision-making process in any way (i.e. genetic counsellor, gynecological oncologist)? How?)*

A.6 Codebook

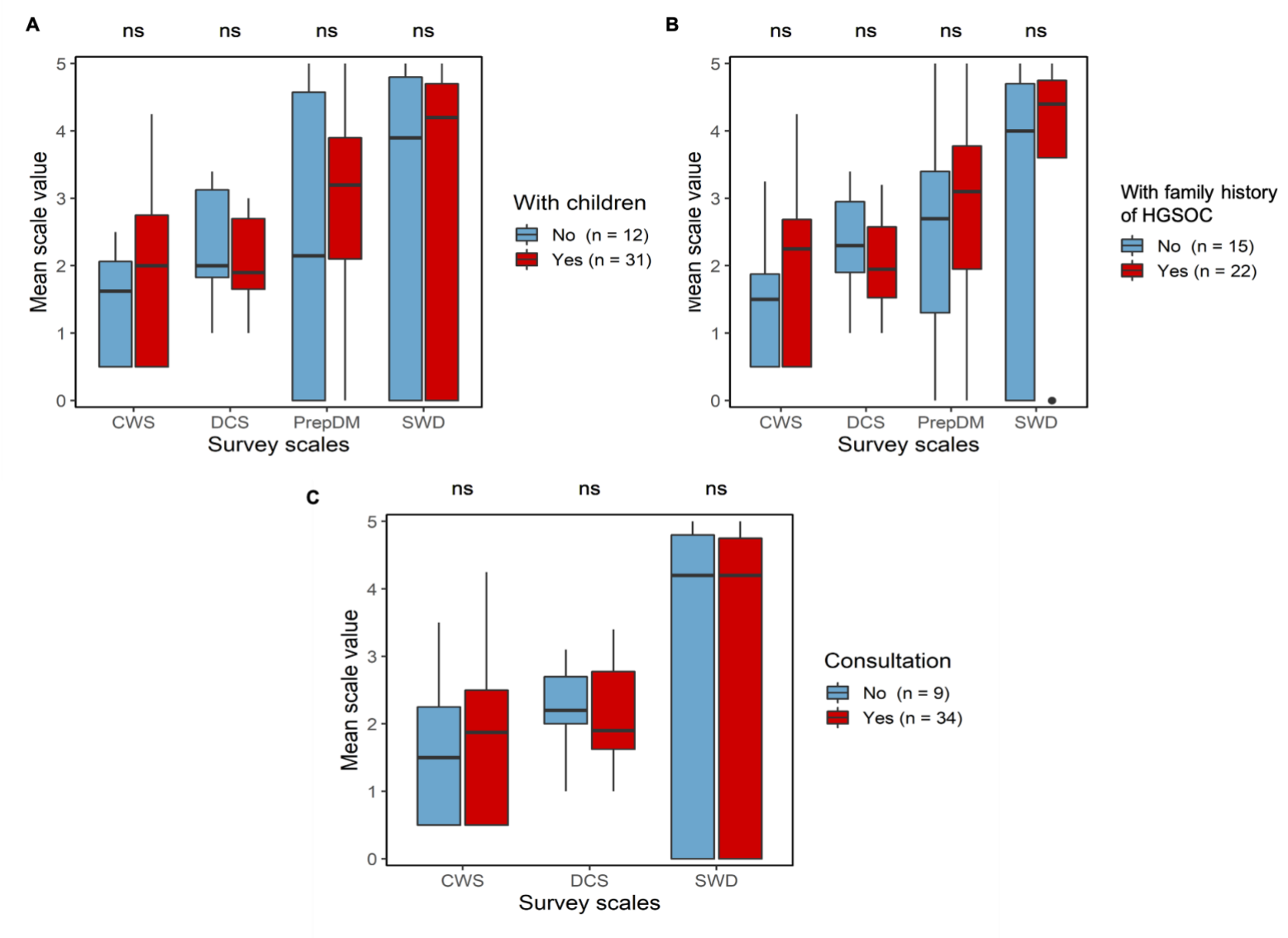
Code name	Description
Contextual factors	Descriptive characteristics including age, number of children, education, ethnicity, menopausal status, occupation, and relationship status.
Coping strategies	Actions that the participant took or mentioned as helpful in coping with all aspects of being *BRCA*-positive.
Learning from others	The participant described learning from others in similar situations (i.e. considering RRSO, or being *BRCA*-positive) and how this may have been helpful in providing support and information that otherwise was not attainable from HCPs.
Support systems	The participant indicated that they required or sought support during the course of their experience (i.e. learning *BRCA* status, deciding for or against RRSO). These included friends, family, HCPs, spiritual leaders, elders, support groups, other doctors, etc.
Taking action	The participant took action or coped by getting involved in their community or starting initiatives aimed at helping other individuals in similar situations (i.e. groups, websites, conducting research, etc.).
Decision-making process	The way a participant went about making a decision. This code encompasses their attitude and style of decision-making, as well as factors influencing their decision-making process.
Control	RRSO provided the participant with a way of "controlling" the situation/their lives and their own cancer risk (i.e. the participant feels in control). The participant may express other ways they took/are taking control of their cancer risk (i.e. changing their diet). On the other hand, the participant may express that they felt/feel a lack of control.
Experiences of family members	The participant's decision about RRSO is influenced by the thoughts and opinions of family members (or friends), or by past and/or current experiences with family members (i.e. with risk-reducing surgeries, past diagnoses, death, etc.).
Family planning	The participant expressed concerns (or did not express concerns) about the timing of RRSO and the want to start a family/have children before RRSO. They may have also discussed romantic relationships when talking about starting a family.
Fear of surgery	The participants indicated that they are scared of the surgical procedure itself (i.e. RRSO), including but not limited to side effects and recovery time.

