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Navigating Previvorship: Exploring the Barriers and Motivators to Lifestyle Behaviour Change in Women with BRCA Pathogenic Gene Variants

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Declaration

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Órla Crowley

Plain English Summary

This project was about understanding how women who have a high risk of getting breast cancer and ovarian cancer (due to a gene change in the BRCA1/2 genes) approach staying healthy. While we know a lot about medical ways to prevent cancer, like surgery, we don't know much about how these women feel about the role that a healthy lifestyle, like diet and exercise, plays in their lives and what helps or prevents them from making healthy lifestyle choices.

Methods: We used a two-step approach:

1. First, this thesis looked at what is already out there, I reviewed scientific papers to see what kind of lifestyle programmes that have been tried with women who have this genetic risk. I used a behaviour model to see what these programmes focused on, dividing it into: Capability (their knowledge and skills), Opportunity (the support and resources available to them) and Motivation (what drives them).
2. The next study in this thesis was designed to talk to the women themselves. I held in depth conversations with a group of women that have this genetic change in the BRCA1/2 genes to hear about their own experiences. This helped understand the real-life challenges and feelings that the scientific papers didn't cover.

Findings: This research showed that while some programmes help with things like exercise, they often miss a big part of the story: the emotional side of living with this genetic risk. The women who took part spoke about feeling a heavy emotional burden. They felt they were in a 'no-man's-land' between being well and being sick. This often left them feeling overwhelmed and exhausted which made it hard to stick to healthy habits. They also felt there was a lack of clear specific information for them unlike for people who have already have cancer.

A powerful finding from this work was that undergoing a risk-reducing surgery (like a mastectomy) could be used as a 'teachable moment'. Many women saw this time as a turning

point and chance to make a positive change to their health and feel in control. It's a key moment where their motivation is particularly high.

Based on these findings, a new way of thinking about support for these women is presented. Instead of generic advice, programmes need to consider the following:

- Personal and emotionally aware: They should be designed to support the mental health load that the women carry.
- Built around a women's journey: They should use key moments like surgery as a chance to help women make lasting changes.
- Connected and supported: There should be a specific person ('liaison') who can guide them through their healthcare journey and connect them with peer groups for support.

In short, this thesis shows that to truly help these women to make positive lifestyle choices, healthcare needs to move beyond simple health tips and create a support system that is as unique and personal as their own genetic journey.

Abstract

Background: Pathogenic variants in the BRCA1 and BRCA2 genes dramatically elevate a women's lifetime risk of breast and ovarian cancer. While clinical strategies such as genetic counselling and prophylactic surgery are well established, growing attention is being placed on modifiable lifestyle factors that may support cancer prevention and overall wellbeing. However, the specific challenges and motivations for adopting healthy behaviours in this genetically high-risk group remain underexplored.

Aims: This thesis investigates the landscape of lifestyle interventions for women with BRCA pathogenic gene variants and seeks to understand their lived experiences, motivations and barriers to behavioural change.

Methods: This research used a sequential qualitative design approach informed by a scoping review. The first study, a scoping review, identified and characterised existing lifestyle interventions for women at high risk of breast cancer, predominantly due to a BRCA1/2 pathogenic gene variant, and examined findings in consideration of the COM-B model (Capability, Opportunity, Motivation, Behaviour) of health behaviour change. Building on this, the second study, a qualitative project, was completed, which utilised focus groups and didactic interviews to explore the behavioural determinants from the perspectives of women with BRCA1/2 pathogenic gene variants.

Results: The review revealed that multicomponent interventions targeting physical capability and opportunity, via homebased and digital platforms, show potential for promoting health behaviour change with studies reporting high adherence rates (above 80%). However, the qualitative insights painted a more complex picture. The findings revealed that while women often have strong intentions to modify their lifestyle, emotional exhaustion and information overload, particularly from medical appointments act as significant barriers. Participants described significant informational gaps, a lack of BRCA-specific resources and a unique

psychological landscape shaped by ‘previvorship’, the emotional tension between proactive control and the inevitability of genetic risk. Barriers related to motivation and psychological capability emerged as particularly influential.

Conclusion: This research demonstrates that promoting health behaviour change in women with BRCA1/2 pathogenic gene variants is a complex process influenced by a nuanced interplay of capability, opportunity and motivation. Future interventions must be psychologically attuned, socially grounded and co-designed with patients to address their distinct emotional and motivational needs. This thesis offers a blueprint for future intervention design that foster sustainable behaviour change and holistic well-being.

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List of abbreviations

Abbreviation	Full term
1RM	One repetition max
AI	Artificial Intelligence
BMI	Body Mass Index
BRCA	BReast CAncer gene
CI	Confidence interval
CLL2	Chemokine (C-C motif) ligand 2
CREST	Cancer Research Stimulus Awards
DCE-MRI	Dynamic Contrast-Enhanced Magnetic Resonance Imaging
DEXA	Dual-energy X-ray Absorptiometry
DIEP	Deep Inferior Epigastric Perforator
DNA	Deoxyribonucleic acid
DPIA	Data protection impact assessment
EIA	Enzyme Immunoassay test
EPCAM	Epithelial cellular adhesion molecule
EU	European union
GP	General Practitioner
HER2	Human Epidermal Growth Factor Receptor 2
HR	Heart rate
IL-6	Interleukin-6
JBI	The Joanna Briggs Institute
MDT	Multidisciplinary team
MECC	Make Every Contact Count
MLH1	MutL protein homolog 1

MMAT	the Mixed Methods Appraisal Tool
MRSA	Methicillin-resistant Staphylococcus aureus
MSH2	MutS homolog 2
MSH6	MutS homolog 6
NCCP	The National Cancer Control Programme
NCRI	The National Cancer Registry Ireland
OR	Odds ratio
PCC/T	Population, Concept, Context/Type of evidence
PIBO	Population, Intervention, Behaviour, Outcome
PMS2	Postmeiotic segregation increased 2
PPI	Patient and public involvement
pQCT	Peripheral quantitative computed tomography
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews
RCT	Randomized controlled trial
RR	Relative Risk
RTA	Reflexive thematic analysis
SD	Standard deviation
SRQR	The standards for reporting qualitative research
TCD	Trinity College Dublin
TNBC	Triple-negative breast cancer
TNF-a	Tumour Necrosis Factor alpha
TSJCI	The Trinity St James's Cancer Institute
USA	United States of America
WCRF	The World Cancer Research Fund

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Chapter 1: Introduction

1.1 Cancer in Ireland

Cancer is a significant global health burden, with Ireland reporting the second highest number of new cancer diagnoses in the EU in 2022 (1). Looking ahead, the European Cancer Information System estimates that cancer cases will increase by 47% between 2022 and 2040 (1). Among women in Ireland, breast cancer is the most common form of cancer with an estimated 3,600 cases diagnosed annually and is the second leading cause of cancer related mortality (2, 3). Breast cancer risk increases with age, with the HSE reporting that about 80% of cases occur in women over 50 years of age (4). Consequently, a substantial proportion of diagnosis are concentrated in middle-aged and older women. Accordingly, the National Cancer Registry Ireland (NCRI) reports that 26% of women diagnosed are between ages of 45-55 years old and 43% of women diagnosed over the age of 55 years (3). It is estimated that 5-25% of breast cancer cases are attributed to hereditary factors (5-7). Although breast cancer is prevalent, the survival rates have improved significantly in Ireland. The NCRI reports that the five-year survival rate is 87%, one of the highest among all cancer types (3). This reflects the advancements in breast cancer treatments which include surgery, chemotherapy, radiotherapy, hormonal therapy and targeted agents.

Treatment for breast cancer in Ireland adheres to a nationally standardised and integrated pathway, overseen by the National Cancer Control Programme (NCCP) (8). This pathway mandates a multidisciplinary team (MDT) approach for all diagnosis cases ensuring comprehensive and coordinated care from diagnosis through to survivorship (8). Patients receive individual treatment plans, determined through expert consensus within the MDT. These plans are tailored based on tumour biology (e.g. hormone receptor status, HER2 status, histological grade), pathological staging and individual patient factors such as comorbidities and genetic predisposition (8). Treatment modalities commonly include surgical interventions (e.g. breast conserving surgery, mastectomy with

or without reconstruction), radiotherapy and systemic therapies such as chemotherapy, hormone therapy and targeted biological therapies.

Cancer prevention strategies are shaped by an understanding of both modifiable and non-modifiable risk factors. Non-modifiable risks include age, genetics and family history, factors which cannot be changed but rather help identify individuals at higher risk (9). In contrast, modifiable risk factors such as smoking, obesity, alcohol consumption and physical inactivity can be influenced through lifestyle changes and public health interventions (9). Lifestyle choices are particularly relevant in cancer prevention and are discussed in detail in section 1.7, under the subheading Modifiable Factors for Cancer Prevention. Obesity, alcohol consumption, and physical inactivity have all been strongly linked to breast cancer development. In Ireland, 29% of all cancer cases are attributed to modifiable risk factors, with breast cancer among the most affected (10). According to the NCRI, in 2016 an estimated 6,238 cancer cases (out of a total of 21,315) may have been prevented in Ireland through lifestyle and environmental interventions (10). These figures underscore the potential of population level strategies, such as those outlined in the National Cancer Strategy 2017-2026 and the HSE Cancer prevention plan 2025-2030, which emphasise public health campaigns targeting obesity, alcohol use and physical inactivity. Initiatives like Healthy Ireland, Making Every Contact Count and the National Skin Cancer Prevention Plan aim to create support and empower individuals to make healthier choices (11, 12). However, while these strategies benefit the general population, they may not address the needs of individuals with inherited cancer syndromes who often face earlier onset and more aggressive disease.

1.2 Hereditary Cancers Syndromes

Hereditary cancer syndromes are genetic conditions that increase a person's risk of developing certain types of cancer, often at a younger age than seen in the general population (13). They have drawn considerable attention due to their impact on cancer risk and the need to develop bespoke

preventative strategies in high-risk cohorts. Approximately 5-10% of all cancer cases in Ireland are linked to inherited genetic mutations (14). The two most common hereditary cancer syndromes are Hereditary Breast and Ovarian Cancer Syndrome which is caused by pathogenic BRCA1 or BRCA2 gene variants and Lynch syndrome which is associated with mutations in mismatch repair genes such as MSH2, MLH1, MSH6, PMS2 and EPCAM (6). Alterations in the BRCA1 and BRCA2 genes are strongly linked to breast and ovarian cancers, whereas Lynch syndrome is linked to an elevated risk of colorectal, endometrial cancer and other malignancies (15-17).

1.3 BRCA Pathogenic Gene Variants

Since their discovery in 1994 and 1995, BRCA1 and BRCA2 pathogenic gene variants have been extensively studied for their impact on hereditary cancer risk (18). These pathogenic gene variants significantly increase the lifetime risk of developing breast, ovarian, prostate, and other cancers (16). BRCA1 and BRCA2 are tumour suppressor genes that play critical roles in maintaining genomic stability through DNA repair processes. These genes act as genomic caretakers, ensuring that DNA damage resulting from environmental or cellular stress is efficiently repaired (15). When a pathogenic gene variant occurs in BRCA1 or BRCA2, their DNA repair functions are compromised, leading to genomic instability, the accumulation of DNA damage, which can result in cancer development. Such mutations are inherited in an autosomal dominant manner, making individuals who carry a single altered copy of these genes particularly susceptible to hereditary cancers (19, 20).

BRCA-associated cancers are distinguished by unique biochemical and clinical characteristics (21). BRCA-related breast cancer differs from sporadic breast cancer which arise from somatic (de novo) mutations acquired during an individual's lifetime rather than inherited germline mutations (22). These inherited cancers tend to appear at a younger age than sporadic cases and are often more aggressive, with a tendency towards higher-grade tumours and triple-negative breast cancer (TNBC) phenotypes (23). TNBC, characterised by the absence of oestrogen receptor, progesterone receptor,

and HER2 expression, is more challenging to treat due to the lack of targeted therapies (23). While TNBC accounts for approximately 10–15% of sporadic breast cancer cases, it occurs in 66–100% of BRCA1 associated breast cancer and 14–35% of BRCA2 associated breast cancer cases (23). BRCA2 associated cancers are more commonly oestrogen receptor-positive, which allows for the use of hormone-targeted therapies (24, 25).

The clinical significance of inheriting a BRCA 1/2 pathogenic gene variant is largely determined by its penetrance, defined as the proportion of individuals with a specific genotype who express the associated phenotype, in this case developing cancer (26). While BRCA1/2 pathogenic gene variants are recognised as highly penetrant, it is crucial to understand that penetrance is incomplete, meaning not all individuals who inherit a harmful BRCA pathogenic gene variant will develop cancer (26). Although penetrance estimates have varied over time due to differences in study populations and methodologies, the current literature suggests that penetrance is not increasing. Rather, it's a dynamic process influenced by a complex interplay of genetic, lifestyle and environmental factors, all of which modify the risk of cancer (27).

Epidemiological studies have provided estimates of cancer risks for BRCA pathogenic gene variant carriers. For example, globally women carrying BRCA1 gene alterations face a lifetime risk of breast cancer between 50–72%, while those with BRCA2 gene alterations have a slightly lower risk, estimated at 45–69% (28, 29). Additionally, the risk of ovarian cancer risk is significantly elevated, with BRCA1 conferring a 39–44% risk and BRCA2 pathogenic gene variants associated with an 11–17% risk (30). It is important to note that these figures represent lifetime cumulative risk and can vary based on several modifying factors including specific pathogenic gene variant, family history, ethnicity and lifestyle choices (26). These elevated risks highlight the profound burden of BRCA gene alterations on affected individuals.

1.4 Hereditary Care Pathways

To address hereditary cancer risk, Ireland has established hereditary cancer services that provide genetic testing, counselling and personalised screening recommendations (6). These services are delivered through family risk clinics which offer tailored risk management strategies, based on a person's genetic profile and family history. In 2023, the NCCP introduced the Hereditary Cancer Model of Care, a strategic framework that enhances service delivery through a three-tiered structure: generalist, regional and specialist cancer genetics services (6). This model strives to ensure timely, equitable and coordinated care. It supports access to genetic assessment, risk reducing interventions, psychological and peer support and includes a focus on workforce development and robust data infrastructure (6).

Once identified, those who carry pathogenic gene variants may opt for enhanced surveillance and/or risk reducing surgeries to reduce their risk of developing cancer (31). As these services grow, there is a growing cohort of pathogenic gene variant carriers that have not and may not progress to a cancer diagnosis. However, the absence of national registries means the size and characteristics of this cohort is unknown, hindering targeted interventions and resource allocation. The key priority for this cohort is cancer prevention through risk mitigation strategies (32). This cohort faces complex decisions regarding the timing of risk reducing surgeries and risk testing for their families (33). As the focus shifts toward preventive strategies, personalised care that incorporates modifiable lifestyle factors is becoming increasingly relevant in reducing hereditary cancer risk and improving long-term outcomes.

1.5 Managing Cancer Risk in People Living with BRCA Pathogenic Gene Variants

For individuals with BRCA pathogenic gene variants, early risk assessment and proactive management are critical. Preventive measures, including enhanced screening, chemoprevention, and prophylactic surgeries (e.g., bilateral mastectomy and salpingo-oophorectomy), play a significant role in reducing

cancer risk and mortality in high-risk individuals (7, 34). Risk-reducing surgeries have proven to be highly effective. Bilateral risk-reducing mastectomies can lower breast cancer risk by 90%, whilst risk-reducing salpingo-oophorectomies reduces the risk of ovarian cancer by 85%-95% (35, 36). While risk-reducing salpingo-oophorectomy is associated with a clear survival benefit due to the high mortality of ovarian cancer, the impact of risk reducing mastectomy and overall survival is more nuanced, recent evidence suggests that for carriers of BRCA1 and BRCA2 pathogenic gene variants, the survival outcomes between those undergoing risk reducing mastectomy and those opting for surveillance are comparable (37). Such surgical interventions are not without challenges or potential adverse effects. Procedures may lead to significant physical and psychological impact, including surgical induced menopause, post-operative infections, and emotional distress (38, 39). Similarly, chemoprevention strategies, such as hormone therapies, carry risks of notable side effects including but not limited to hot flushes, vaginal discharge, and adverse sexual function symptoms (34).

Given the health challenges faced by individuals with BRCA pathogenic gene variants, there is an increasing focus on lifestyle risk factor management to support overall health (40, 41). Lifestyle behaviours among this cohort are generally poor (42, 43), therefore lifestyle modifications are essential for chronic disease prevention, cancer risk management and reducing the side effects associated with risk-reducing surgeries. While diet, physical activity and environmental exposure cannot eliminate genetic predisposition, there is evidence which suggests that healthy lifestyle modifications may compliment medical interventions (44). Thus, adopting a holistic model that integrates genetic insights with behavioural interventions, provides an opportunity to develop comprehensive, patient-centred care that potentially contributed to cancer risk management.

1.6 Lifestyle Behaviours Among BRCA Pathogenic Gene Variant Carriers

Research exploring the issue of unhealthy lifestyle patterns in individuals with BRCA1/2 pathogenic gene variants is expanding. A cross-sectional study of Irish BRCA pathogenic gene variant carriers

(N=75) reported that 94% of participants did not meet the physical activity levels recommended by the American College of Sports Medicine (45), with majority being overweight (39%) or obese (32%) and 73% exhibiting central obesity (42). A larger study from the Netherlands (N= 268) reported similar findings, with 41% of their study cohort classified as overweight as well as 48% of BRCA gene carriers of childbearing age reported to be physically inactive (43). While adopting a healthier lifestyle is recognised for reducing cancer risk, growing evidence suggests that lifestyle modifications improve overall quality of life, enhance treatment responses and significantly reduces post-operative complications, potentially leading to better long-term health outcomes for BRCA pathogenic gene variant carriers (43, 46, 47). Nonetheless, women with BRCA1/2 pathogenic gene variants face unique challenges in adopting lifestyle recommendations and therefore understanding the unique challenges that drive or impede behaviour change in this cohort is essential for designing effective interventions that promote sustained healthy lifestyles.

1.7 Modifiable Factors for Cancer Prevention

Cancer prevention is increasingly focused on modifiable risk factors; evidence suggests that 30–40% of all cancers worldwide can be prevented through lifestyle changes (9). Unlike genetic predispositions, modifiable factors such as diet, physical activity, smoking, alcohol consumption, body weight, and environmental exposures can be altered to reduce all cancer risk.

1.7.1 Diet, Physical Activity and Obesity

Diet can play a major role in cancer prevention, with epidemiological studies demonstrating strong associations between dietary patterns and cancer risk (48). Diets high in refined carbohydrates and unhealthy fats have been associated with higher insulin resistance which can promote harmful cell proliferation, whereas fibre rich diets enhance gut microbiome diversity which is linked to better immune function and a reduction in chronic inflammation (49, 50). Cohort studies from the United States, and Europe have consistently shown that diets rich in whole grains, vegetables, fruits, and

legumes are associated with a 10–20% reduction in cancer incidence, particularly for colorectal and sporadic breast cancers (51-53). In relation to BRCA-associated breast cancer specifically, data is sparse but is emerging. One cohort study found that higher meat intake of 3–10 meat food-items/day was linked with a nearly doubled breast cancer risk amongst people living with BRCA pathogenic gene variants (HR 1.97, 95% CI 1.13,3.4; p = 0.026) (54). Another case control study found that total energy intake > 2339 kcals/day was associated with increased BRCA-related breast cancer risk when compared to women who consumed <1724 kcal/day (OR 2.76, 95% CI: 1.10–7.02; p=0.026 for trend) (55). These findings suggest that a balanced diet, appropriate calorie intake, weight management and healthy diet patterns may have an important role to play and are consistent with broader dietary recommendations aimed at promoting overall health and reducing disease risk.

Regular physical activity has a well-established inverse association with cancer risk, exerting protective effects through multiple biological pathways (56). Meta-analyses and large prospective cohort studies demonstrate that engaging in at least 150 minutes of moderate-intensity exercise per week can reduce the risk of sporadic breast cancer by 20–30% and colon cancer by approximately 15–20% (57, 58). Proposed mechanisms of action include improved immune function, reduced systemic inflammation and improved hormonal regulation, in particular oestrogen and insulin levels (59). Especially for individuals with BRCA1 or BRCA2 pathogenic gene variants, emerging evidence suggests that regular exercise may be associated with a decreased breast cancer risk (41, 60). One systematic review found that physical activity during adolescence and young adulthood may play a protective role, with higher physical activity during these formative years linked to a delayed age of breast cancer diagnosis (p=0.03) (60). Additionally, sedentary behaviour may have negative implications. One pilot study observed a significant inverse correlation ($\rho = -0.32$; $P = 0.02$) between long uninterrupted sedentary bouts and reduced BRCA1 mRNA expression, suggesting that extended periods of sitting are leading to poor health behaviours that could potentially increase cancer risk in individuals with BRCA pathogenic gene variants (61). Given these findings, integrating exercise-based interventions

into hereditary cancer prevention strategies could provide individuals with BRCA pathogenic gene variants with a proactive approach to optimising their health and potentially minimising cancer risk.

Body weight significantly influences cancer risk, with obesity being a major preventable cause of several cancers, including those of the breast, colon, liver, and pancreas (62). Studies report that women with obesity (BMI ≥30) have up to a 50% increased risk of developing post-menopausal sporadic breast cancer (63). Fat distribution has also been shown to be a relevant factor with central obesity posing a higher risk compared to overall obesity (63). Excess body fat promotes chronic inflammation, hormonal imbalances, and metabolic dysfunctions, creating an environment conducive to tumour development (62). Proinflammatory cytokines such as IL-6 and TNF-a, along with excess oestrogen production in adipose tissue may drive carcinogenesis (64). One study found that cancer risk was notably influenced by body fat levels, particularly for BRCA1 pathogenic gene variant carriers (65). They reported that women with higher body fat levels had a significantly higher risk of developing BRCA1-related cancer (HR 1.87, 95% CI, 1.21-2.88), whereas people living with BRCA2 pathogenic gene variants who have four to five metabolic syndrome risk factors (high blood pressure, weight circumference >85cm, abnormal cholesterol, high fasting blood glucose and triglycerides) had an increased cancer risk (HR, 1.87; 95% CI, 1.11-3.19) (65). While evidence in this area remains limited, it is increasingly recognised that weight management alongside healthy dietary practices and regular physical activity may play a contributory role in broader risk management strategies and improving overall health outcomes for individuals with BRCA1/2 pathogenic gene variants.

1.7.2 Smoking and Alcohol

Smoking is one of the leading preventable causes of cancer worldwide. It accounts for nearly 90% of lung cancer cases and is strongly linked to cancers of the oral cavity, oesophagus, bladder, pancreas, and cervix (66). A meta-analysis of the prospective studies conducted in the general population suggested that current smokers have a 13% increased risk of sporadic breast cancer compared to non-smokers (95% CI 1.09–1.17) (67). Tobacco smoke contains carcinogens that cause DNA damage and promote tumour development, making smoking cessation a critical strategy for cancer prevention

(68). Although evidence amongst individuals with BRCA1 and BRCA2 pathogenic gene variants is limited, preliminary evidence has suggested that smoking within five years of a pregnancy may exacerbate breast cancer risk (69). Some cohort studies indicate that for BRCA1 carriers, a history of smoking is linked to significant increase (OR = 1.27; 95% CI 1.06–1.50) of breast cancer, suggesting tobacco exposure interacts with underlying genetic susceptibility (70).

Alcohol consumption has been a well-documented risk factor for several cancers including those of the mouth, throat, oesophagus, liver, colon, and sporadic breast (71). Alcohol metabolises into acetaldehyde, a carcinogen that damages DNA and promotes tumour development. A meta-analysis based on 53 epidemiological studies indicated that an intake of 35-44 grams of alcohol per day (approximately 3.5 to 4.4 standard units, in Ireland, one standard drink contains 10 grams of pure alcohol) can increase the risk of sporadic breast cancer by 32% (72, 73). The role of alcohol in cancer prevention primarily revolves around public health strategies to reduce alcohol intake and promote awareness of its carcinogenic effects. While alcohol's carcinogenic effect is recognised, its role in BRCA-related cancers remains poorly described (27). One study reported a modest inverse association between breast cancer and current alcohol consumption among women with a BRCA1 pathogenic gene variant (OR = 0.82, 95% CI 0.70–0.96) but found no association among carriers of BRCA2 pathogenic gene variants (OR = 1.00; 95% CI 0.71–1.41). Interestingly, in the same study, exclusive wine consumption was linked to a significant reduction in breast cancer among BRCA1 carriers (p-trend = 0.01) (74). While another study observed that alcohol consumption, excluding wine, was significantly associated with increased breast cancer risk among carriers of the BRCA2 pathogenic gene variant (OR=2.15, 95% CI 1.03–4.49) (75). Given that BRCA2 related breast cancers are more commonly oestrogen receptor positive they hypothesised that alcohol may increase risk in BRCA2 pathogenic gene variant carriers via hormonal pathways, particularly by elevating oestrogen levels (75).

1.8 Cancer Prevention Guidelines

Given the established evidence highlighting suboptimal lifestyle patterns of this cohort, there is a clear need to explore how general cancer prevention guidelines can be meaningfully integrated into BRCA-specific healthcare (42, 43). The World Cancer Research Fund (WCRF) in collaboration with the American Institute for Cancer Research has developed evidence-based guidelines to help individuals adopt healthier behaviours (Figure 1) (76, 77). While these guidelines are not tailored specifically to individuals with hereditary cancer syndromes, they represent the most comprehensive framework currently available for reducing modifiable cancer risk through lifestyle adjustments. This study seeks to understand how such generalised guidance can be embedded into the lived realities of women managing elevated cancer risk due to BRCA1/2 pathogenic gene variants. In doing so it shifts the focus from theoretical gene-environment interactions to the practical application of public health recommendations.

Figure 1. WCRF Cancer prevention recommendations from https://www.wcrf.org/preventing-cancer/cancer-prevention/our-cancer-prevention-recommendations/

1.9 Project Context and Personal Motivation

This project was supported by the CREST awards (Cancer Research Stimulus Awards) through The Trinity St James's Cancer Institute (TSJCI), a research funding scheme that provides seed funding to foster and develop new research collaborations across the Cancer Institute. This project was conducted in collaboration with 'the CREST multidisciplinary research team' with expertise spanning cancer genetics, medical oncology, breast care, physiotherapy, health psychology and nursing. The team consisted of: Physiotherapist (OC -Lead researcher), An Associate Professor in Cancer Rehabilitation and Survivorship (EG- thesis supervisor) and PhD Candidate from Trinity College Dublin (DC- who supported project implementation through double screening and double coding). The advisory team included a Health Psychologist from the University of Galway (JG), a patient representative (KC), Consultant Breast Surgeon (EC), Consultant Medical Oncologists (KC, NC), Project Manager/ Research Coordinator in Breast Care (SMcG) and Advanced Nurse Practitioner (YH) from St James Hospital Dublin.

As a senior oncology physiotherapist, I encounter women with BRCA pathogenic gene variants regularly, typically immediately following risk reducing surgery such as mastectomies and breast reconstruction procedures. These patients often present with pain, restricted range of motion, fatigue, and postural changes associated with reduced scapular, upper limb and thoracic movement. For many, this is in the context of managing surgical induced menopause brought on by previous risk reducing salpingo-oophorectomy. These factors significantly impact their recovery and engagement in rehabilitation. During treatment sessions, common barriers to full recovery include persistent pain, changes to body image, fatigue, delayed scar healing, hot flushes and the psychosocial stress associated with contemplating a return-to-work date. These challenges are compounded by familial

experiences, many women are simultaneously navigating risk reducing pathways alongside sisters and cousins who are undergoing, have undergone or anticipating the same procedures and cancer treatment. A common trend was a lack of knowledge about lifestyle factors following disclosure of BRCA pathogenic gene variant as many women seek advice for relatives that may be at the beginning of their BRCA journey.

These real-world encounters highlight the cross-generational and collective dynamics of hereditary cancer risk management and underscores the need for comprehensive interdisciplinary approaches that extend beyond the surgical pathway. By integrating physiotherapy, psychological support and evidence-based lifestyle interventions, we can effectively address the complex, layered recovery needs of this population, facilitating not just rehabilitation, but also restoration of confidence, autonomy and long-term wellbeing.

1.10 Aims and Objectives of Thesis

The overarching aim of this thesis is to explore the lifestyle interventions and behaviour change among women with BRCA pathogenic gene variants, with the goal of identifying the core components necessary to inform the future development of more tailored, patient-centred interventions for this specific population.

Specific objectives:

- Scoping review: To identify and describe the key characteristics of existing lifestyle interventions (e.g. weight loss, physical activity) for cancer prevention in women with germline BRCA pathogenic gene variants**.**
- Qualitative study: To examine how women with known BRCA pathogenic gene variants (but unaffected by cancer) perceive, interpret, and potentially implement the WCRF recommendations for cancer prevention.

1.11 Thesis Structure

This thesis is organised into five chapters. Chapter one introduces BRCA genes, lifestyle interventions for cancer preventions, the current cancer prevention recommendations, and the significance of this study. Chapter two outlines the methodological approach, the COM-B theoretical model underpinning this work and provides a brief overview of the two projects that make up this thesis. Chapter three presents the methods and results of the scoping review, mapping lifestyle interventions for BRCA pathogenic gene variant carriers to the COM-B model of behaviour change. Chapter four outlines the methodology and results of the qualitative study, reporting the focus group findings which explored the current levels of knowledge and motivations that women with BRCA1/BRCA2 pathogenic gene variants have towards modifiable lifestyle factors of cancer risk, and to what extent are they aware of, understand, and implement the WCRF cancer prevention recommendation. Chapter five engages in a discussion of the results, interpreting their implications in the context of existing literature, summarising key findings, acknowledging the study's limitations and suggesting directions for future research.

Chapter 2: Methodological Approach

2.1 Methodological approach

This thesis uses a mixed-methods approach to explore lifestyle interventions and behaviour change among women with BRCA pathogenic gene variants. By integrating insights from behavioural science with cancer prevention research, this thesis seeks to identify the core components necessary to inform the future development of more tailored, patient centred interventions for individuals carrying BRCA pathogenic gene variants.

The first study, presented in Chapter three, was a scoping review, undertaken to identify and describe existing evidence on lifestyle interventions as modifiable risk factors in BRCA-associated cancer risk. By characterising these interventions and mapping them to the COM-B model the review provided a foundation for understanding current behavioural approaches and their relevance within broader preventive strategies.

The second study, presented in Chapter four, examined women's perspectives on the World Cancer Research Fund (WCRF) recommendations for cancer prevention in the context of BRCA-associated cancer risk. Through qualitative focus groups and didactic interviews, the study explored how women, with known BRCA pathogenic gene variants but unaffected by cancer themselves perceive, interpret, and potentially implement these recommendations. These insights provided valuable understanding of practical challenges, personal motivations and contextual factors that influence behaviour change.

The decision to utilise both a scoping review and a qualitative study allowed for a comprehensive examination of existing literature and an in-depth understanding of real-world perspectives from the women who are directly affected by BRCA pathogenic gene variants.

2.2 Research Design

2.2.1 An Overview of Sequential Qualitative Methodology

This Study Adopts a sequential qualitative design informed by a scoping review. In this approach, a review-based phase precedes primary data collection, allowing for deeper exploration and the identification of gaps before applying a structures analysis to participant experiences (78). This design is typically used to first identify themes, concepts, or gaps, which can then inform subsequent investigations.

2.2.2 Rationale

A sequential design was selected because it establishes a strong evidence base, it contextualises theoretical findings, and it enhances depth and validity. The scoping review establishes a foundational mapping of existing studies to the COM-B model for behaviour change to structure understanding. The qualitative study builds on this, providing first-hand insights into how women with BRCA pathogenic gene variants perceive and engage with behaviour change interventions. Findings from both studies were synthesised to strengthen conclusions, ensuring the results are not solely based on theoretical frameworks but also reflect real-world experiences. This approach is particularly beneficial in behavioural research and health sciences, as it ensures that subsequent interventions are not only informed by existing theoretical evidence but also by practical human experiences.

2.3 Theoretical Framework

Central to this thesis, the COM-B model for behaviour change served as a foundational theoretical framework guiding two key areas of investigation. This approach provided a clear and practical structure for pinpointing the specific determinants of behaviour within this population, ensuring the research went beyond simply what interventions exist to examine how and why they may or may not be effective. In chapter three, this model was systematically applied to map and categorise interventions identified within the scoping review.. Subsequently in chapter four, the model was

instrumental in the development of the interview guide for the qualitative study, ensuring a comprehensive exploration of behavioural determinants. The COM-B model is a widely used framework for understanding and influencing behaviour change. The model emphasises three core components (79):

1. Capability: the individual's physical and psychological ability to perform a behaviour.
2. Opportunity: External factors that facilitate or hinder the behaviour.
3. Motivation: Internal processes, both reflective (e.g., intentions) and automatic (e.g., habits).

The COM-B model postulates that changes in any of these three elements can influence behaviour and successful interventions often focus on one or more to drive meaningful change. By analysing how these factors interact, interventions can be designed to address specific barriers or enablers, leading to more effective and lasting change (80). COM-B serves as both an explanatory and design framework, making it a valuable tool for identifying behavioural determinants and informing interventions strategies. Often used alongside the Theoretical Domains Framework, COM-B provides a practical structure for designing context sensitive interventions in a wide range of sectors including health, sustainability, and education (80).

The value of the COM-B model lies in its structured approach to behavioural assessment, enabling researchers and practitioners to pinpoint which component requires intervention in a given context, be it improving psychological readiness, reshaping external environments or enhancing physical capacity. Widely applied in healthcare, this model has been utilised to improve adherence to medical advice and enhance overall health outcomes (81). For example, one study used the COM-B framework to categorise and analyse perceived barriers to uptake of population genomic screening and management options for breast and prostate cancer (82). By capturing these barriers within the framework, the study was able to provide mapped strategies from the behaviour change wheel to address specific barriers and increase uptake in an evidenced manner. Another study, which used the

model by mapping free-text survey responses to the COM-B components allowed them to identify specific barriers and enablers to weight management and suggest targeted strategies amongst women with breast cancer (83). They identified that environmental restructuring, incentivisation, persuasion/coercion, and equipping participants with specific knowledge and skills would facilitate optimal lifestyle behaviours and weight management for women with breast cancer (83). These examples highlight the model's versatility and effectiveness in addressing diverse healthcare challenges. Given the unique challenges faced by BRCA pathogenic gene variant carriers, the COM-B model allows for a deeper analysis of the factors shaping their decisions. Understanding how to drive change requires a layered look at three key factors capability (the knowledge, skills and confidence required to make changes), opportunity (the environmental and social enablers and barriers that impact daily choices) and motivation (the fears and beliefs that drive engagement or resistance). As such this model offers a meaningful bridge between abstract behavioural therapy and lived realities of BRCA pathogenic gene variant carriers illuminating not only what interventions exist but how and why they may, or may not, resonate with BRCA pathogenic gene variant carriers in real world contexts.

Chapter 3: Examining the Role of Lifestyle Interventions for Managing Modifiable Risk Factors in Women with Germline BRCA Pathogenic Gene Variants: A Scoping Review

3.1 Introduction

Current clinical guidelines for women with BRCA pathogenic gene variants predominantly emphasise genetic counselling and surgical or chemo-preventive options, with relatively limited attention to behavioural interventions (84). However, growing interest in non-pharmacological approaches particularly among women seeking to delay risk-reducing surgery, has prompted investigation into the role of lifestyle factors such as physical activity, diet and weight management (85). As presented in section 1.7 preliminary evidence suggests that physical activity and higher diet quality may influence breast cancer risk in BRCA1/BRCA2 pathogenic gene variant population (44). Notably, the variable penetrance of BRCA pathogenic gene variants underscores the possibility that environmental and behavioural modifiers contribute to differences in cancer risk expression (86, 87). While several studies have examined individual lifestyle components and a small number of reviews have explored their potential impact on cancer risk in BRCA pathogenic gene variant carriers, there is no study that has systematically mapped these interventions or considered how women engage with or adhere to them. This scoping review addresses that gap by synthesising existing evidence on lifestyle interventions for BRCA pathogenic gene variant carriers and mapping them to the COM-B model of behaviour change, with particular focus on intervention design, delivery and behavioural engagement.

3.2 Rationale for Scoping Review Methodology

Scoping reviews are a form of knowledge synthesis that aim to map the breadth and nature of evidence on a given topic, particularly when the field is complex, heterogeneous or emerging. Unlike systematic reviews, which focus on narrowly defined questions and outcome measures, scoping

reviews offer a broader lens to chart the landscape of research activity and inform future study design, clinical guidelines, and patient education efforts (88).

The methodological foundation for a scoping review was first laid out by Arksey and O'Malley, who proposed a five-step framework : 1) identify research question, 2) identify relevant studies, 3) study selection, 4) charting the data, 5) collating, summarising and reporting results (89). Levac et al. (2010) later refined this model to emphasise the importance of iterative team-based decision making, stakeholder consultation and transparent reporting (90). More recently the Joanna Briggs Institute (JBI) has developed comprehensive methodological guidance for conducting scoping reviews (91). Compared to earlier frameworks the JBI approach offers clearer guidance on protocol development, inclusion criteria, data extraction and the optional integration of quality appraisal tools (91). The structure enhances transparency, reproducibility and methodological consistency, qualities important when synthesising literatures in emerging or heterogenous fields such as BRCA-related lifestyle interventions. By building upon and consolidating previous frameworks, JBI offers a more operationalised and health research focused structure making it appropriate and rigorous choice for the current study. This framework supports a structured and replicable approach to evidence synthesis particularly in areas where literature is diverse and fragmented**.**

To date, no single review has mapped the current state of knowledge regarding how lifestyle interventions impact BRCA-associated cancer risk. Therefore, a scoping review, particularly one guided by the JBI framework, is well-suited to comprehensively map the heterogeneous and emerging evidence on lifestyle interventions for BRCA pathogenic gene variant carriers, thereby laying the groundwork for future research and patient-centred care.

3.3 Protocol Publication

The protocol for this scoping review is published to open access on open science framework (92).

Citation: Crowley O. Scoping review protocol: Examining the Role of Lifestyle Interventions for Managing Modifiable Risk Factors in Women with Germline BRCA Pathogenic Variants. [Internet]. OSF; 2025. Available from: osf.io/ka75z/files/osfstorage

3.4 Objectives

This scoping review aims to identify and describe the key characteristics of existing lifestyle interventions (e.g. weight loss, physical activity) for cancer prevention in women with germline BRCA pathogenic gene variants**.**

Specifically, it seeks to:

1. Identify and describe the characteristics of existing lifestyle interventions targeted at individuals with germline BRCA pathogenic gene variants.
2. Map these characteristics to the COM-B model to evaluate behaviour change elements, as well as key indicators of intervention, feasibility and acceptability, with a view to informing the development of future interventions tailored to the BRCA pathogenic gene variant population.

3.5 Methods

This scoping review follows the JBI methodology and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines (91, 93). While critical appraisal is not required by PRISMA-ScR, it was integrated into this review using the Mixed Methods Appraisal Tool (MMAT) version 2018 (94). This deliberate step was undertaken because in a heterogenous and emerging field like modifiable risk factors in BRCA pathogenic gene variant carriers, assessing methodological rigor allows for a more nuanced and

informed interpretation of findings (91). Understanding the quality of the included studies help to contextualise their results and to identify more robust evidence, strengthening the recommendations for future research and intervention development.

3.5.1 Primary Research Question

What is currently known from empirical research about the design, delivery and behavioural mechanisms, such as motivation, capability and adherence, through which lifestyle interventions support risk reduction in women with germline BRCA pathogenic gene variants?

3.5.2 Search Strategy

A three-step search strategy, as outlined by JBI, was used to ensure a comprehensive identification of relevant literature:

1. Preliminary Search: A limited search was conducted in PubMed to identify relevant papers and analyse index terms.

2. Comprehensive Search: A full search using identified keywords and index terms (Table 1) was conducted in MEDLINE, Embase, Web of Science, and CINAHL databases, in collaboration with an experienced subject librarian to enhance search precision. The extended search strategy is presented in Appendix 1.