Code name	Description
Image	The participant mentioned self-image, for example the norm of "femaleness" and what that means in relation to physical appearance and their body, as a contributing factor to their decision about RRSO.
Differing impact of mastectomy	The participant talked about how the impact of RRSO on image differed from that of mastectomy.
Sexuality	The participant discussed the impact of RRSO on sexuality including sexual intimacy with their partner, as well as sexual side effects (i.e. vaginal dryness and decreased libido).
Induced menopause	Anything the participant mentioned regarding induced menopause and their decision about RRSO (i.e. thoughts, concerns).
Risk perception	Dialogue related to how the participant perceived their cancer risk (i.e. Low or high, binary/black and white, in percentages, on a continuum, etc.). The participant may have expressed fear or worry about their increased cancer risk and use it as a driver towards getting surgery, or is not worried about their cancer risk/perceives it as low and as a result does not feel as pressured to make a decision about RRSO.
Previous personal cancer diagnosis	The impact of a previous cancer diagnosis influenced the participant's perception of their current cancer risk and the potential implications of being diagnosed with cancer again. They used this as a factor in their decision about RRSO for fear of being diagnosed with cancer again (or not).
Surgery for the benefit of others	The participant decided to have/is in support of having RRSO for the benefit of someone else in their life. For example, they may decide to have RRSO so that they can reduce their cancer risk and "be around for their children."
Effect on daily life	How the participant described their *BRCA* status or decisions about RRSO as affecting their day-to-day life. This included the impact on their beliefs, way of thinking, and actions.
Changing lifestyle	As a result of learning they were *BRCA*-positive, the participant implemented lifestyle changes. These included anything from changes to diet and exercise, to changes in their mentality/belief systems.
Information	Comments related to information received or yet to be received, or information sought out by the participant. The participant felt/is feeling like they need more information, that information was/is unclear, or that they experienced/are experiencing