3. Additional Searches: To supplement the database search, both backwards and forward citation searching were performed. Backwards citation searching involved reviewing reference lists of included studies to identify further relevant papers. Forward searching citation searching was conducted using Google Scholar, tracking newer papers that cited each included study to capture emerging literature. Grey literature searches were performed following a similar methodology.

	Key Words
Population	Women Female BRCA1 BRCA2 Germline mutation Pathogenic gene variant
Interventions	Lifestyle intervention Lifestyle modification Training Education Group based
Behaviours	Improved diet Improved nutrition Increase exercise Decreased sedentary Increased physical activity Reduction or cessation of smoking Reduction or abstinence from alcohol
Outcomes	Weight loss Reduced BMI Increased physical fitness.

Table 1: The search terms were organized using a modified PIBO framework (Population, Intervention, Behaviour, Outcome) to guide the search strategy for the scoping review. BRCA: Breast cancer gene; BMI: Body Mass Index.

To ensure a structured and comprehensive search strategy, the search terms were organised according to established scoping review frameworks. Specifically, the PIBO structure (Population, Intervention, Behaviour, Outcome) was applied to guide term selection related to behavioural change (Table 1), while PCC/T (Population, Concept, Context/Type of evidence) was used to align with the JBI methodology (Table 2) (95). PIBO helped delineate terms related to target behaviours and intended

outcomes (e.g., physical activity, improved diet, reduced cancer risk), while PCC/T ensured the broader conceptual scope of modifiable lifestyle interventions among BRCA pathogenic gene variant carriers was captured across diverse study designs and contexts. Using both frameworks enabled the review to remain behaviourally focused while accommodating the complexity and heterogeneity of the literature.

	Inclusion criteria
Population	The review considered all Women with Germline BRCA pathogenic gene variants, with or without a diagnosis of cancer. Studies were included if at least some of the participants were reported as BRCA pathogenic gene variant carriers, even if they were part of a broader 'high-risk' population. This approach was taken to capture all relevant evidence, as some studies may not have exclusively focused on women with a confirmed BRCA pathogenic gene variant.
Concept	The review considered all studies and publications that provide information about lifestyle interventions and approaches that are used to address cancer risk in all women with Germline BRCA pathogenic gene variants.
Context	The review considered studies that describe modifiable lifestyle interventions for women with BRCA associated inherited risk.
Type of studies	The review considered all types of quantitative, qualitative, or mixed-methods studies including RCTs, non-RCTs, pre-post studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies were considered for inclusion.

Table 2: PCC/T: Population, Intervention/Concept, Context, and Study types. This table presents the inclusion criteria used for the systematic review. BRCA: Breast cancer gene; RCTs: Randomized Controlled Trials.

3.5.3 Study Selection

All retrieved publications were uploaded into Covidence, and duplicates were removed. Covidence software was used to facilitate study selection and screening, providing a streamlined platform for managing title/abstract review, full-text inclusion and data charting. Following this, two researchers

(OC and DC) independently screened titles and abstracts based on the predefined inclusion criteria (Table 2). Full-text articles were assessed independently and studies that did not meet the criteria were excluded. Rationale for exclusion are detailed on PRIMSA diagram Figure 2. In the case of disagreement between the two researchers, a discussion took place, and conflicts were resolved via consensus. If consensus was not reached a third researcher (EG) was consulted. If articles were unavailable, authors were contacted directly. Final included studies were then stored and managed using Endnote reference management software.

3.5.4 Inclusion Criteria

The inclusion criteria was developed to ensure the review remained focused on literature directly relevant to women with germline BRCA1/2 pathogenic gene variants and the specific context of lifestyle-related cancer risk reduction. By targeting empirical studies that examined modifiable behavioural interventions, such as diet, exercise, smoking cessation, and alcohol use, across diverse healthcare and community settings, the criteria allowed for a comprehensive yet purposeful synthesis. This focus aligns with the behavioural aims of the review and ensures that findings are meaningful for informing intervention development and clinical practice tailored to this high-risk population.

3.5.5 Charting the Data

A standardised data extraction form was developed before the data extraction. The lead researcher (OC) extracted data from the included studies. The following data were extracted: Author, country, study design, participants, intervention, feasibility metrics, study duration, primary and secondary outcomes (Table 3). OC discussed the extracted data from all included studies with two researchers (EG and JG) to ensure reliability of the extraction process.

3.5.6 Data Analysis

Intervention content and delivery details from the included studies were systematically reviewed and mapped onto the COM-B model of behaviour change: Capability, Opportunity and Motivation (Table 4) (79). The COM-B model served as an organising framework to classify behavioural determinants at

both individual and contextual level. Codes were developed based on the core constraints and subcomponents of the model (e.g. physical Vs psychological capability, social Vs physical opportunity, reflective Vs automatic motivation). Two researchers (OC and JG) independently applied this framework, discrepancies in classification were then resolved through consensus.

3.6 Results

3.6.1 Study Selection

In total 2,954 studies were identified in PubMed, MEDLINE, Embase, Web of Science and CINAHL. Following the removal of duplicates, 1889 studies were screened for eligibility based on their title and abstracts. This initial screening process led to the exclusion of 1,882 articles, leaving seven full-text articles for more detailed assessment. Of these, three articles were subsequently excluded: one due to publication's full text was not in English, another conducted their trial on the general population with no reporting of BRCA or 'high risk' cohorts and the third did not assess the delivery or uptake of the intervention in sufficient detail to inform behavioural mechanisms. No additional studies were included from citation searching. Ultimately four studies met all inclusion criteria and were included in the scoping review (Figure 2).

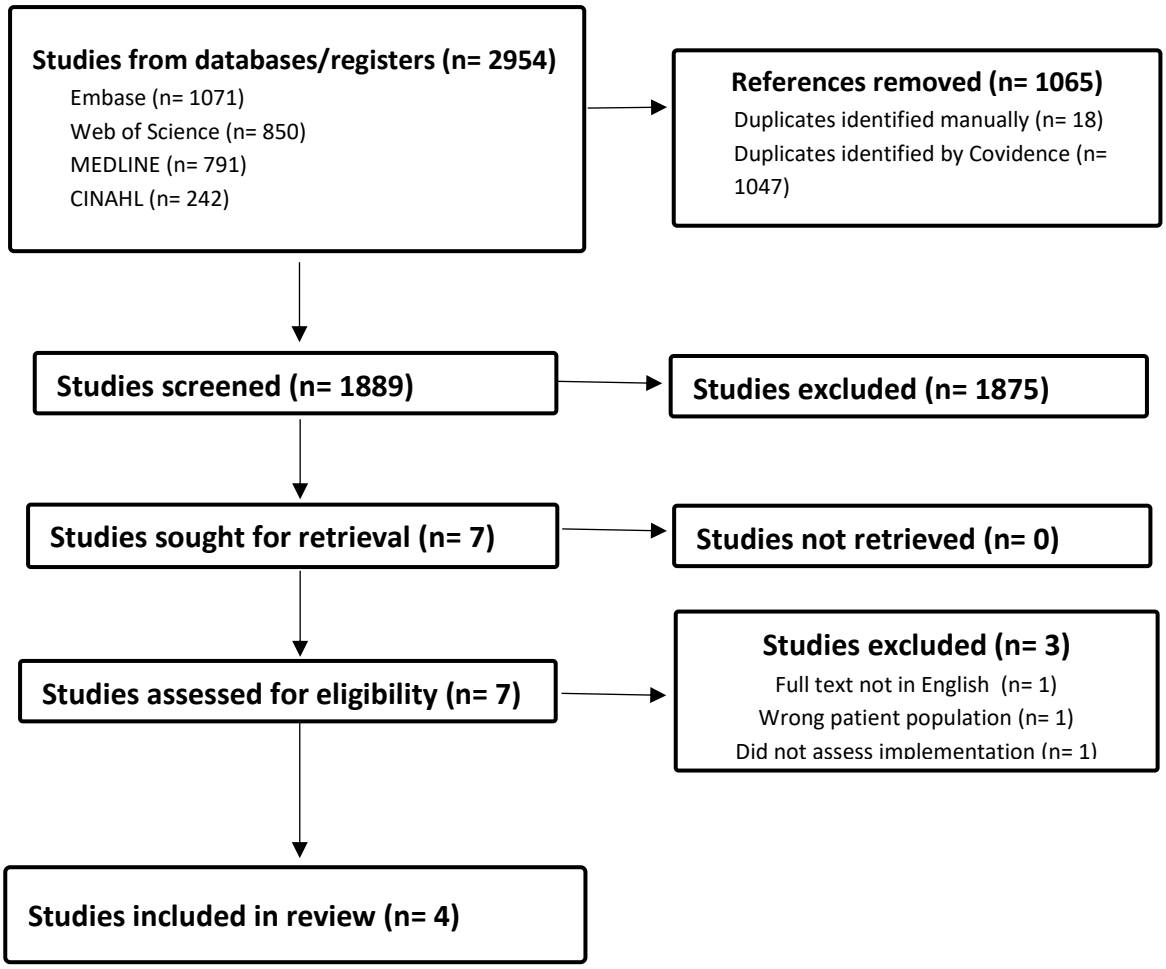

Figure 2. PRISMA diagram.

3.6.2 Study Characteristics

Study characteristics of the four studies included are presented in Table 3. All four studies were conducted in the United States of America; three of the four studies consisted of randomized controlled trials (96-98) and the fourth study was a single arm control trial (99). All studies were published between 2011-2020 (96-99). Sample sizes varied significantly, ranging from 7 to 122 enrolled participants (96-99). Eligibility criteria also differed, only one study exclusively included confirmed BRCA1/2 pathogenic gene variant carriers (98), while the other three studies included 'high risk' participants and included people with genetic mutations such as BRCA1/2 pathogenic gene variants, women identified as high risk through prediction models, or women with significant family history (96, 97, 99).

Study Characteristics

Study	Haley et al. (2020) (96)	Schmitz et al. (2015) (97)	Sturgeon et al. (2017) (98)	Kossman et al. (2011) (99)
Country	USA	USA	USA	USA
Study Design	Randomized controlled trial	Randomized controlled trial	Randomized controlled trial	Single arm intervention
Sample Size (N=)	• 132 enrolled • 43 control group • 44 low dose group • 45 high dose group • 116 completed	• 139 enrolled • 46 control group • 45 low dose group • 48 high dose group • 122 completed	• 35 enrolled • 16 control group • 19 intervention group • 32 completed	• 10 enrolled • 7 completed
Population	Premenopausal women at high risk of breast cancer.	Premenopausal women at high risk for breast cancer with no prior breast cancer diagnosis.	BRCA1/2+ breast cancer survivors who underwent risk-reducing RRSO, who were cancer free at time of study.	Premenopausal women at high risk for breast cancer with no prior breast cancer diagnosis who have not had risk reducing surgery.
Genetic and Risk Profile of sample	The breakdown of how many had confirmed BRCA1/2 pathogenic gene variants is not provided, all participants were considered high risk for breast cancer.	N=49 (35%) participants tested who had positive for BRCA1/2. N= 12 (9%) participants who tested negative for both BRCA pathogenic gene variants N=78 (56%) participants who were not tested for BRCA pathogenic	N=32 (100%) participants tested who had positive for BRCA1/2. Note that only BRCA1/2 carriers were eligible for inclusion.	N=3 (42.9%) participants tested who had positive for BRCA1/2 N= 4 (57.1%) were not tested, 3 had a 50% prior probability of carrying a BRCA pathogenic gene variant, and 1 participant had a 25% probability based on family history.

		gene variants but were considered high risk for breast cancer.		
Study Duration	5 menstrual cycles*	5 menstrual cycles*	12 months	7 menstrual cycles*

Table 3: Study Characteristics *Menstrual cycles were defined as 25–32 days in length. RRSO- risk-reducing salpingo-oophorectomy. The term 'high risk' in these studies included confirmed BRCA1/2 pathogenic gene variant carriers, women with a lifetime breast cancer risk of ≥18% (as determined by Gail or Claus prediction models), and those with a documented deleterious mutation in a relative that conferred a risk of over 25% to the participant.

3.6.3 Risk of Bias, Quality Assessments

An assessment of study quality was included using the MMAT (2018 version). Of the four studies included, two met all five MMAT criteria indicating strong methodological rigour (96, 98). One RCT met four out of the five MMAT criteria, falling short on criterion 2.3 (complete outcome data) (97). While overall follow-up was high (88% across all four studies), key limitations included incomplete hormonal data for four participants which may have impacted internal validity (97). The final study met three out of five MMAT criteria for quantitative descriptive (99). It was limited by a small sample size (n=7), lack of diversity with all participants identifying as Caucasian and no reporting of the characteristics of participants who withdrew (30% attrition) (99). The absence of these details raises the potential for nonresponse bias and limits generalisability. A detailed breakdown of the quality assessments for each study is presented in Table 4 and in Appendix 2. Given the limited pool of eligible studies and exploratory nature of this scoping review, no studies were excluded because of their methodological quality.

Quality Assessment Table According to the MMAT

Category of study designs and MMAT Questions			Haley et al 2020 (96)	Schmitz et al 2015 (97)	Sturgeon at al 2017 (98)	Kossman et al 2011 (99)
Screening Questions	S1	Are there clear research questions?	Yes	Yes	Yes	Yes
	S2	Do the collected data allow to address the research questions?	Yes	Yes	Yes	Yes
Quantitative randomised controlled trials	2.1	Is randomisation appropriately performed?	Yes	Yes	Yes	
	2.2	Are the groups comparable at baseline?	Yes	Yes	Yes	
	2.3	Are there complete outcome data?	Yes	Can't tell	Yes	
	2.4	Are outcome assessors blinded to the intervention provided?	Yes	Yes	Yes	
	2.5	Did the participants adhere to the assigned intervention?	Yes	Yes	Yes	

Quantitative Descriptive	4.1	Is the sampling strategy relevant to address the research question?				Yes
	4.2	Is the sample representative of the target population?				No
	4.3	Are the measurements appropriate?				Yes
	4.4	Is the risk of nonresponse bias low?				No
	4.5	Is the statistical analysis appropriate to answer the research question?				Yes

Table 4: Quality Assessment Table According to the MMAT. This table provides a detailed breakdown of the methodological quality for each included study, with non-relevant cells shaded in light grey.

3.6.4 Programme Characteristics of Included Interventions

The four included studies predominantly focused on physical activity programming, though design and evaluation focus varied (Table 5). Three studies prescribed structured exercise programmes, facilitated through treadmill-based interventions (96, 97, 99). In contrast, the final RCT prescribed a broader online lifestyle modification intervention (98). The latter intervention included strength training, health education, personalised coaching along with financial incentives to reinforce adherence. Notably, only this intervention incorporated lifestyle components beyond physical activity, and none of the reviewed interventions specifically included diet modification as a primary focus. Two RCTs used a dose comparison design, comparing low-dose (150 minutes/week) and high-dose (300 minutes/week) aerobic exercise (96, 97). In terms of primary outcomes, the included studies focused on distinct physiological endpoints. Two trials reviewed examined hormonal changes, including changes in oestrone and oestradiol, as their primary outcomes (97, 99). The study by Haley and colleagues (2020) primarily focused on biomarkers such as CCL2 (C-C motif chemokine ligand 2) and TNF-a (Tumour Necrosis Factor-alpha) which are key markers of inflammation, as their main endpoint (96). The fourth study listed primary endpoints that measured cardiovascular fitness and bone mineral density (98).

Study Interventions and Outcomes

Study	Haley et al. (2020) (96)	Schmitz et al. (2015) (97)	Sturgeon et al. (2017) (98)	Kossman et al. (2011) (99)
Intervention	**Aerobic exercise**: 150 min/week (low dose), 300 min/week (high dose) using treadmills provided to the participants. No other lifestyle components reported.	**Aerobic exercise**: 150 min/week (low dose), 300 min/week (high dose) using treadmills provided to the participants. No other lifestyle components reported.	**3 daily activities**: 160 min/week online progressive strength training + aerobic exercises. Education– reading on health, nutrition, fitness or behaviour change. Habit – completing a new lifestyle habit every two weeks. All participants assigned a level 1 precision nutrition trained female coach to support behaviour change.	**Aerobic exercise**: 45mins/week to 300 min/week at 80-85% max aerobic capacity – using treadmills and heart rate monitors provided to the participants. Certified trainer visited participants homes for the first session of each of the first 5 weeks thereafter participants had the option to attend weekly YMCA exercise classes which none attended. No other lifestyle components reported.
Control group	Maintain normal PA levels, <75 min/week	Advised not to change daily activities	Advised not to change daily activities	N/A
Primary Outcome	Inflammatory biomarkers (ELLA simple plex)	Hormonal changes (AUC for urinary oestrogen)	Cardiovascular fitness (Bruce Protocol) and bone mineral density (DEXA and pQCT).	Hormonal changes (Daily urine collection over menstrual cycles)
Additional measures taken	Physical activity levels (Modified activity questionnaire) Body composition (DEXA)	Physical activity levels (exercise logs and Modified activity questionnaire) Body composition (DEXA)	Physical activity levels (Modified activity questionnaire) Body composition (digital scales and stadiometer)	Physical activity levels (exercise logs) Body composition (DEXA, BMI)

	Cardiopulmonary fitness (Bruce Protocol) Dietary intake (3-day diet log)	Cardiopulmonary fitness (Bruce Protocol, HR monitors) Dietary intake (3-day food log)	Cardiopulmonary fitness (HR monitors) Muscle strength (1RM) Dietary intake (food log)	Cardiopulmonary fitness (Bruce Protocol)
Primary Findings	Aerobic exercise in healthy premenopausal women at high risk for breast cancer dose-dependently increased proinflammatory biomarkers (CCL2, IL-12, and TNF-α), suggesting that reduced breast cancer risk from physical activity may not be mediated by a reduction in inflammation.	Dose-response reduction in oestrogen (estrone and oestradiol) levels due to aerobic exercise in healthy premenopausal women at high risk for breast cancer.	A commercially available web-based lifestyle modification program improved cardiovascular fitness and body composition in BRCA1/2+ breast cancer survivors after risk-reducing salpingo-oophorectomy.	A structured exercise intervention significantly reduced total oestrogen and progesterone exposure, primarily during the luteal phase, while also improving body composition and aerobic fitness in healthy premenopausal women at high risk of breast cancer.

Table 5: Programme interventions and study outcomes. DEXA: Dual-energy X-ray absorptiometry; pQCT: peripheral quantitative computed tomography; AUC: Area under the curve; ELLA: Enzyme-Linked Immunoabsorbent Assay; TNF-a: tumour necrosis factor alpha; CCL2: chemokine (C-C motif) ligand 2; BMI: body mass index; 1RM: one-repetition maximum

3.6.5 Intervention Outcomes

Included studies reported a range of preliminary biological and physiological outcomes relevant to cancer risk and comorbid health conditions.

Inflammatory markers: One RCT evaluated the impact of aerobic exercise on systemic inflammation, a recognised contributor to tumorigenesis (96). This study found that increasing aerobic exercise appeared to increase levels of proinflammatory biomarkers in a dose-dependent manner in high-risk women. The percentage change for TNF-a was a significant increase of 9.51% in the low-dose group and 15.7% in the high-dose group compared to the control group (P=.01 and P< .001, respectively). The change in CCL2 was -0.03% in the low-dose group and 1.54% in the high-dose group. This suggests that the mechanism for reduced breast cancer risk from physical activity may not be mediated by a reduction in inflammation, but rather via a different biological process.

Hormonal markers: Two studies reported that regular aerobic exercise could influence endogenous sex hormones associated with breast cancer (97, 99). The single arm intervention trial reported significant reduction in oestradiol and progesterone levels among premenopausal women after a five-month aerobic exercise intervention, with total oestrogen exposure reduced by 18.9% and total progesterone exposure reduced by 23.7% (99). While the other RCT extended this finding with a dose-response design, showing that for every 100 minutes of exercise there was a 3.6% lower follicular phase oestrogen area under the curve (AUC) (97). These hormonal shifts suggest there is a role for physical activity in modulating cancer-related hormone pathways.

Cardiovascular fitness and bone health: One RCT focused on the dual burden of cardiovascular disease and osteoporosis, common comorbidities following surgical induced menopause. The study reported that the intervention group maintained their cardiovascular fitness level over 12 months, with an average change of 1.1% (± 8.1 %), while the control group had a statistically significant decreased their fitness capacity by -4.0%(± 7.7 %, P = 0.04). Furthermore, the intervention group showed an improved

bone health outcome, as evidenced by a significant difference between groups in the percent change of whole-body bone area, with a change of −0.8% ± 2.5% control and 0.5% ± 1.30% in the intervention. This highlights the broader systemic health benefits of lifestyle intervention (98).

3.6.6 Feasibility and Safety

A constant finding across all four studies was the high programme feasibility for women at increased risk of breast cancer predominantly due to the BRCA1/2 pathogenic gene variant, including those who had undergone risk reducing surgeries (Table 6) (96-99). This positive assessment of feasibility was supported by various indicators including participant adherence, retention and the absence of serious adverse events. Adherence rates were consistently high, generally above 80%. The single arm intervention reported an adherence range from 70-97% with an average of 85% adherence of total prescribed exercise minutes (99), Similarly, two other RCTs reported similar adherence rates from 81-85% for their exercise interventions (96, 97). While the remaining RCT reported an overall adherence rate of 74.8%, broken down as 80% to their exercise intervention, 75% for habit formation and 68% to the education component (98). Participation retention was also generally strong, indicating good acceptability of the interventions. Follow-up rates for the three RCTs were notably high, above 88%, while the single arm intervention had a follow-up rate of 70% (96-99). Crucially, no serious adverse events were reported in any of the studies (96-99). The high adherence rates coupled with the absences of adverse events strongly suggest that both structured exercise and broader lifestyle modification programmes were well tolerated and acceptable within a genetically high-risk population. Interventions were designed and delivered through accessible formats such as home-based equipment or online platforms, further supporting their practicality.

Feasibility and Safety

Study	Haley et al. (2020) (96)	Schmitz et al. (2015) (97)	Sturgeon et al. (2017) (98)	Kossman et al. (2011) (99)
Adherence	>80% of prescribed exercise minutes	>80% of prescribed exercise minutes	74.8% overall programme adherence • 80% exercise component • 75% habit formation • 68% education component	85% of prescribed exercise minutes (Range 70-97%)
Retention Rate	88%	88%	91%	70%
Adverse evens	No adverse events reported	No adverse events reported	No adverse events reported	No adverse events reported

Table 6: Feasibility and safety indicators of included studies. Adherence refers to the percentage of the intervention protocol that participants completed. Retention indicates the percentage of participants who completed the study from initial enrolment.

3.6.7 Behavioural Mechanisms Targeted by Interventions (COM-B Mapping)

While these studies collectively demonstrate the feasibility and potential benefits of lifestyle interventions for women at increased risk of breast cancer predominantly due to the BRCA1/2 pathogenic variant, understanding how and why these interventions drive behaviour change is key for optimising future strategies. The COM-B model provides a useful lens for examining the mechanisms through which these interventions influence participants ability, environment and motivation to adopt and sustain healthy behaviours which potentially mitigate cancer risk (i.e. physical activity and improved nutrition). By mapping these findings to the COM-B framework, we gain valuable insight

into behavioural components that underpin effective lifestyle interventions in genetically high-risk populations. Results of this mapping exercise is summarised in Table 7 and discussed below.

Authors	Haley et al. (2020) (96)	Schmitz et al. (2015) (97)	Sturgeon et al. (2017) (98)	Kossman et al. (2011) (99)
Target Behaviours	Increasing physical activity	Increasing physical activity	Increasing physical activity Improving diet	Increasing physical activity
Intervention Function	● Enablement ● Environmental Restructuring ● Education	● Enablement ● Environmental Restructuring ● Education ● Modelling	● Enablement ● Education ● Training ● Incentivisation	● Enablement ● Environmental Restructuring ● Education ● Training
COM-B Components /Description	**Physical opportunity**: The provision of treadmills enabled participants to engage in regular exercise at home. **Psychological capability**: Weekly telephone-based health coaching, where participants received tailored guidance on increasing PA levels. **Reflective Motivation**: Participants were encouraged to set weekly goals based on prior progress, physical condition and feedback to achieve progressive PA goals.	**Physical opportunity**: The provision of treadmills enabled participants to engage in regular exercise at home. **Psychological Capability:** Information was provided on how aerobic exercise can reduce breast cancer risk increasing participants' knowledge and understanding of the importance of PA. **Reflective Motivation**: Information given framed PA as meaningful and personally relevant to evoke positive feelings about PA and	**Physical opportunity**: Web-based delivery platform, allowing participants access to exercise and nutrition guidance at their convenience. **Psychological capability**: Participants received weekly one to one behaviour changes coaching on fitness, diet, and health. **Physical capability**: Participants engaged in structured exercise and diet changes tailored to their abilities **Reflective Motivation**: Reinforced through weekly coaching feedback,	**Physical opportunity**: The provision of treadmills enabled participants to engage in regular exercise at home. **Psychological Capability**: Targeted by offering training on heart rate monitor use alongside education content to enhance understanding of exercise intensity and its relation to health outcomes. **Reflective Motivation**: Heart rate monitors enabled participants self-monitor to track progress, enhancing motivation through performance feedback.

		strengthen participants' intention to engage. **Social Opportunity**: Group-based exercise settings allowed for peer-support and modelling to promote physical activity.	where progress was reviewed by using self-monitoring logs. **Automatic Motivation**: Financial incentives ($120 reimbursement for 80% adherence) acted as reinforcement, encouraging habit formation.	

Table 7: Intervention characteristics of included studies mapped to COM-B framework.

3.6.7.1 Capability

Physical capability was addressed in one RCT through structured exercise programmes tailored to participants' individual physical abilities (98). The programme accounted for variation in fitness levels and physical limitations, enabling engagement in exercise within a safe and manageable range.

Psychological capability was addressed across all studies through education, training or coaching. Two RCTs provided participants with general health education and information about the benefits of physical activity (96, 97), one in particular included specific information about the potential for aerobic exercise training to reduce breast cancer risk (97). The single arm intervention trial offered training on the use of heart rate monitors to support exercise engagement and self-monitoring (99). Just one RCT incorporated behaviour change-coaching focused on fitness, diet and health knowledge (98). This component aimed to build skills and increase participants ability to engage with the intervention over time.

3.6.7.2 Opportunity

Physical opportunity was enabled in all four studies, primarily through access to equipment or programme delivery platforms that enabled physical activity. Three of the studies provided participants with treadmills to facilitate home-based exercise (96, 97, 99). While the fourth study used a web-based platform to deliver exercise and nutrition guidance which allowed participants to access resources at their convenience (98).

Social opportunity was addressed in one RCT through group-based exercise sessions (97). These group settings provided peer interaction and opportunities for modelling physical activity behaviours within a supportive environment.

3.6.7.3 Motivation

Reflective motivation was supported across all four studies through goal setting, self-monitoring, education and feedback. For instance, in one RCT reflective motivation was supported by encouraging participants to set progressive weekly goals related to physical activity (96). The single arm intervention trial included self-monitoring tools (i.e. heart rate monitors) which allowed participants to track their exercise, providing ongoing performance feedback that reinforced engagement (99). Another RCT provided educational content linking physical activity to breast cancer risk reduction, aiming to influence beliefs above the value of exercise, they also incorporated group-based settings which could offer social modelling and peer reinforcement for adherence (97). One more RCT incorporated behavioural coaching to reinforce benefits of engagement and support continued adherence (98).

Automatic motivation was only addressed in one RCT, where the intervention included a financial incentive (98). Participants received up to $120 for meeting an adherence threshold of 80%, which served as a reinforcement mechanism.

Collectively, these studies demonstrated that various strategies including explicit instruction to meet exercise targets (e.g. 150 minutes of aerobic exercise) and the use of tools like heart rate monitors for tracking progress were employed to enhance reflective motivation. Integrated goal setting and feedback mechanisms to encourage sustained participation. While reflective motivation was widely addressed the systematic incorporation of strategies to foster automatic motivation, such as consistent behavioural nudges or intrinsic rewards beyond financial incentives, remains largely unexplored.

3.7 Discussion

This scoping review provides the first summary of lifestyle interventions in women at increased breast cancer risk, including those with BRCA1/2 pathogenic variants, discussed in the context of a health behaviour change model. Findings suggest that multi-component interventions targeting physical capability (e.g. personalised structured exercise (99) and physical opportunity (e.g. access to equipment or delivery platforms (96-98) show potential in promoting health behaviour change. High adherence rates (typically above 80%) across studies suggest these interventions were acceptable and feasible within this population. However, motivation enhancing strategies varied in design and intensity across studies. Elements such as social modelling (97) self-monitoring and financial incentives (98), were all employed to varying degrees and may have influenced adherence and engagement. The extent to which these motivational mechanisms effectively address barriers to long-term behavioural maintenance will be discussed in greater detail in Chapter 5. Nonetheless, the included studies collectively offer preliminary evidence integrating physical activity and structured behaviour change interventions into care pathways at supporting long-term health outcomes in women with BRCA1/2 pathogenic gene variants.

This review has several strengths and limitations which are acknowledged. A key strength of this review is its application of a behavioural science lens to synthesize findings. The COM-B model offered a systematic framework to explore the drivers of health behaviour change in a high-risk genetic population. Furthermore, the review adhered to PRISMA-ScR guidelines, ensuring methodological transparency.

There are however several limitations including the small number of eligible studies, heterogeneity in intervention design and outcomes, and limited ability to draw conclusions about causality or clinical effectiveness. Additionally, the review was limited to English-language studies and may have missed relevant non-English publications. Acknowledging that not all included studies were exclusively comprised of women with known BRCA pathogenic gene variants and that some were post-cancer diagnosis is a key limitation that adds to the heterogeneity of the population. This was deemed a

necessary trade-off to capture relevant data, as women known pathogenic variants, regardless of their cancer status, likely share a similar psychological burden and face comparable challenges in health behaviour change to those with an elevated breast cancer risk (100).

3.8 Conclusion

This scoping review synthesizes emerging evidence on the role of lifestyle interventions, particularly structured exercise programs, as modifiable risk factors in the context of BRCA-associated cancer prevention. While the current evidence base remains modest in scope and scale, the reviewed studies offer proof-of-concept that aerobic exercise may influence biologically relevant cancer risk markers and is safe, feasible, and acceptable (as inferred from adherence rates) for BRCA pathogenic gene variant gene carriers. The findings of this review will be discussed further in the context of the overall thesis in Chapter Five.

Chapter 4: Understanding the Views of Women with BRCA1/BRCA2 Pathogenic Gene Variants on Lifestyle Choices for Cancer Prevention: A Qualitative Study

4.1 Introduction

Women with BRCA1/2 pathogenic gene variants face a significantly elevated lifetime risk of developing breast and ovarian cancers, often requiring them to make complex decisions regarding screening, prophylactic surgery and lifestyle modification (28, 30, 33, 44). While much of the existing research has focused on clinical outcomes and decision making around risk reducing surgery (33), less is known about how these women experience and navigate their genetic risk in everyday life, particularly in the absence of a cancer diagnosis. This study addresses that gap by exploring the lived experiences, psychosocial impacts and behavioural influences among women with BRCA1/2 pathogenic gene variants. By using qualitative methods rooted in reflexive thematic analysis and guided by the COM-B model of behaviour change, this research provides nuanced insights into the motivators and barriers that shape health related behaviours in this population (101). These findings aim to inform more person-centred interventions and contribute to better patient education and communication strategies. This chapter presents the thematic findings that emerged from focus groups and dyadic interviews, illuminating the diverse experiences and needs of this understudied group.

4.2 Rational for Qualitative Methodology

Qualitative research is an approach focused on understanding the meanings, experiences and perspectives of individuals within their social and cultural contexts (102). Rather than seeking to measure or predict, it aims to explore depth and nuance through methods such as interviews and focus groups (103, 104). This approach was chosen for the current study because it was most appropriate to address the primary research question. While quantitative data from the preceding scoping review highlighted that structured interventions were generally safe and well adhered to, it offered limited insight into the 'why', the deeply personal motivations, psychosocial impacts and

practical barriers that influence health behaviours. By prioritising the participant's voice, a qualitative approach allows for a rich, contextual understanding of these experiences, which is essential for informing the design of person-centred interventions and improving patient education tailored to this specific population (105). Acknowledging the inherent limitations of this methodology, the findings are not intended to be generalisable to the broader population. Instead, they provide in-depth, transferable insights that can inform future research and clinical practice. This methodology is grounded in an interpretivist paradigm, which seeks to understand how individuals make sense of their world and will use reflexive thematic analysis to present themes directly from the participants' narrative (104, 106).

4.3 Objectives

The aim of this qualitative study was to examine how women with known BRCA pathogenic gene variants (but unaffected by cancer) perceive, interpret, and potentially implement the World Cancer Research Fund (WCRF) recommendations for cancer prevention.

Specifically, it seeks to:

1. To explore the lived experiences and psychosocial impacts of BRCA1/2 pathogenic gene variants.
2. To identify the key motivators and barriers to adopting health behaviours, specifically the WCRF cancer prevention recommendations, by women with BRCA1/BRCA2 pathogenic gene variants.
3. To understand the extent to which these women are aware of, understand and implement the WCRF cancer prevention recommendations.

4.4 Methods

Qualitative research is a nuanced and rigorous approach to inquiry that requires careful planning and execution. This section details the methodological choices made to ensure the studies credibility. It outlines the specific steps taken including the research design, participant recruitment and selection,

data collection procedures, and the analytical framework used to interpret the findings. The methods were guided by the principles of reflexive thematic analysis and the COM-B model of behaviour change, providing a structured approach to exploring the complex experiences of women with BRCA pathogenic gene variants.

4.4.1 Design

This study utilised a combination of focus groups and dyadic interviews to explore key themes related to the objectives outlined in section 4.3. Data was analysed using an inductive reflexive thematic analysis to identify emerging patterns (103). Reflexive thematic analysis ensured the participants' subjective experiences were addressed while considering the researchers' biases in data analysis (101). The standards for reporting qualitative research (SRQR) were followed to report the findings of this study (Appendix 3) (107). The GRIPP-SF2 was used to report public patient involvement (Appendix 4) (108).

4.4.2 Participants

Participants were eligible for inclusion if they self-reported a confirmed BRCA1 or BRCA2 pathogenic gene variant, identified as female, were aged 18 years or older and had no personal history of cancer. Individuals were excluded if they did not meet the age, gender or genetic eligibility criteria, had a prior cancer diagnosis or were unable to provide informed consent. The study aimed to recruit a minimum of 10 participants across four focus groups/dyadic interviews. While research suggests that thematic saturation typically occurs within two to three groups, reflexive thematic analysis does not rely on predefined saturation criteria (109). Instead, the final sample is contingent on the perceived quality of data collected.

4.4.3 Participant Recruitment

Participants were recruited through purposeful sampling which was facilitated by gatekeepers (BRCA Ireland co-founder Krista Costello and Marie Keating's BRCA peer group nurse manager Bernadette Carter) who disseminated recruitment posters within their networks. Additional posters were placed

in the family risk clinic at St James Hospital, enabling self-referral. Snowball sampling was later used, where participants were encouraged to share study details within their own networks to reach individuals who may not engage with formal recruitment channels (110). Potential participants were provided with a patient information sheet outlining study objectives, confidentiality policies, and voluntary participation guidelines (Appendix 5). There was no monetary compensation for participants in this study. All participants were informed that participation was voluntary, and they could withdraw at any time up until focus groups had transcribed approximately one month after the groups took place.

4.4.4 Patient and Public Involvement

Patient and public involvement (PPI) refers to the active partnership of patients, caregivers or members of the public in shaping research design, conduct and dissemination, ensuring that studies are relevant, accessible and informed by lived experience. PPI is typically defined as research carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them (111).

PPI was an integral component of this project, providing insights based on personal experiences outside of academic or clinical settings. A patient representative (KC) was consulted during the initial conceptualisation and protocol development phase of the study to ensure that the research question remained relevant and help promote inclusivity. Communication was conducted online via email and zoom call. The patient representative (KC) reviewed and approved recruitment materials and interview schedule, providing feedback on language and tone. Throughout this thesis, the term 'pathogenic gene variant' is consistently used to describe genetic alterations that are known to cause disease, this terminology is specifically chosen for its precision and alignment with modern genetic language. However, in collaboration with the patient representative it was decided that for all patient facing materials, including recruitment posters, consent forms and interview guides, the term 'gene alteration' would be more accessible and appropriate. The patient representative also played an active role in disseminating recruitment posters through their personal networks. To uphold participation

confidentiality and avoid exposure to identifiable data the patient representative was not involved in transcription or coding of interview material. Their contributions enriched the study design and ensured participant facing materials were sensitive to language and communicated the appropriate message.

4.4.5 Development of the Interview Guide

An interview guide was developed to explore lifestyle behaviours, motivators and barriers in cancer preventive behaviours. It also aimed to assess the perceptions of lifestyle recommendations and baseline knowledge about BRCA genes and their associated cancer risk among BRCA1/2 pathogenic gene variant carriers (Appendix 6). The guide was informed by the COM-B model of behaviour change, with questions mapped to the constructs of capability, opportunity and motivation to ensure theoretically grounded exploration of behavioural determinants (as detailed in Table 8). The interview guide was designed, reviewed and piloted in close consultation with the CREST multidisciplinary team and the patient partner collaborating on this project. This team's clinical expertise helped ensure appropriateness and sensitivity. Feedback from the team helped shape the overall scope of inquiry.

Interview guide question	Mapped COM-B component	Mapped Study Objective	Rationale
"Can you share what you know about BRCA genes, and the cancer risks associated with them?"	Capability (Psychological)	To explore lived experiences and psychosocial impacts	Directly assesses the participant's knowledge and understanding of the foundational genetic information relevant to their health.
"Has having a BRCA pathogenic gene variant influenced your lifestyle choices?"	Motivation (Reflective) & Behaviour	To explore lived experiences and psychosocial impacts	Explores how their understanding has translated into an internal drive or decision to change or maintain specific actions.
"What do you think about the role of lifestyle factors—such as diet and exercise—in modifying cancer risk for people with BRCA1/BRCA2 Pathogenic gene variants?"	Capability (Psychological)	To identify key motivators and barriers	Assesses their understanding and beliefs about the efficacy of lifestyle interventions in their specific context.
"How many of you are familiar with the World Cancer Research Fund's cancer prevention guidelines?"	Capability (Psychological)	To identify key motivators and barriers	Direct assessment of their awareness and knowledge of specific, evidence-based guidelines.
"What specific recommendations from these guidelines do you think are most important for	Capability (Psychological)	To identify key motivators and barriers	Explores their interpretation, prioritisation, and perceived relevance of the guidelines, indicating their cognitive processing and understanding.

women with BRCA1/BRCA2 pathogenic gene variants?"			
" What do you believe a typical healthy diet looks like?"	Capability (Psychological)	To explore lived experiences and psychosocial impacts	Assesses their knowledge and conceptual understanding of healthy eating.
"Are there any specific foods/food groups or supplements you personally avoid or include for health reasons?""	Behaviour & Motivation (Reflective)	To identify key motivators and barriers	Captures their actual practices and the underlying personal beliefs or reasons driving those choices.
"How about physical activity? What would you consider a physically active lifestyle?"	Capability (Psychological)	To identify key motivators and barriers	Assesses their knowledge and conceptual understanding of physical activity.
"How often do you think people should engage in physical activities like walking, sports, or more formal exercise	Capability (Psychological)	To identify key motivators and barriers	Explores their knowledge of recommended frequencies or intensity for physical activity.
"Do you drink alcohol? What do you consider a reasonable amount of alcohol consumption?"	Behaviour & Capability (Psychological)	To explore lived experiences and psychosocial impacts	Captures current behaviour and their understanding of safe consumption levels.
"Has the idea of cancer prevention ever made you think about reducing alcohol? Why or why not?""	Motivation (Reflective)	To identify key motivators and barriers	Directly asks about the influence of a health goal (cancer prevention) on their decision-making and intentions regarding alcohol consumption.