Code name	Description
	information overload, leading to uncertainty about various outcomes.
Emerging research	The participant commented on new information regarding RRSO/HGSOC emerging from new research, or that more research should be conducted to explore these topics.
Risk-reducing behaviour	The participant wanted more information on other ways to reduce their HGSOC risk. For example, questions about diet, exercise, alternative non-western medicinal strategies, etc. This code also included information they received on risk-reducing surgery.
Sharing	The participant struggled with sharing information related to their diagnosis or implications of *BRCA* status with others. On the other hand, they may have encouraged and participated in information sharing with others.
Side effects	The participant mentioned information specifically pertaining to the side effects of surgery, induced menopause, etc. They may have expressed feeling uncertain about side effects. Concerns about side effects ranged from physical symptoms to behavioural changes.
Previous health-related experiences	Previous experiences the participant had with disease and the implications of that diagnosis, including personal and family history. This also included previous treatment, surgeries, side effects, etc. (including RRSO, mastectomy). Also more broadly encompassed past experiences with the healthcare system.
Quality of care	Patient commented on the quality of care they received from HCPs. For example, the patient may felt like the care they received is "special" or more than what a normal patient would receive because they are *BRCA*-positive. They may have expressed gaining additional access to resources or screening as a result. Also encompassed descriptions of poor quality of care.
Reaction to being *BRCA*-positive	The participant's reaction to learning they were *BRCA*-positive and their feelings about being *BRCA*-positive.
Fate	The participant discussed the implications of being *BRCA*-positive in terms of their fate. They may have seemed fatalistic, optimistic, pessimistic, etc. For example, they expressed that being *BRCA*-positive is something they cannot control and accepted that they cannot change their genes.
Fear	The participant expressed that they were scared after being told they were *BRCA*-positive (i.e. scared of getting cancer, of uncertainty, etc.).

Code name	Description
Speed of RRSO decision	The participant either feels/felt like RRSO should be done as quickly as possible, or that it is not something that they need to rush into and have time to decide before committing to surgery. For example, individuals who "rushed" felt like they needed to take immediate action while individuals who “waited” did not.
Trajectory of care	The trajectory or path a patient took along their healthcare continuum or journey. For instance, their appointments with primary care physicians, genetics specialists, GCs, and GOs/gynecologists.
Experiences with GCs	The participant discussed experiences or interactions with a GC at the HCC.
Experiences with GOs/gynecologists	The participant discussed experiences with a GO at the HGC, or gynecologist outside of HSC.
Experiences with other HCPs	The participant discussed experiences with HCPs other than a GC or GO/gynecologist.
Genetic testing process	The participant discussed the process by which they made a decision to have or not have genetic testing, as well as when/how they learned their results. For example, when did they decide to have genetic testing and why? Were they hesitant to pursue testing or motivated? When did they learn their results, and how (i.e. over phone or in person)?
Trust in HCPs	The participant trusts/trusted and listens/listened to their HCP's recommendations and suggestions, they do not/did not question their expertise. On the other hand, the participant may have indicated that they do not/did not trust their HCPs.

A.7 Box plots for non-significant results



The median of the mean scale values (listed in Table 3.2) are represented by the horizontal black lines within each bar. Outliers are represented by black dots. A; Differences in mean scores on the CWS ($p = 0.257$), DCS ($p = 0.408$), SWD scale ($p = 0.825$), and PrepDM scale ($p = 0.369$) were not significant between women with and without children, although there was a trend towards greater HGSOC-related worry and preparedness for decision-making in women who have children versus those who do not. B; Differences in mean scores on the CWS ($p = 0.120$), DCS ($p = 0.149$), SWD scale ($p = 0.449$), and PrepDM scale ($p = 0.647$) were not significant between those with and without a family history of HGSOC. There was a trend towards increased HGSOC-related worry, satisfaction and preparation for decision making, as well as decreased decisional conflict in those with a family history of HGSOC compared to those without. C; Differences in mean scores on the CWS ($p = 0.474$), DCS ($p = 0.580$), and SWD scale ($p = 0.891$) were not significant between women who consulted a GO/gynecologist versus those who did not. Satisfaction with RRSO decision was very similar between groups, however there was a slight trend towards increased HGSOC-related worry and decreased decisional conflict for those who consulted a GO/gynecologist compared to those who did not consult a GO/gynecologist. PrepDM scores were not included for this group as those who did not attend the HGC were not able to evaluate it as an intervention using the PrepDM scale. ns, non-significant.