"Do any of you smoke/vape or have you ever smoked/vaped?"	Behaviour	To explore lived experiences and psychosocial impacts	Gathers information on current or past engagement in these behaviours.
"What do you believe the impact of smoking/vaping is?""	Capability (Psychological) & Motivation (Reflective	To identify key motivators and barriers	Assesses their knowledge of the health impacts and their beliefs about the consequences, which can drive motivation.
"Are there any other health practices or routines you follow specifically because of your BRCA+ gene test result	Behaviour	To explore lived experiences and psychosocial impacts	Identifies other specific actions taken in response to their genetic status.
"How did you decide to include these habits or routines in your lifestyle?"	Motivation (Reflective)	To explore lived experiences and psychosocial impacts	Explores the decision-making process, values, and reasons behind adopting these specific behaviours.
"What motivates you to follow or not follow a healthy lifestyle / cancer prevention recommendation?"	Motivation (Reflective & Automatic)	To identify key motivators and barriers	This is a direct question about their internal drivers and inhibitors, covering both deliberate plans/evaluations and more automatic impulses/habits.
"What challenges or barriers have you encountered in trying to follow the World Cancer Research Fund guidelines?"	Opportunity (Physical & Social), Capability (Psychological &	To identify key motivators and barriers	This is a broad question designed to uncover obstacles across all COM-B domains.

	Physical), Motivation (Reflective & Automatic)		
"Are there specific social, financial, or personal obstacles that make it more difficult to follow these guidelines?""	Opportunity (Social & Physical), Motivation (Reflective	To identify key motivators and barriers	Explicitly probes for external (social, financial) and internal (personal obstacles like self-efficacy, competing priorities) barriers.
"What kind of information or support would you find most useful in managing your cancer risk?"	Capability (Psychological) & Opportunity (Social/Physical)	To identify key motivators and barriers	Identifies perceived gaps in knowledge/skills and desired external resources or assistance.
"Are there any areas, such as diet, exercise, or mental health, where you feel like you could use more guidance?""	Capability (Psychological)	To identify key motivators and barriers	Pinpoints specific areas where they feel a lack of knowledge or skills, indicating a need for capability-building interventions.
"If you could design a lifestyle support program specifically for women with pathogenic gene variants in BRCA1/BRCA2 genes, what would it look like?"	Opportunity (Social/Physical) & Capability (Psychological)	To identify key motivators and barriers	Explores their ideal external support structures and resources, and implicitly what kind of learning or skill-building components they would value.
"How would you prefer to receive this information, through workshops, online resources, or one-on-one counselling?"	Opportunity (Physical/Social)	To identify key motivators and barriers	Focuses on the preferred channels and modes of delivery for support and information, which are aspects of physical or social opportunity.

Table 8: Interview Questions Mapped to (C)apability (O)pportunity (M)otivation-(B)ehaviour and Study Objectives. This table outlines the interview guide questions and their corresponding COM-B components, demonstrating how the guide was systematically developed to address the study's objectives

4.4.6 Data Collection and Management

Focus groups and dyadic interviews were facilitated by the lead researcher OC, with the thesis supervisor EG serving as an observer, providing field notes (Appendix 7) and providing feedback to ensure methodological rigor and consistency. To optimise attendance and accommodate participant preference, focus groups were conducted in person at the Trinity Centre for Health Sciences and virtually via TCD-licensed Microsoft Teams (registered to EG). No participants were known to either OC or EG.

Audio files, recorded via Microsoft Teams, were transcribed initially by Microsoft teams build in artificial intelligence (AI) software, and then checked and transcribed verbatim by the lead researcher (OC). Any errors were omitted or corrected. Any identifiable information was then pseudonymised to maintain participant confidentiality. The final transcripts were then imported to NVivo 14, a qualitative data management software and double checked for accuracy before coding.

4.4.7 Ethical Considerations

Ethical approval for this study was obtained from the Faculty of Health Sciences Research Ethics Committee on February 20th, 2025 (Approval No. 250106) (Appendix 8). In addition to ethical approval, a data impact assessment (DPIA) was completed and finalised on March 14th, 2025, to ensure compliance with data protection and privacy regulations (Appendix 9). To ensure ethical integrity, all participants received a detailed information sheet outlining the study's purpose, procedures, voluntary participation, and withdrawal options (Appendix 5). Informed consent was obtained in writing before participation (Appendix 10), and all data was stored securely using TCD licensed SharePoint, with access restricted to the lead researcher (OC).

4.4.8 Data Analysis

Reflective thematic analysis (RTA) was conducted using an iterative approach, allowing a flexible and adaptive method (101). RTA involves a six-step process which allows flexibility while still allowing the researcher to be systematic and rigorous, the six phases of the reflexive thematic analysis are outlined in Table 9, with an overview of how these phases were followed within this study (106). The study adopted a bottom-up, inductive approach, allowing for themes to arise naturally instead of relying on predefined themes.

The six step process of thematic analysis as proposed by Braun & Clarke, and how these were adhered to within this study	
Step 1: Become familiar with the data	The lead researcher (OC) conducted all focus groups/dyadic interviews with all 11 participants. Following each session, she used the Microsoft teams AI transcriptions as a starting point and from there conducted a thorough verbatim transcription, allowing for initial understanding of the data collected. The lead research then read the final transcripts multiple times prior to analysis to further familiarise the data.
Step 2: Generate initial codes	Both the lead researcher and the second coder (DC) used NVIVO14 software to code data into codes and subcodes separately to allow for a deeper interpretation of the data. The second coder had prior experience in thematic analysis and had conducted research with this study population which gave her insights into key concepts.
Step 3: Search for themes	The lead researcher and second coder met to discuss codes and establish initial overarching themes. Through subsequent discussions both the lead researcher and the second coder agreed on two overarching themes which best represented the data.
Step 4: Review themes	These themes were then discussed with the research supervisor who attended the focus groups as an observer.
Step 5: Define themes	The lead researcher then spent some time defining and naming each theme to best represent the essence of what was discussed during the focus groups and dyadic interviews.
Step 6: Write up	The lead researcher conducted the write up phase in stages, defining each theme identified, contextualising each theme and subtheme, then supporting each one with relevant participant quotes.

Table 9: Steps 1-6 of reflexive thematic analysis

4.4.9 Limitations and Reflexivity

To enhance academic rigor and mitigate potential researcher bias, reflexivity was embedded into the analytical framework. The lead researcher (OC), a senior oncology physiotherapist, had direct clinical experience working with women with BRCA pathogenic gene variants, this facilitated deep understanding of physical and practical challenges faced by the participants and fostered rapport. However, this clinical familiarity also introduced the potential for pre-existing assumptions or an overemphasis on physical and rehabilitation related aspects of lifestyle. To actively mitigate this bias and strengthen analytical credibility, a second independent coder (DC), a PhD student with a background in health psychology, contributed to data interpretation. Her strong theoretical lens in health behaviour complemented the primary researcher clinical perspectives, and her previous work, completing a master's thesis involving the same cohort of women, further enriched the analysis. This dual-coding approach, supported by iterative discussions and consensus-building sessions, allowed for the negotiation of diverse interpretations and strengthened the credibility of the thematic findings. Additionally, strategies such as peer debriefing were employed to enhance credibility and minimise interpretation subjectivity. The potential for volunteer bias is acknowledged due to the self-selected nature of recruitment, and to uphold participant confidentiality and foster a safe environment for open participant all data was pseudonymisation and stored securely.

4.5 Results

Data collection was conducted between 15th April - 6th May 2025, fourteen patients contacted the research team expressing interest in joining the study. Following eligibility screening, two did not meet inclusion criteria due to having a prior cancer diagnosis and another was unavailable to attend their scheduled focus group time due to other life commitments. Three focus groups and one dyadic

interview were conducted. Demographic characteristics are presented in Table 10. The four sessions lasted between 50–75 minutes, with an average duration of 59 minutes.

Characteristics	Categories / Summary (N=11)
BRCA genotype	
BRCA1	4 (36.4%)
BRCA2	7 (63.6%)
Age (years)	Mean 43.5 (SD 6.04) years Range 34-52 years
Risk Reducing Mastectomy	
Yes	7 (63.6%)
No	4 (36.4%)
Risk Reducing Salpingo-oophorectomy	
Yes	6 (54.5%)
No	5 (45.5%)
Highest level of education	
High School*	1 (9%)
Undergraduate	3 (27.4%)
Postgraduate	7 (63.6%)
Provance of residence	
Munster	3 (27.4%)
Leinster	6 (54.5%)
Connaught	2 (18.1%)
Marital status	
Married	5 (45.5%)
Single	5 (45.5%)
Divorced	1 (9%)
Children	
Yes	7 (63.6%)
No	4 (36.4%)
Age at BRCA gene testing confirmation (years)	Mean 40.5 (SD 6.6) years Range 30-49 years

Table 10: Key Demographic Characteristics. Continuous level data are presented as mean (standard deviation). Categorical data are presented as frequency (percentage). SD: Standard deviation.

*One participant reported 'high school' as their highest level of education.

4.6 Thematic Analysis

Analysis of the data generated two overarching themes with three and four subthemes each. The interview guide as presented in Table 8, was underpinned by both the objectives of the study and the COM-B model, aiming to focus on lifestyle behaviours in the context of cancer risk management. Interestingly, in all focus groups and didactic interviews, surgical risk reduction was the predominant discussion point, and participants naturally discussed lifestyle factors in the context of their surgery. Therefore, the results presented below place considerable emphasis on surgical risk reduction. All codes, subthemes and themes for the results are presented in Appendix 11.

4.6.1 Theme one. Challenges in Accessing and Interpreting Information: The BRCA1 and BRCA2 Experience

This theme highlights the challenges women with BRCA1 and BRCA2 pathogenic gene variants face in accessing and interpreting information in relation to both the medical management of their risk and how they can manage their risk more broadly through lifestyle. Participants reported difficulties in understanding medical terminology and obtaining clear guidance on risk-reducing surgery, leading to uncertainty about their choices. Participants relied heavily on online and peer support networks and charities, seeking accessible and trustworthy information outside formal healthcare settings. This theme consists of three subthemes as depicted in Figure 3.

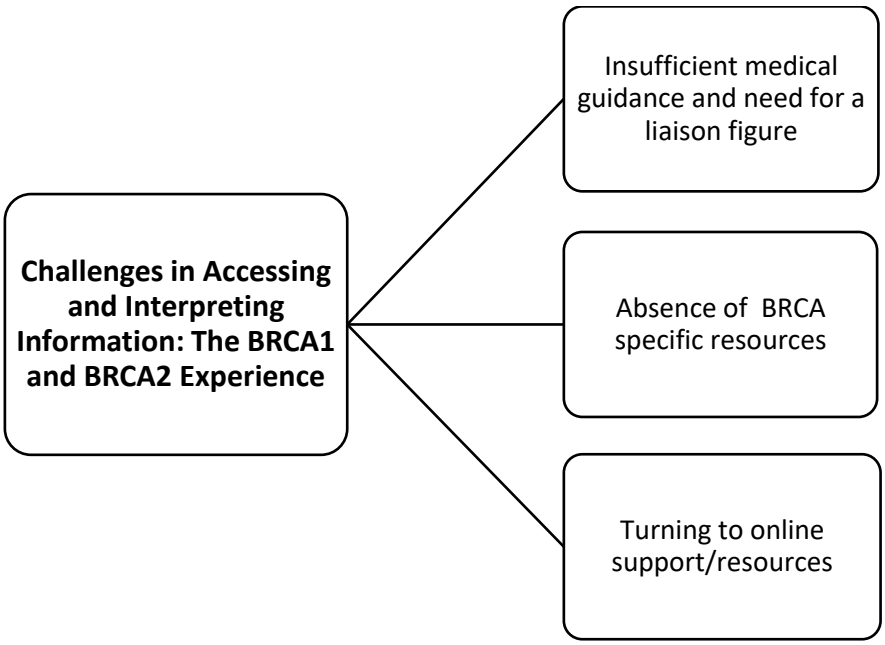

Figure 3. Theme one with associated sub-themes.

4.6.1.1 Subtheme one: Insufficient Medical Guidance and the Need for a Liaison Figure

Participants reported inconsistencies in the medical advice that they received with information, particularly regarding risk-reducing surgery, varying from one healthcare professional to another. The lack of standardised guidance created confusion with many reporting their choices related to risk reducing surgery were guided by their doctor's preference. Many expressed frustrations at the absence of a clear pathway for BRCA1 and BRCA2 pathogenic gene variant carriers. A strong need for a dedicated liaison figure was identified with participants advocating for a centralised medical professional or service that could provide consistent, evidence-based information. Many participants felt their surgical decisions were dictated by medical preference and scheduling constraints, rather than being guided by their personal needs. One Participant reported her experience discussing options with her surgeon:

'It was just assumed that especially because I didn't have cancer, that if I'm going in for risk reducing that that's just it's a double mastectomy reconstruction with implants. I had done my research, so I knew there was the option to do the DIEP. But I went into the appointment to discuss you know the

pros and cons of either of those, it just wasn't even really a discussion. It was kind of like, well, if you do choose that option, it's a much bigger surgery. It's a much longer surgery. And the thing that they really pushed was if you're going for that, you will have a much longer waiting time. And for me, I just wanted the surgeries because I didn't want to feel like a ticking time bomb' - (P12 FG4)

Similarly, another participant reflected on the lack of discussion around surgical options, emphasising how reconstruction was assumed as the default choice:

'*In terms of the consultant, neither the plastic or the general consultant gave me, or didn't outline all the options in terms of surgery like. In terms of you know it was assumed I was going for reconstruction', 'No, no, no, no. You know, it was like you're a woman. No, no, no. You shouldn't be going flat like. I just think that his dismissal of me really impacted me, and I know I am in a case where I've kind of opted for reconstruction and I don't really want it'* - (P6 FG4)

Many other participants also expressed similar events, that surgeon's personal preference and availability led to their risk reducing surgery choice. The 'disjointed' system was described by one participant:

'it's been very disjointed, like when we'll say initially when I got all these different consultants, different disciplines, appointments I was under the impression that it was up to me as to whether I do the top half surgery first or the lower, in fact, and I spent ages trying to figure out, you know, doing my own research going, which is the most likely to be the one to cause cancer first, which I should never be put in that position. In fact, what's after happening is it's the surgeon's diary which has dictated the surgery.' - (P6 FG4)

'*I saw the consultant he was like, well, I recommend you go for hysterectomy and that took me aback because I was like, I didn't even know it was going to be that extreme, and he was like; you don't have to. You can just have your ovaries and fallopian tubes out. You don't have to have a*

hysterectomy, but that's my recommendation, and it's just more straightforward and if it was my wife, that's what I'd tell her to do.'- (P13 FG4)

The need for a clear pathway and/or liaison figure to help navigate medical jargon, presurgical decisions and post-surgical complications was highlighted by many of the participants. Medical jargon and word framing was reported by many as an issue in accessing reliable information:

'I took upon myself all this research, which didn't mean anything to me, this was way too medical for me to be. I needed better guidance on it.' - (P13 FG4)

The breast surgery nurses service, well established to support women having breast surgery for cancer, also provided support to those having prophylactic mastectomy and was highlighted as an excellent resource. However, many of the participants felt that a BRCA specific service would be more useful as there is a mismatch between the risk reducing breast surgery and risk reducing gynae surgery follow up care:

'*The breast care nurses were outstanding for me in terms of practical support, emotional support. And there was a real difference between getting that support on the breast side and then nothing on the kind after the oophorectomy and stuff.'* - (P12 FG4)

The appreciation for the breast care nurses led service was affirmed by another participant:

'Those breast care nurses are brilliant. And they were the ones at your bedside when you were in tears after it and in shock and in trauma. You know, not the consultant. The consultant comes in for, like, 60 seconds and goes again. But so, something like that, I guess might. But female led I think, you know, I think that is important because they get it.' - (P13 FG4)

A clear need for a specific BRCA liaison figure was voiced by many of the participants:

'I just think having like a nurse type liaison officer or somebody that you can talk to and guide you and steer you in like, OK, you know, let's get a push on with the this or lets you know just to run things by, but particularly someone who has, yeah like knowledge and qualification or whatever in those areas (both breast and ovarian) to support women I think is actually vital, yeah.' - (P12 FG4)

'*You know, you have no one to bounce those questions off.*' - (P5 FG4)

This was reaffirmed by another participant who highlighted the lack of knowledge by general practitioners to support women going through risk reducing surgery.

'I just had the surgery and went home and had to deal with the surgical menopause and hot flushes and all this stuff, it was traumatic for me, you know, at 36 and like, there's no follow up nobody there. Like, you're discharged now from gynaecology. I talked to my GP, who is amazing, but she was like this out of my kind of scope of expertise.' - (P12 FG4)

These findings reinforce the need for a standardised, patient-centred approach in BRCA care. Participants emphasised the importance of establishing a dedicated liaison figure, improving interdisciplinary coordination between breast and gynaecological surgery, and ensuring clear presurgical guidance and structured post-surgical support.

4.6.1.2 Subtheme two: Absence of BRCA Specific Resources

Participants reported that all the information provided to them following their BRCA pathogenic gene variant confirmation was generic in nature. Many stated that they received only broad public health resources or nonspecific links. Several of the participants emphasised a preference for in person guidance or peer-based conversations. Several participants noted that more practical detail about

what constitutes a 'healthy diet' would be valuable particularly for those unsure how to translate vague advice into daily habits:

'I think more information even around foods and things like, you know, people probably think overall a healthy diet. But like what that looks like, you know that kind of stuff would be helpful you know.' - (P7 FG2)

The disconnect between diagnosis and tailored guidance often left participants feeling unseen by the healthcare system, compounded for those navigating care in more rural areas:

'I went to my GP with my letter, and I live in a small town in [Rural Ireland]. I mean, she knew what BRCA was, but she'd never in her 25 years seen a person with BRCA. So, she was asking me, what do you want me to do.' - (F1 P2)

A recurrent identity issue emerged with participants feeling excluded from cancer services while carrying the burden of having an increased inherited cancer risk and therefore were not like the general population:

'*I think probably in my earlier years of having it like I used to, nearly like when I was going to James's nearly felt like you were taking time away from people that actually had cancer and nearly apologising for being there*.' - (P7 FG2)

'*I didn't join anything before because I was like, oh, well, I don't technically have cancer*.' – (P9 FG2)

Others called for more visibility and recognition of those with BRCA pathogenic gene variants within the healthcare system:

'I think it will be great to have a specific BRCA, or I don't know or 'other' maybe cancer section because we're still like both, like were saying we're still part of the cancer model, you know, and we just don't fit in.' - (P2 FG1)

These reflections suggest that tailored information isn't just about clarity it's also about validation. For participants, better education strategies would help close the gap between lived experience and meaningful action.

4.6.1.3 Subtheme three: Turning to Online Support/Resources

Participants frequently expressed that the lack of centralised, BRCA specific guidance, particularly around lifestyle behaviours and cancer risk reduction, often led them to rely on online research, peer support groups and social media as a means of getting information. While these resources provided community driven insights, many felt that self-directed research was insufficient and often resulted in conflicting advice, and significant uncertainty and emotional burden.

Several participants described how they relied on Google searches and independent research to stay informed about BRCA-related treatments:

'I do sort of every now and again it's just Google really just go in and see are there any new studies and then I go to the Marie Keating BRCA seminar, and you get lots of information there and just keep your ears open yeah.' - (P11 FG3)

Others noted that despite their proactive efforts, they frequently encountered contradictory findings, making it difficult to determine which information is reliable:

'I find you have to do a lot of research yourself, you know, and then you get conflicting, you know, results.' - (P2 FG1)

Participants emphasised that being left to navigate complex medical information independently contributed to feelings of uncertainty and lack of support:

'Yeah, you are left to your own devices, and it would be good to see that changed.' - (P11 FG3)

While charities such as the Marie Keating Foundation played an important role in supporting women with BRCA pathogenic gene variants, participants noted that these organisations were not exclusively focused on BRCA leading to gaps in specialised support:

'*There's no kind of one place that that isn't a charity that you can go to get proper, reliable kind of facts and stuff that I feel it's lacking*.' - (P12 FG4)

The mental health impact of the peer-led meetings by charity organisations was described as valuable by many participants:

'*Meeting other women that had come through the other side and their lives weren't over was really like a big thing for me*.' - (P12 FG4)

'*Talking to other people who are going through the same thing as you, is really, really important*.' - (P9 FG2).

But there was a strong feeling amongst participants that charities should not be relied upon for mental health support:

'*So again, that reliance on charity. I just think that shouldn't be down to charities like I think there should be, just to have the availability of some kind of mental health support when you have been given something like the news that you have a BRCA gene. I think that should be a standard given you know*.' - (P12 FG4)

Participants heavily depended on online peer groups for emotional reassurance and practical advice. Although the groups provided a sense of community, some participants noted that they only accessed or found out about these groups after going through their risk reducing surgeries:

'*I had already gone through all my operations, and I could see people about to go through theirs asking for advice, we would all give it. I would have loved that before my operation, I had no one*.' - (P9 FG2)

Others reinforced the importance of one to one counselling or structured workshops to complement online groups:

'*A workshop, online resources, or one-to-one counselling would be helpful. Everything and anything that can be done with support groups helps*.' - (P9 FG2)

Due to lack of BRCA specific formal healthcare resources, many participants turned to social media groups to BRCA-related guidance:

'*Most of the research I've done is through joining groups on Facebook or Instagram and learning from people who have the same problem*.' - (P3 FG1)

However, some questioned the reliability of medical advice shared in online spaces, expressing concern over self-interpreted information and difficulty of verifying sources:

'*Not that everyone's operation will go exactly the same or whatever, but it definitely the support of a group is amazing, who are going through and have the same, is so much different, and you need the one-on-one because you can really feel different to another person or might be going through things differently*.' - (P9 FG2)

Feeling misunderstood by the public, particularly regarding their decision to undergo preventative surgeries was also highlighted by one participant:

'*People thought it was like a free boob job, so that wasn't very helpful*.'- (P7 FG2)

The same participant also noted that society's lack of awareness of BRCA led to stigmatisation and dismissive attitudes towards preventative healthcare choices:

'*People don't really understand why you would do that when you didn't have cancer, even though your risk was very high*." - (P7 FG2)

The absence of structured BRCA specific medical guidance led to participants to rely heavily on online resources, peer support groups and social media. While these platforms provided community driven insights, many of the participants acknowledged that information was not sufficient and advocated for a service which integrated structured peer and professional support with reliable evidence based medical information which would reduce the need for self-navigation through fragmented online resources.

4.6.2 Theme two: Drivers of Behaviour change

This theme explores the key factors influencing behaviour change among BRCA1 and BRCA2 pathogenic gene variant carriers, particularly in relation to engaging in a healthy lifestyle, it consists of four subthemes as depicted in Figure 4. Many participants described how their long-term outlook shaped their willingness to engage in lifestyle behaviours, empathising the role of risk-reducing surgeries as a motivator for change. Social circumstances also played a pivotal role, with participants frequently citing life events, family responsibilities and peer influences as both facilitators and barriers to change. Additionally, the psychological impact of the BRCA and the desire for control emerged as a

significant driver in decision making. Together these elements illustrate how personal, social and emotional factors intersect to shape behavioural responses.

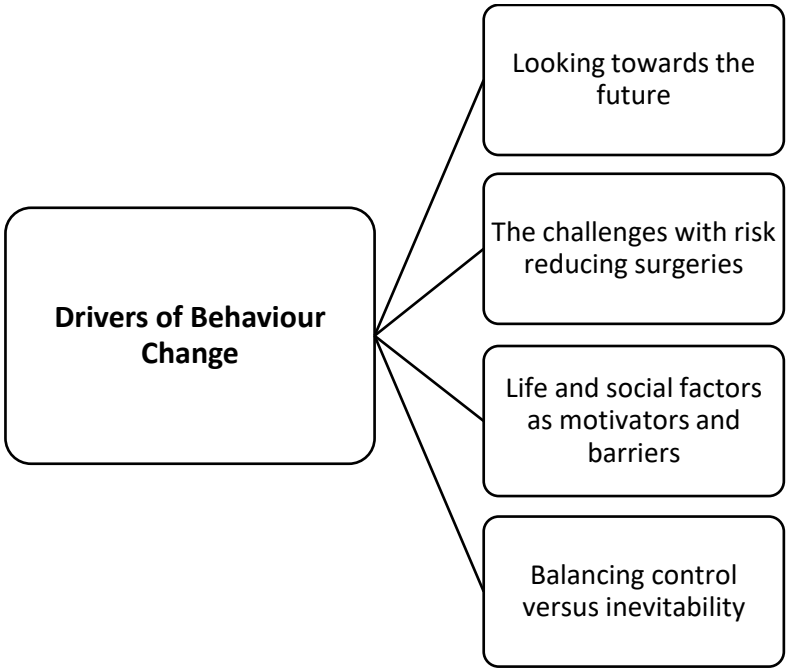

Figure 4. Theme two with associated sub-themes.

4.6.2.1 Subtheme one: Looking towards the future

Participants frequently emphasised the importance of future focused thinking in their decisions, particularly regarding longevity, the perceived value of health investment and surgical planning. Many describe their motivations for adopting health-conscious behaviour focusing on long-term well-being, quality of life and maintaining mobility as they age. For many participants the desire to stay healthy for loved ones was a key motivator for lifestyle changes:

'*I want to stay as healthy as long as I can for him (Son).*' - (P3 FG1)

Others framed their health goals in terms of life expectancy and generational differences, expressing commitment to living longer than their parents and remaining active in later years:

'To live longer than my parents, really. Just to be able to see my grandchildren, that's my aim.' - (P11 FG3)

'*To have a good quality of life, especially when I'm a little bit older.*' - (P4 FG1)

Many of the participants spoke about maintaining physical strength and focus on ageing well:

'I think just to feel good, you know, and longevity. So, you know, growing older in a sustainable, healthy way.' - (P13 FG4)

'*It's the motivation of feeling good and feeling strong and thinking long term as well like if you know not just living a long life but just actually being as mobile and healthy as possible*.'- (P12 FG4)

Beyond general wellness, participants discussed strategies to prepare for surgical intervention aimed at reducing cancer risk and promoting long-term health:

'*Before the operation, she'd (holistic therapist) do certain things and give me ideas on taking certain supplements to try and build myself up beforehand*.' - (P9 FG2)

Many acknowledged that once they committed to risk-reducing surgeries, they felt a responsibility to fully embrace other health behaviours:

'*If you're going to do it, you have to do it all the way, there's no point in smoking and drinking after making that sacrifice.'* - (P9 FG2)

4.6.2.2 Subtheme two: The challenges with Risk reducing surgeries

Participants described how undergoing risk-reducing surgery was a pivotal moment in their lives. While surgery provided a sense of control over cancer risk, it also came with profound physical, emotional and psychological consequences. Many described their surgery as a turning point that pushed them to adopt healthier lifestyle habits, including nutrition, physical activity and overall self-care. Participants frequently highlighted the mental strain associated with surgery. While some expected to feel immediate relief, they found that anxiety about future health risks persisted:

'*You think when you do all your surgeries, you're just going to wake up and go, 'That's great, it's done, now I can get on with life.' But it's not like that at all*.' - (P2 FG1)

For many participants, surgery prompted a renewed focus on health behaviours reinforcing the need to maintain a strong physical health post-surgery:

'If I hadn't done the surgeries, I don't know if I would be thinking this way or making these changes, but surgery definitely spurred all of that on.' - (P12 FG4)

Participants also described a greater awareness of surgical induced menopause, motivating them to take proactive steps towards bone health and strength training:

'*Going through surgical menopause in my 30s made me much more health conscious. I track my bone density, go to the gym, and do strength training because I know how important it is*.' - (P12 FG4)

Some emphasised the holistic approach they adopted following surgery, ensuring their diet supported their recovery:

'*Since surgery, I've been more focused on getting a balanced diet, protein, fats, carbs, and fibre, because I know my body needs it*.' - (P5 FG4)

While surgery was empowering for many, participants also faced complications and setbacks that affected their ability to maintain an active lifestyle. One participant reported:

'*I spent the last couple of years going through surgeries, stuck in the hospital, unable to move much, and completely drained of energy*.' - (P12 FG4)

This was reiterated by another participant who had her risk reducing surgery more recently:

'*I'm not very physically active at the moment because yeah the complications with the surgeries*. - (P9 FG2)

Several individuals experienced significant post op surgical complications, including infections, MRSA and repeated hospitalisations:

'*Especially with all the operations and having, you know, I've had a lot of as I said every-one of my operations has gone wrong and when I had the ovaries, fallopian tubes, everything I got a bad infection and was in hospital for two weeks. During one of my breast operations contracted MRSA went through hell with that*.' - (P9 FG2)

These challenges impacted their ability to engage in exercise and other healthy lifestyle behaviours with the same participant reporting feeling physically limited due to ongoing recovery issues:

'*I haven't been able to carry on my usual. I used to do yoga, Pilates, and different things. But because I've been going through double mastectomies, and everything went wrong. And I'm still 6/7 operations later and I've got expanders in, so I still must get the implants in later*.' - (P9 FG2)

While many participants adopted health-conscious behaviours, some questioned whether lifestyle alone was enough to mitigate their genetic predisposition:

'*Like if you were leading an unhealthy lifestyle and overweight and someone was like, well, you know, maybe if you change your diets and exercise a bit more you might just be like, sure, I could get cancer anyway, I have this gene.*' - (P7 FG2)

'*So, I think you know lifestyle definitely has a role yeah, but I think yeah, for when you have a genetic disposition it's the mental, the mental side of it that it's the stress and the worry really that's the trying to calm that and manage that*.' - (P2 FG1)

Others acknowledged that while diet and exercise are important, risk reducing surgery was necessary to effectively lower cancer risk:

'*I don't think when the percentages and the risks are so high with BRCA like I don't think that just doing all those things is definitely going to be enough. Without kind of the risk reducing surgeries, especially as you get a little bit older. But equally I think it's important to follow all those guidelines anyway just for overall risk of all cancers, I guess*.' - (P12 FG4)

For many their focus on nutrition and exercise was more about general wellbeing rather than BRCA specific prevention:

'I'm really trying to eat more Whole Foods and avoid processed foods but that's more for my general health than, you know, the fact that I have a BRCA status.' - (P7 FG2)

4.6.2.3 Subtheme three: Life and Social Factors as Motivators and Barriers.

Participants spoke about the day-to-day realities that influence their ability to engage with lifestyle recommendations. Rather than a simple matter of motivation or knowledge, behaviours were shaped by a combination of time constraints, caregiving responsibilities, financial limitations and preexisting health conditions. This subtheme illustrates how personal circumstances act as significant barriers or facilitators to change.

Struggling to find time, amidst demanding roles as mothers, caregivers and full-time workers was highlighted repeatedly. Many participants shared that time scarcity, not lack of knowledge or intent, was the primary barrier to maintaining healthy habits:

'I'm a full-time mom, if you're working full time and then you're trying to do something for yourself. It's just that sometimes you have to pick and mostly I'm picking my son who needs more than myself.' *- (P3 FG1)*

'But like, who has the time? You know, people are sitting in a 2-hour kind of traffic every day (commuting to and from work) so like who has time for that.' - (P4 FG3)

These competing demands which often included parenting and caring for aging relatives left little space for planning and prioritising physical activity or meal preparation:

'*We'll say like over the bank holiday weekend now I spend most of the time caring for my mother. I was in and out of hospitals, you know, that's outside having a job, having children, having other health issues is just that's my barrier*.' - (P6 FG4)

However, for some, time became a facilitator, particularly when life circumstances shifted:

'The youngest (Child) went to secondary school and now I have loads of time. Yeah. When they were small it was really difficult like you'd feel frustrated because, you know, I should be trying to do this, but I just don't have time.'- (P11 FG3)

Planning or lack of it, also emerged as a practical barrier, highlighting the importance of routine and structure in facilitating behaviour change. One participant highlighted the domino effect of poor planning:

'If you have a good weekend and you're not around then that feeds into the week. If you haven't done your planning for your food or decided like when you're going to do things because you must plan but you have other people to consider.' - (P1 FG1)

Financial barriers were prominent, particularly in accessing nutritious food and structured exercise, although many valued the benefits of healthy living, they acknowledged that cost impacts their choices in sustainability of habits:

'*To eat really well in this country costs a lot of money and it's cheaper to eat a poorer diet and it should actually be the other way round*.' - (P4 FG3)

'*Well, the exercise classes I've chosen or the ones I'm doing are actually very expensive, but I won't do it forever*.' - (P11 FG3)

Participants' motivation for adopting healthy lifestyles often extended beyond BRCA related cancer risk, reflecting broader concerns about personal values, pre-existing health conditions and overall wellbeing. Some shared how managing conditions like high cholesterol and celiac disease already

made them health conscious. For others cancer prevention was one of many health considerations, but not specifically tied to their BRCA status:

'*It's not just this BRCA. No, it's. I'm more worried about lung cancer. Really. And bowel cancer and yeah. I never really think of the link as much but, I more think of lung, but in general it's just such an increased risk of all cancers I suppose*.' - (P11 FG3)

These perspectives illustrate that lifestyle decisions were often multifactorial rather than a narrow focus on genetic predisposition alone with participants describing a general desire to live a healthier life, regardless of their BRCA status:

'*I think it is vitally important to just have a healthy lifestyle. I do think it's, you know, whether it is BRCA or whatever you have just. You know, I think it's better for you and on your body and on your mind and health and everything*.' - (P9 FG2)

4.6.2.4 Subtheme four: Balancing Control Versus Inevitability

Participants spoke powerfully about the emotional impact of living with a BRCA pathogenic gene variant, describing how cancer risk shaped not only their behaviours but their mental health, relationships and identity. This has been shaped by past trauma, ongoing grief, and persistent feelings of vulnerability, creating both barriers and motivators for health-related behaviours.

Many participants described counselling, journaling and mindfulness as essential tools in managing the emotional toll of living with a BRCA pathogenic gene variant. These practices offered space to process the weight of BRCA beyond medical decision making:

'*I think the counselling is brilliant. I found that helpful because it allowed me to be sad, happy, angry about it, resentful and go through the emotions, not just getting information*.' - (P1 FG1)

‘*Since I've had BRCA and all the operations yeah, If I could go (to counselling) every day I would*.’ - (P9 FG2)

Many participants described living with constant stress, sometimes manifesting through heightened food vigilance and emotional fatigue:

’It's like literally anything I put into my mouth I'm thinking, oh my God is they're going to cause (cancer)’ - (P3 FG1)

‘*It's kind of like music playing in the background in your life sometimes the music is loud, sometimes you can barely hear it. You know that kind of way*.’ - (P7 FG2)

This metaphor captured how for many participants, cancer risk wasn’t just something they thought about during medical appointments, it is always there in the background, as one participant reflected that even when trying to stay healthy:

‘*You kind of forget that you have control over the lifestyle side of things*.’ - (P12 FG4)

At times participants felt the presence of cancer in their thoughts made it hard to feel in control, especially during big life moments, affecting choices about the impact on their children or making long term plans. Participants also expressed frustration at others inability to understand the hidden emotional load they were carrying:

‘*Mentally, you know, at certain days I just don't want to listen to people moaning about stupid things when I'm like, I've a lot more going on in my head right now and you don't even understand what's going through my head and you're moaning, you're moaning about something small. So sometimes I have to take myself away from people*.’ - (P9 FG2)

4.7 Discussion

This is the first study to qualitatively examine the key barriers and motivators for health behaviour change in women with known BRCA1/2 pathogenic gene variants, with no personal history of cancer. The narratives shared in this study reveal that cancer risk management was not the primary driver of lifestyle change among women with BRCA1/2 pathogenic gene variants. Instead, participants described motivations rooted in broader values, such as maintaining long-term health for caregiving responsibilities, preserving personal identity and achieving a sense of control over their bodies and futures, this aligns with prior research in hereditary cancer cohorts which reported cultural identity, familial roles and emotional attachments often underpin health behaviours (112).

Participants consistently described a sense of uncertainty, characterised by occupying a transitional space between health and illness and further challenged by inconsistent healthcare communication. This echoes previous research highlighting the psychological burden of 'previvorship' and the emotional fatigue associated with navigating risk without a current diagnosis (32). The interplay between control and inevitability also emerged as a key factor influencing decisions and behaviours. While some participants found empowerment in proactive choices, others expressed fatigue from self-navigating risk and health recommendations.

The consistent call for BRCA-specific support services, both informational and emotional, was consistently highlighted. These qualitative insights highlight critical gaps in BRCA care pathways and underscore the importance of structured, person-centred support systems. In Chapter 5, these findings will be further synthesised and examined in relation to existing literature through triangulation with the scoping review to deepen the understanding of facilitators and barriers to health engagement in this population.

The qualitative findings, while rich and detailed, also have several limitations. The small sample size of n=11, while sufficient to reach data saturation and capture the depth of participant experiences, limits generalizability of the findings. Furthermore, the sample was homogenous, consisting of all

white female participants, with a high level of educational attainment. Nearly all have a university degree and over half a postgraduate degree. While their experiences are valuable, they do not represent the broader population of BRCA pathogenic gene variant carriers, particularly those from different ethnic and socioeconomic backgrounds.

4.8 Conclusion

This chapter synthesises the lived experiences of women with BRCA pathogenic gene variants, highlighting the complex, multifactorial nature of their journey. The qualitative data reveals that lifestyle change is not solely a response to genetic risk but is deeply intertwined with personal identity, social roles, and the emotional burden of "previvorship." The findings underscore a critical need for a structured, patient-centred support pathway that includes a dedicated liaison figure and a more holistic approach to care, moving beyond the current disjointed and information-focused model.

Chapter 5: The Discussion

5.1 Introduction

While much of the existing behavioural intervention literature in oncology focuses on cancer survivors or those undergoing active treatment, where lifestyle choices are often necessitated by diagnosis or managing treatment side effects, the context for women with BRCA pathogenic gene variants but unaffected by cancer is fundamentally different. Their journey involves proactive preventive measures and requires a long-term approach to self-management that integrates seamlessly into busy daily lives. This chapter, therefore, synthesises findings from both the scoping review (Chapter 3) and the qualitative data (Chapter 4) to explore how women at an elevated genetic risk of cancer perceive, engage with and are supported in adopting health-promoting lifestyle behaviours.

Guided by the COM-B model (Capability, Opportunity, Motivation and Behaviour), this integration provides a behavioural science lens for interpreting the determinants of change. By aligning empirical findings with behavioural theory, this chapter critically appraises existing interventions, identifies key enablers and barriers, and outlines implications for future programme design, clinical practice and health policy. It also contributes to a deeper conceptual understanding of hereditary cancer prevention, highlighting the need for emotionally responsive, patient-centred care models.

5.2 Aligning findings with existing literature

The scoping review presented in Chapter 3, revealed modest yet encouraging evidence supporting the feasibility, acceptability and biological efficacy of lifestyle interventions, particularly structured physical activity, for women at high risk of breast cancer, predominantly due to a BRCA1/2 pathogenic gene variant. Despite methodological variability, reviewed studies reported beneficial outcomes in hormone modulation (97, 99), cardiovascular fitness and bone health (98). However, a key limitation across most interventions was the absence of explicit behaviour change components. These programmes tended to focus on physical opportunity (e.g. providing exercise equipment) and

reflective motivation (e.g. coaching, goal setting) (96-99), but rarely addressed psychological capability (e.g. health literacy or self-regulation skills) or automatic motivation (e.g. habit formation or intrinsic rewards).

This omission is particularly significant given the qualitative findings, presented in Chapter 4, which highlighted the profound emotional burden of living with a BRCA pathogenic gene variants and the voiced frustration over the lack of personalised, psychologically informed support. This pattern of promising but limited evidence is not unique to the BRCA context. For instance, studies in individuals with Lynch Syndrome, who face an elevated lifetime risk for colorectal and other cancers, similarly highlight the potential of lifestyle interventions in risk reduction, yet often report challenges in adherence and sustainability due to a lack of tailored, psychosocially informed support and locus of control (113). The anxiety around surveillance and difficult preventative choices, also resonates strongly with the psychological distress experienced by individuals navigating other hereditary cancer syndromes, such as Li-Fraumeni Syndrome or Familial Adenomatous Polyposis (114). Across these diverse high-risk cohorts, a consistent theme emerges, while genetic information empowers prevention the practical and emotional infrastructure to support sustained health behaviour change remains underdeveloped.

Existing literature affirms the benefits of physical activity, dietary modification and weight management in cancer prevention, even among genetically high-risk populations (43, 44). However, this thesis contributes distinctively by embedding these findings within a behavioural science framework and centring the lived experience of BRCA pathogenic gene variant carriers. The notable lack of diet and alcohol focused interventions in the literature is particularly striking given emerging evidence of their relevance to cancer risk and the documented trend toward unhealthier dietary and lifestyle profiles among women with BRCA pathogenic gene variants (42, 43). Furthermore, while outside the primary scope of this study, it is worth acknowledging emerging hypotheses regarding the potential endocrine-disrupting effects of environmental contaminants such as microplastics (115). As

research in this area evolves, it may represent an additional facet of risk-reduction and lifestyle management for BRCA pathogenic variant carriers . This gap underscores a need to broaden the scope of lifestyle interventions moving beyond physical activity alone to encompass dietary modifications, alcohol reduction and other relevant environmental components of healthy behaviour strategies for cancer prevention and improving overall health outcomes.

This omission of explicit behaviour change components identified amongst studies reviewed in Chapter 3, particularly concerning psychological capability and automatic motivation, appears to be a broader challenge within hereditary cancer risk management. While some interventions for Lynch Syndrome carriers emphasise surveillance adherence and basic health information (116), a systematic review identified that comprehensive programmes explicitly building skills for sustained lifestyle change (e.g., specific dietary modifications for colorectal cancer risk) or leveraging habit formation are similarly scarce (117). The striking lack of diet and alcohol-focused interventions within the BRCA literature, despite their documented relevance, may reflect a broader trend in high-risk populations where intervention development has traditionally prioritised physical activity (117). Physical activity is often seen as more easily standardised and measurable intervention, with clear metrics such as duration and intensity, whereas alcohol reduction interventions can be more challenging to operationalise in a research context, often requiring more complex measures, longer follow up periods and more detailed level of personalisation (79). This collective oversight across various hereditary cancer cohorts underscores a systemic need for interventions that proactively build psychological skills and leverage automatic motivation, moving beyond mere information to help individuals sustain health promoting behaviours in their daily lives.

5.3 Behavioural Determinants of Change

5.3.1 Psychological and Physical Capability: A Dual Imperative.

Across both strands of research presented in this thesis, psychological capability emerged as inconsistently supported. Participants' understanding of specific health behaviours, particularly dietary and exercise guidelines, was often fragmented (Chapter 4, Theme 1, Subtheme 2). While many expressed a general awareness of the importance of 'eating healthy', few could confidently articulate what that entailed in practice. One participant's reflection encapsulated this disconnect: "People probably think a healthy diet… but like what that actually looks like, you know?" (P7, FG2). This illustrates a concerning gap between broad public messaging and the actionable context specific guidance needed to build psychological capability (118). The findings highlight the necessity for not just clinical information but also actionable self-management skills that enable individuals to proactively adopt and maintain healthy habits. Examples in the literature such as the Stanford's Chronic Disease Self-Management Programs have consistently shown that teaching skills such as goal setting, problem-solving, and decision-making leads to significant improvements in health behaviours, even in a diverse range of conditions like diabetes, heart disease, and arthritis (119).

The focus is on empowering the individual with skills, not just providing information. Both the scoping review (Chapter 3) and the qualitative findings (Chapter 4) emphasised that targeted education and practical skills training are essential in bridging this gap. Interventions that incorporated health coaching, instructional materials and structured exercise plans not only enhanced knowledge, but in one study included the scoping review, was associated with measurable reductions in oestrogen levels, demonstrating a direct behavioural-to-biological link (99). This finding is consistent with other population studies that have demonstrated the impact of structured lifestyle changes on biological markers (120). That said, the qualitative data in Chapter 4 also highlighted that information alone is not enough, participants repeatedly emphasised the need for BRCA-specific resources such as plain

language aids and tailored BRCA exercise regimes. Such resources were perceived as useful for building the confidence and competence required to make sustained lifestyle changes in the face of uncertainty and emotional strain. This finding is consistent with other qualitative studies, which have also demonstrated that motivation to maintain lifestyle change is influenced by a combination of internal and external barriers, highlighting the need for tailored support beyond initial information delivery (121).

In contrast, physical capability received far less attention in existing interventions. Only one study tailored its fitness programme to account for post-surgical recovery and menopausal symptoms (98). This omission contrasts starkly with the lived experiences of the participants, presented in Chapter 4, who described fatigue, pain and reduced mobility following risk reducing surgery. These accounts underscore the need for adaptable programmes that include home-based strength training, low impact options, and phase specific exercise prescriptions that ease transitions from pre-operative conditioning to post-operation rehabilitation. This call for tailored interventions aligns with a growing body of literature demonstrating the effectiveness of home-based exercise in improving adherence and the benefits of low-impact activities like yoga for symptom management in cancer survivors (122, 123). Furthermore, the concept of a phase-specific approach is consistent with established prehabilitation and rehabilitation protocols in oncology, which have been shown to enhance recovery and functional outcomes (124-126).

Prehabilitation is a tailored, proactive approach to preparing a patient for a significant medical event, such as surgery (125, 127). It typically involves a combination of exercise, nutritional optimization and psychological support, all aimed at improving a patient's physical and mental resilience before their procedure. This contrasts with traditional rehabilitation which occurs only after surgery (127). There is compelling justification for incorporating structured prehabilitation into BRCA care pathways. Evidence from non-BRCA populations demonstrates that preoperative exercise can significantly reduce postoperative complications (OR = 0.25, 95% CI = 0.10-0.66) (128). Adapting this approach for

BRCA pathogenic gene variant carriers may enhance surgical resilience, reduce recovery time and serve as a springboard for sustained lifestyle change (127). In this way, surgery emerges not only as a physical challenge but also as a behavioural inflection point, 'a teachable moment' that can be leveraged to great effect. As several participants described the decision to undergo surgery as an opportunity to re-engage with their health 'If I hadn't done the surgeries, I don't know if I would be thinking this way or making these changes'(P12 FG4) (Chapter 4, Theme 2, Subtheme 2), suggesting that for these women, the surgical period is a unique, highly motivated window for incorporating new behaviours. It provides a tangible goal that can anchor long-term changes, such as improved nutrition, strength training and mindfulness practices, transforming the emotional and physical ordeal into a positive catalyst for change.

Furthermore, while prehabilitation is typically framed as a preparation for surgery, its principles should be extended to the many women who opt for surveillance rather than immediate risk-reducing surgery. For these women, a 'prehabilitation-type' approach serves as a proactive health optimisation strategy. By maintaining high levels of cardiovascular fitness and nutritional health during the surveillance period, patients are essentially 'primed' for treatment. Should a malignancy be detected during surveillance these individuals would enter the cancer care pathway from a position of functional reserve and improve recovery outcomes. Reframing lifestyle interventions as a form of continuous functional readiness, regardless of surgical intent, validates the importance of healthy behaviours for all 'previvors'.

Taken together, findings from both the literature and lived experiences suggest that psychological capability is foundational but inconsistently supported, and that physical capability though equally vital is even more neglected. Without targeted practical and emotionally attuned support across both domains, behaviour change efforts for women with BRCA pathogenic gene variants are unlikely to achieve their full potential.

5.3.2 Opportunity: Structural Gaps and Social Potential.

Interventions examined in the scoping review (Chapter 3) consistently enhanced physical opportunity by supplying home based equipment (e.g. treadmills) and delivering programmes though online platforms, strategies intended to minimise logistical barriers like travel and time constraints (96-99). However qualitative findings, presented in Chapter 4, complicate this narrative suggesting that these logistical issues are not the only barriers to consider. Many described financial constraints as a major obstacle: the high cost of healthy food, limited access to locally sourced organic produce and rising fees for fitness classes creating an uneven playing field (Chapter 4, Theme 2, Subtheme 3). This finding resonates with another review which investigated the health disparities before and after non-communicable disease diagnosis, which highlighted socioeconomic status as a key determinant of health behaviours (129).

In addition, participants highlighted the absence of a coordinated clinical pathway following their confirmed BRCA pathogenic gene variant as a major challenge to navigating risk management. Rather than receiving integrated ongoing support, many described navigating lifestyle decisions and care plans in isolation. To address this fragmentation, participants repeatedly called for the introduction of a dedicated BRCA specific liaison figure, a clinical role combining medical expertise with behavioural and psychosocial insight to provide continuity of care (Chapter 4, Theme 1, Subtheme 2).

The social opportunity dimension of the COM-B model was almost entirely overlooked in the intervention literature. In contrast the qualitative data, presented in Chapter 4, highlighted peer support as a pivotal enabler of sustained behaviour change (Chapter 4, Theme 1, Subtheme 3). Participants described informal networks and structured peer-led interventions as vital in normalising health behaviour, alleviating emotional burden and facilitating mutual learning, which is consistent with findings in other populations, such as those living with mental health disorders (130). The call for professionally facilitated peer-led forums acknowledges the essential role of a community in fostering engagement, trust and reducing isolation.

To move beyond the narrow focus on equipment provision, programmes should consider partnering with community organisations and embedding peer support mechanisms to address structural gaps. Peer connection is not merely a supplement but is a vital tool. Systematic reviews and meta-analysis have shown that peer support interventions improves quality of life (SMD = 0.48, 95% CI 0.21–0.75; $p < 0.001$), depression (SMD = −0.23, 95% CI −0.39 to −0.07; $p = 0.005$), anxiety (SMD = −0.24, 95% CI −0.45 to 0.03; $p = 0.03$), and self-efficacy (SMD = 0.22, 95% CI 0.03–0.42; $p = 0.03$) among people with cancer relative to controls (131). Notably, in those reviews, mixed mode delivery (e.g. combining face-to-face and virtual format) yielded greater improvements in quality of life than single-mode approaches (131).

5.3.3 Motivation: Sustaining Change in the Face of Emotional Exhaustion

All Interventions reviewed in the scoping review presented in Chapter 3 explicitly targeted reflective motivation through structured goal setting, educational content and self-monitoring tools (96-99). Participants were encouraged to set weekly or dose-dependent exercise goals and track progress via logs or wearable devices. The underlying aim was to foster deliberate, intentional engagement with health behaviour through cognitive planning and self-regulation. Qualitative findings presented in Chapter 4 confirmed that women often held strong intentions to modify their lifestyle, however, many described emotional exhaustion and information overload that accompanied medical appointments for surveillance, and recent or upcoming surgeries (Chapter 4, Theme 1, Subthemes 1 and 2). This cognitive and affective burden often disrupted their ability to maintain focus on long-term health goals, suggesting while reflective motivation may initially be high sustaining the engagement requires support which actively manages emotional fatigue. Interventions that combine multiple techniques such as pacing information delivery, embed stress reduction techniques and offer periodic motivational ‘boosts’ may be more effective in maintaining momentum (118). Programmes could also

benefit from aligning action planning with personally meaningful milestones, such as surgery and family events, to reinforce internalised goals and strengthen long-term adherence.

In contrast, automatic motivation, which includes habit formation, emotional reinforcement and behavioural nudges was rarely leveraged across intervention literature. Only one study included financial incentives and none systematically incorporated cues, reminders or affective rewards to promote healthy routines (98). In the qualitative study presented in Chapter 4, many participants described feelings of guilt and overwhelm underscoring how negative emotion when left unmanaged can hinder rather than catalyse change (Chapter 4, Theme 2, Subtheme 3). Promising opportunities exist to tap into positive affect and identity reinforcement (118). Simple strategies such as digital badges for consistency, congratulatory notifications upon milestone completion or 'habit-stacking' prompts linked to existing routines may help embed new behaviours into daily life (132).

The qualitative findings presented in Chapter 4 revealed a far richer and more emotionally charged motivational landscape than the intervention literature suggests. Women spoke of fear, guilt, hope and trauma and evolving bodily identity particularly in relation to decisions related to surgery and menopause (Chapter 4, Theme 2, Subtheme 2). These emotional drivers point to the conclusion that motivation for behaviour change among women with BRCA pathogenic gene variants is rarely rooted solely in the goal of cancer risk reduction. Rather, it is often driven from a broader desire to regain a sense of control in the face of uncertainty, sustain longevity and nurture present day well-being. These findings are consistent with existing literature on those living with BRCA pathogenic gene variants (100, 133). One qualitative study, although modest in size (n=6) and highly homogenous (exclusively included women with BRCA1/2 pathogenic gene variants actively under surveillance for breast cancer only) reported that women carrying BRCA1/2 pathogenic gene variants experiences mirror those of individuals living with a chronic illness, and they must therefore adapt accordingly in a physical, psychological, and social manner (133). Another report by the same research group based on the same sample also found that there appears to be many commonalities between the descriptions of

uncertainty made by individuals fighting cancer and women living with the BRCA1 or BRCA2 pathogenic gene variants (100). This intrinsic drive speaks to the importance of emotionally attuned and trauma informed approaches that support identity, agency and healing.

5.4 Theoretical Implications

This study extends the utility of the COM-B model by demonstrating its relevance in evaluating interventions for genetically high-risk populations. However, BRCA pathogenic gene variant carriers often experience a liminal “no-man’s-land” between wellness and illness status, which traditional behavioural models may fail to accommodate. Integrating the COM-B framework with concepts from self-determination theory and trauma informed care could better support the unique psychological profile of this population (134, 135).

Self-determination theory suggests that intrinsic motivation is enhanced when individuals feel autonomy (control over their choices), competence (confidence in their ability), and relatedness (a sense of connection with others) (134). This aligns directly with the qualitative findings in Chapter 4, which highlighted the need for personalised support and peer connection to build confidence and agency. Similarly, a trauma-informed approach recognises that living with a genetic risk for cancer and undergoing preventative surgeries can be a traumatic and emotionally overwhelming experience (135). Such an approach could focus on creating emotionally safe environments, promoting trust, and empowering individuals rather than reinforcing a sense of helplessness, which is crucial given the profound emotional burden voiced by participants.

5.5 Implications for Practice and Policy

To embed lifestyle changes effectively within hereditary cancer care, programmes must be both individually tailored and responsive to the unique psychosocial burden carried by those living with BRCA1/2 pathogenic gene variants. Based on the synthesis of the scoping review (Chapter 3) and the

qualitative findings (Chapter 4) and underpinned by behavioural theory and a trauma informed approach, the following recommendations are proposed to address the identified gaps in BRCA care. These recommendations represent a pragmatic roadmap derived directly from the lived experiences of the participants in Chapter 4 and substantiated by behavioural change theory.

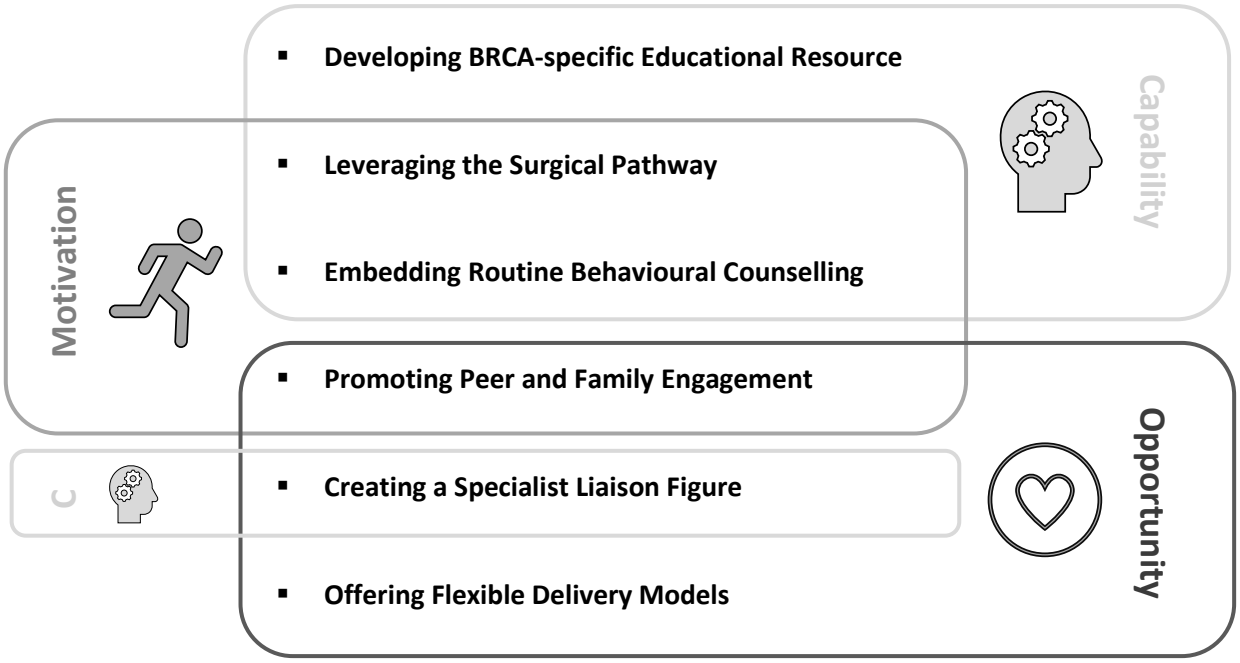

Figure 5: A conceptual framework for holistic, patient-centred interventions, designed to support proactive and sustained health behaviours in women with a BRCA pathogenic gene variants. Guided by the COM-B model, the framework illustrates how the six key recommendations derived from the study's findings can be integrated to address the specific behavioural determinants of change. Each recommendation is strategically positioned to enhance capability, opportunity, and motivation, ultimately fostering a resilient and proactive approach to "previvorship."

<u>Developing BRCA-specific educational resources</u>

This recommendation directly targets psychological capability. The results from this thesis revealed a significant gap in accessible, tailored information. By providing plain language, tailored information, these resources build health literacy, empowering individuals to take proactive steps for their long-term health. The use of plain-language written resources is a well-established strategy for improving health literacy and empowering individuals to engage in self-management, a crucial component of long-term behaviour change (136).

Leveraging the surgical pathway as a 'teachable moment'

This recommendation primarily targets motivation (reflective and automatic) and physical capability. It leverages a period around a high reflective motivation (decision to undergo surgery) as a powerful inflection, transforming the emotional and physical ordeal into a positive catalyst for change. Drawing on the established prehabilitation and rehabilitation protocols, it is recommended that proactive, phase-specific programmes be interested into surgical pathway (124, 126, 127). A prehabilitation phase should focus on improving a patient's physical and mental resilience before their procedure through a combination of tailored exercise and nutritional optimization directly enhancing physical capability. Following surgery, a bespoke rehabilitation programme could build on this momentum, integrating low-impact activities and mindfulness practices to aid recovery and embed lasting habits (automatic motivation).

Embedding routine behavioural counselling

To address the motivational and capability barriers identified in this thesis, behavioural counselling sessions should be embedded into standard care. This approach aligns with the Making Every Contact Count (MECC) initiative, which encourages healthcare professionals to use routine interaction opportunities to engage individuals in conversations about their health. By teaching skills like goal setting and action planning, it builds psychological capability. Additionally, specific behavioural

counselling sessions, led by trained counsellors or health care professionals, could employ evidence-based techniques such as motivational interviewing to reinforce reflective motivation and empower individuals to seamlessly integrate health promoting behaviours into their daily lives for long-term well-being.

Promoting peer and family engagement

This recommendation strengthens opportunity (social) and motivation (automatic and reflective). The findings highlighted that online peer groups provided a crucial focus of emotional reassurance and practical advice. To counteract the feelings of isolation and the 'identity issue' of falling between categories, it is prudent to actively incorporate peer-led initiatives and family-supported forums. Organizations and peer-led support networks such as the Marie Keating foundations BRCA support group and BRCA Ireland offer unique form of 'experiential knowledge' which bridges the gap between clinical advice and daily life. These platforms serve multiple functions, they normalise health behaviours, alleviating emotional burden and foster a sense of relatedness which is a key driver of intrinsic motivation (reflective) (134). The shared experiences also provided social accountability, acting as a behavioural nudge (automatic motivation).

Creating a specialist liaison figure

This recommendation addresses psychological capability and social opportunity. The qualitative data provided compelling evidence of a fragmented and disjointed healthcare system. The creation of a dedicated BRCA-focused liaison figure within a family risk clinic is therefore a critical recommendation. This individual would coordinate multidisciplinary care, ensure consistent messaging and provide a centralised point of contact to guide individuals through complex pre-surgical and self-management

decisions. This recommendation aligns with the NCCP Hereditary Cancer Model of Care which identified a need for dedicated roles to address the fragmented care pathways and is currently establishing positions such as a 'national MDT coordinator and advanced nurse practitioners (6). A liaison figure is crucial for health behaviour change as they directly enhance an individuals' psychological capability by providing actionable information, improve social opportunity by fostering a consistent and trusting relationship and improve motivation by offering tailored support during critical junctures such as the surgical pathway.

Offering flexible delivery models

This recommendation addresses physical opportunity. The findings consistently highlighted that competing life demands, financial limitations and post-surgical recovery periods act as significant barriers. Therefore, interventions should offer flexible, home-based models that can accommodate varying physical capabilities and time constraints. These modular programmes should be adaptable to different phases (e.g. pre- or post- risk-reducing surgery), allowing individuals to maintain a healthy lifestyle throughout their life, even during periods of recovery or heightened stress. This approach promotes long-term adherence and acknowledges the dynamic nature of a 'previvor's' journey.

5.6 Limitations and Strengths

Despite its contributions, this thesis is subject to several limitations. Firstly, the scoping review presented in Chapter 3 was restricted to English-language publications and yielded only four eligible studies, all conducted in North America. This narrow evidence base may limit the transferability of findings to other cultural or healthcare contexts, and important intervention domains, such as dietary modification, alcohol reduction, and smoking cessation, remain underexamined.

Secondly, the qualitative study presented in Chapter 4 drew on a small, self-selected cohort of Irish BRCA1/2 pathogenic gene variant carriers. Participants who volunteered were highly educated with almost all to a degree level and many with postgraduate qualifications. This level of education likely provided the skills to access and critique information, meaning participants may have been particularly motivated and well-informed. Conversely, the perspectives of more isolated individuals, such as those from rural areas or lower socioeconomic backgrounds, are underrepresented. Furthermore, navigating a complex hereditary care pathway requires high levels of health literacy recent migrant populations in Ireland may face unique challenges in 'Previvorship,' including language barriers and limited access to culturally tailored genetic services. As these groups are often underrepresented in hereditary cancer research, future studies should prioritize inclusive recruitment and the development of linguistically accessible lifestyle resources to ensure health equity within Ireland's increasingly diverse population.

Thirdly, the sequential qualitative design informed by a scoping review facilitated rich theory-informed insights, it precludes definitive conclusions regarding intervention efficacy or long-term adherence. Without quantitative follow-up or longitudinal tracking, the durability of observed behaviour changes and their impact on cancer incidence cannot be established.

Finally, the integration of scoping and qualitative findings rests on a conceptual mapping via the COM-B framework rather than on statistical synthesis. While this approach deepens our understanding of behavioural mechanisms, future research should incorporate larger, more diverse samples and mixed-methods evaluation to validate and extend these preliminary recommendations. For example, a future meta-analysis could statistically combine the effect sizes from studies to provide a more precise estimate of the overall impact of specific interventions such as physical activity on hormonal biomarkers. This would move beyond a conceptual synthesis to provide a definitive quantitative measure of efficacy (91).

5.7 Conclusion

This chapter demonstrated that lifestyle behaviour change among BRCA pathogenic gene variant carriers is shaped by a complex interplay between psychological readiness, structural access and distinct motivational drivers. While medical prevention strategies remain foundational, the integration of behavioural support offers a complementary and empowering pathway to improved health outcomes. The COM-B framework provides a pragmatic and theoretically grounded model for designing future interventions that are sensitive to the lived realities of this population.

This thesis underscores that effective cancer-prevention for women with BRCA pathogenic gene variants demands an approach that is distinct from what is offered to the general population. Successful outcomes require a shift from generic advice to bespoke lifestyle programmes rooted in behavioural science. By mapping existing evidence and lived experiences onto the COM-B framework, we demonstrate how this population perceives and prioritises health behaviours in a unique way. The findings highlight that their motivation for change is distinct, necessitating more nuanced, tailored strategies to support them. This work illuminates a clear roadmap for a new generation of interventions that are not only biologically sound but also psychologically resonant, socially embedded, and logistically feasible.

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Appendices

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Appendix 1- Extended Search strategy

EMBASE (1220)

'Hereditary breast and ovarian cancer syndrome'/exp

('BRCA1 and BRCA2-associated hereditary breast and ovarian cancer' OR 'HBOC Syndrome' OR 'familial breast and ovarian cancer' OR 'hereditary breast and ovarian cancer (HBOC)' OR 'hereditary breast and ovarian cancer syndrome'):ti,ab,kw

'BRCA1 protein'/exp OR 'BRCA2 protein'/exp

BRCA*:ti,ab,kw

#1 OR #2 OR #3 OR #4

'lifestyle'/exp

((life OR lifestyle OR life-style) NEAR/2 (style* or change* OR modify OR modifi* OR intervention* OR program* OR promot* OR educat*)):ti,ab,kw

'self concept'/de

(self NEAR/1 (efficac* OR help OR manag* OR care)):ti,ab,kw

'health promotion'/exp OR 'health education'/de

(health NEAR/1 (promot* or educat* OR intervention*)):ti,ab,kw

(motivat* NEAR/1 (therap* or interview*)):ti,ab,kw

#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12

'weight loss program'/exp OR 'body weight loss'/exp OR 'body weight management'/exp OR 'obesity'/exp

(('Weight loss' OR 'weight reduc*' OR slimming OR 'weight management') NEAR/3 (program* OR class* OR session* OR intervention*)):ti,ab,kw

('slim* class*' OR 'weight watchers' OR 'slimming world' OR 'obesity manage*'):ti,ab,kw

((weight OR 'body mass index' OR BMI OR 'Waist circumference' OR 'Waist size') NEAR/3 (los* or reduc* or decreas* or low* OR management)):ti,ab,kw

'energy restrict*':ti,ab,kw

(calor* NEAR/2 (restrict* or reduc* or low*)):ti,ab,kw

'antiobesity agent'/exp

(('anti obesity' OR 'antiobesity') NEAR/2 (agent* OR intervention* OR therap*)):ti,ab,kw

(appetite NEAR/2 suppress*):ti,ab,kw

(Orlistat OR Xenical OR alli OR tetrahydrolipstatin OR phentermine OR phenyl-tertiary-butylamine OR Ionamin OR adipex-P OR anoxine-AM OR duromine OR metermine OR mirapront OR obephen OR obestin-30 OR phentremene OR phentrol OR phenterex OR phentromin OR 'pro-fast SA' OR redusa OR panbesy OR 'phentermine trenker' OR Obenix OR Oby-trim OR Teramine OR Zantryl OR Sinpet OR Supremin OR Umine OR Weltmine OR Aplenzin):ti,ab,kw

'semaglutide'/exp

(Ozempic OR rybelsus OR wegovy OR semaglutide*):ti,ab,kw

#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25

'diet therapy'/exp OR 'nutritional counseling'/exp

((Diet* OR nutrition*) NEAR/3 (intervention* OR treatment OR therap* OR treatment* OR supplementation* OR support* OR counsel* OR education OR sheet OR intake OR program*)):ti,ab,kw

(lacto-vegetarian* OR 'lacto vegetarian*' OR vegetarian* OR non-vegetarian* OR 'lactose free' OR non-vegetarian* OR vegan OR Cretan OR mediterranean):ti,ab,kw

'diet restriction'/exp

((intermittent* OR alternat* OR modified) NEAR/3 fast*):ti,ab,kw

(food NEAR/1 (abstinence or fast*)):ti,ab,kw

((protein OR purine OR fat OR cholesterol OR triglyceride OR diet*) NEAR/2 (restrict* or reduc* or low* or elim*)):ti,ab,kw

#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33

'lactose free diet'/exp

('lactosefree diet*' OR 'lactose free diet*' OR 'dairy free'):ti,ab,kw

((milk OR cheese* OR yog*urt OR dairy) NEAR/2 (restrict* OR reduc* OR low* OR elim*)):ti,ab,kw

#35 OR #36 OR #37

'alcoholism'/exp OR 'drinking behavior'/exp OR 'alcohol consumption'/exp

((Alcohol OR etahnaol) NEAR/2 (drinking OR behaviour* OR behavor* OR habit* OR pattern* OR restrict* OR reduc* OR low* OR elim* OR control* OR consum* OR intake)):ti,ab,kw

alcohol*:ti,ab,kw

#39 OR #40 OR #41

'caffeine'/exp

Caffeine:ti,ab,kw

#43 OR #44

'exercise'/exp OR 'kinesiotherapy'/exp OR 'physical activity'/exp OR 'physical activity, capacity and performance'/de OR 'training'/de OR 'endurance'/de OR 'exercise tolerance'/de OR 'physical capacity'/de OR 'sport'/exp

((resistance OR strength*) NEAR/3 (train* OR exercis*)):ti,ab,kw

((physical* or motion* or cardiopulmonary or cardiorespiratory) NEAR/3 (fit* or therap*)):ti,ab,kw

(treadmill* or cross-train* or rowing or sport* OR exercis* OR ‘physical activit*’ OR aerobic* OR run or jog* or running OR walk or walks or walking OR gym* OR yoga OR pilates OR ‘recreation* activit*’ OR zumba or salsa* OR cycling or bicycle or bike or swim* or dance or dancer* or dances or dancing or HIIT):ti,ab,kw

(circuit* NEAR/1 train*):ti,ab,kw

(keep* NEAR/2 (active or fit)):ti,ab,kw

#46 OR #47 OR #48 OR #49 OR #50 OR #51

'tobacco dependence'/exp OR 'smoking cessation'/exp OR 'smoking'/exp

((quit* or stop* or ceas* or giv* or replace* OR cessation OR Abstinence OR abstain* OR prevent*) NEAR/5 (smoking or tobacco or nicotine OR cigarette*)):ti,ab,kw

(cigarette* or cigar* or pipe* OR vape* OR vaping):ti,ab,kw

'nicotinic agent'/exp

(nicotine NEAR/1 (replacement or patch* or gum or nasal)):ti,ab,kw

'hypnosis'/exp

hypnosis:ti,ab,kw

'counseling'/de OR 'genetic counseling'/exp

counsel*:ti,ab,kw

#53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61

#13 OR #26 OR #34 OR #38 OR #42 OR #45 OR #52 OR #62

'behavior change'/exp AND ('health behavior'/exp OR 'cancer risk'/exp)

(Behavio?r* NEAR/3 (change* OR intent* OR modify OR modifi* OR intervention* OR program* OR promot* OR educat* OR health OR 'cancer risk*')):ti,ab,kw

'behavior therapy'/exp

(behavio?r* NEAR/3 (psychotherapy OR training OR treatment OR therapy)):ti,ab,kw

'risk reduction'/exp

((Risk* OR harm*) NEAR/3 (reduce* OR reduction OR modify OR modifi* OR perception* OR perceive*)):ti,ab,kw

#64 OR #65 OR #66 OR #67 OR #68 OR #69

#5 AND #63

Appendix 2- Mixed method appraisal tools

Haley et al 2023
Dose-dependent effect of aerobic exercise on inflammatory biomarkers in a randomized controlled trial of women at high risk of breast cancer.

Part I: Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	X			to investigate the dose-dependent effects of aerobic exercise on inflammatory biomarkers in premenopausal women at high risk of breast cancer.
	S2. Do the collected data allow to address the research questions?	X			randomized controlled trial (RCT) methodology, biomarker assays, and validated instruments to measure pro-inflammatory (e.g., TNF-α, IL-12) and anti-inflammatory (e.g., IL-10) markers.
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				

	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?	X			randomized into control (<75 min/week), low-dose (150 min/week), and high-dose (300 min/week) exercise groups. Randomization was stratified by BMI and time since menarche
	2.2. Are the groups comparable at baseline?	X			no significant differences in age, BMI, or fitness levels across groups
	2.3. Are there complete outcome data?	X			16 participants were lost to follow-up (mainly from the intervention groups), reasons for dropout were reported (e.g., time pressures, family issues)
	2.4. Are outcome assessors blinded to the intervention provided?	X			Yes assessor were blinded appropriately
	2.5 Did the participants adhere to the assigned intervention?	X			High adherence to groups (85% and 81%) Adherence was monitored through exercise logs and heart rate data
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?				

	4.2. Is the sample representative of the target population?				
	4.3. Are the measurements appropriate?				
	4.4. Is the risk of nonresponse bias low?				
	4.5. Is the statistical analysis appropriate to answer the research question?				
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Schmitz et al 2015

Dose–response effects of aerobic exercise on estrogen among women at high risk for breast cancer: a randomized controlled trial

Part I: Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	X			the study focuses on the dose-response effects of aerobic exercise on oestrogen and breast cancer risk markers among women at high risk for breast cancer..
	S2. Do the collected data allow to address the research questions?	X			
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?	x			blocked randomization process with a 1:1:1 allocation ratio

	2.2. Are the groups comparable at baseline?	x			age, BMI, education, marital status, etc. of the three groups are reported, and no significant differences seen between groups
	2.3. Are there complete outcome data?			x	most participants provided complete data (88% follow-up rate). A subset of participants (n=68) underwent imaging due to budget constraints. Missing hormonal data for 4 participants are also acknowledged.
	2.4. Are outcome assessors blinded to the intervention provided?	x			Staff conducting measurements- hormone levels, MRI imaging- were blinded to group allocation
	2.5 Did the participants adhere to the assigned intervention?	x			Objective heart rate monitor data showed that participants in the exercise groups adhered to 81-85% of prescribed exercise minutes.
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?				
	4.2. Is the sample representative of the target population?				

	4.3. Are the measurements appropriate?				
	4.4. Is the risk of nonresponse bias low?				
	4.5. Is the statistical analysis appropriate to answer the research question?				
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Sturgeon at al 2017

Commercially available lifestyle modification program: randomized controlled trial addressing heart and bone health in BRCA1/2+ breast cancer survivors after risk-reducing salpingo-oophorectomy

Part I: Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	X			Yes, it investigates the efficacy and safety of a web-based lifestyle modification program (Precision Nutrition Coaching) to improve cardiovascular and bone health outcomes among BRCA1/2+ breast cancer survivors following risk-reducing salpingo-oophorectomy.
	S2. Do the collected data allow to address the research questions?	X			the data include appropriate outcomes such as cardiovascular fitness, dietary intake, bone density, and body composition,
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				

	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?	x			Randomization was performed using stratified random sequence assignment within four BMI and age-based strata,. Allocation was concealed prior to group assignment
	2.2. Are the groups comparable at baseline?	x			Baseline characteristics (e.g., age, BMI, and other demographic factors) were reported, and there were no significant differences between the intervention and control groups.
	2.3. Are there complete outcome data?	x			the study achieved a follow-up completion rate of 91% (32/35 participants completed the trial)
	2.4. Are outcome assessors blinded to the intervention provided?	x			study indicates that assessors for body composition, bone density, and fitness outcomes were blinded to group allocation
	2.5 Did the participants adhere to the assigned intervention?	x			an overall adherence rate of 74.8%. Substantial proportions of participants completed at least 80% of the exercise (62%), habit formation (75%), and reading activities (68%), demonstrating strong participant engagement.
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				

	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?				
	4.2. Is the sample representative of the target population?				
	4.3. Are the measurements appropriate?				
	4.4. Is the risk of nonresponse bias low?				
	4.5. Is the statistical analysis appropriate to answer the research question?				
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Kossman et al 2011
Exercise lowers oestrogen and progesterone levels in premenopausal women at high risk of breast cancer

Part I: Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	X			Looks at if a structured exercise intervention reduces oestrogen and progesterone levels in premenopausal women at high risk for breast cancer.
	S2. Do the collected data allow to address the research questions?	X			collects daily urine samples over seven menstrual cycles and uses AUC (area under the curve) hormone measures, used for assessing cumulative hormonal exposure.
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				

2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?	X			N=10 women with high breast cancer risk through convenience sampling
	4.2. Is the sample representative of the target population?		x		No n=7 completed the study, all Caucasian. Lacks diversity
	4.3. Are the measurements appropriate?	x			uses validated assays for estrone-1-glucuronide (E1G) and pregnanediol-3-glucuronide (PdG) to measure hormone levels
	4.4. Is the risk of nonresponse bias low?		x		Does not discuss the characteristics of those that dropped out (30%) and if they differ from those that stayed in the study
	4.5. Is the statistical analysis appropriate to answer the research question?	x			Paired t-tests and AUC comparisons pre- and post-exercise intervention

5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Appendix 3- SRQR

Standards for Reporting Qualitative Research (SRQR)

Title and abstract		Page number
	Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1, 60
	Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	5-6
Introduction		
	Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statemen	60-61
	Purpose or research question - Purpose of the study and specific objectives or questions	61
Methods		
	Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	28,61-62
	Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the re	72
	Context - Setting/site and salient contextual factors;	62-63
	Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	62-63
	Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	69

	Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection, if/how the instrument(s) changed over the course of the study	64-69
	Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	72-73
	Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	70-72
	Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	70-72
	Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	70-72
Results/findings		
	Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	72-92
	Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Appendix 7
Discussion		
	Integration with prior work, implications, transferability, and contribution(s) to the field - short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	93-94
	Limitations - Trustworthiness and limitations of findings	93-94, 108-109
Other		
	Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	72
	Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	n/a

Appendix 4- GRIPP-SF2

GRIPP2 short form

PPI=patient and public involvement

Section and topic	Item	Reported on page No
1: Aim	Report the aim of PPI in the study	63
2: Methods	Provide a clear description of the methods used for PPI in the study	63
3: Study results	Outcomes—Report the results of PPI in the study, including both positive and negative outcomes	63-64
4: Discussion and conclusions	Outcomes—Comment on the extent to which PPI influenced the study overall. Describe positive and negative effects	63-64
5: Reflections/critical perspective	Comment critically on the study, reflecting on the things that went well and those that did not, so others can learn from this experience	72,93-94

Appendix 5 – Participant information leaflet

Participant Information Leaflet

Study title:

Understanding the views of women with BRCA1/BRCA2 pathogenic gene variants on lifestyle choices for Cancer prevention.

Lead Researcher:	Ms Orla Crowley	MSc Physiotherapy, School of medicine TCD. Contact: Ocrowley@tcd.ie
Primary investigators:	Dr Emer Guinan	Associate Professor in Cancer Rehabilitation and Survivorship, Trinity College Dublin. Guinane1@tcd.ie
Study team:	Ms. Diana Cooke	PhD candidate, School of Medicine Trinity College Dublin.
	Dr Jenny Groake	School of Psychology, University of Galway jenny.groarke@universityofgalway.ie
	Dr Karen Cadoo	Medical Oncologist and Cancer Geneticist at St. James's Hospital
	Ms. Kelly Coghlan Lynch	Acting Clinical Specialist Physiotherapist (Cancer Services), St James's Hospital
	Dr Niamh Coleman	Consultant Medical Oncologist, St James's Hospital
	Ms. Elizabeth Connolly	Consultant Breast Surgeon, St James's Hospital
	Dr Sarah McGarrigle	Project Manager & Research Coordinator, Breast Care Department, St James's Hospital and Adjunct Assistant Professor, Dept. Of Surgery, Trinity College Dublin
	Ms. Yvonne Hanhauser	Advanced Nurse Practitioner, Breast Care Department, St James's Hospital
Data Controller	Trinity College Dublin (research data)	

Data Protection Officer (Research data)	Data Protection Officer Secretary's Office Trinity College Dublin Dublin 2

Introductory Statement

We would like to invite you to take part in a research study. Before you decide whether or not you wish to take part, please take time to read this information leaflet carefully and discuss it with your family, friends or healthcare team. If there is anything which is not clear, or if you would like more information, please ask any of the research team.

Do I have to take part?

No, joining this study is your choice. You can say no, and this will not affect your medical care in any way. If you join but change your mind later, you can stop at any time.

Part 1 - The Study

Why have I been invited to take part?

We are interested in understanding the views of women aged 18 years and older, who have an alteration in BRCA1/2 genes, towards lifestyle factors for cancer prevention. Lifestyle choices may include for example diet and exercise. We will gather this information through focus group discussion. You are invited because you are a woman over 18 years old with BRCA1/BRCA2 gene alteration, who hasn't had a prior diagnosis of cancer. We hope to include 20–25 women in this study.

Why is this study being done?

Lifestyle factors, such as diet and physical activity, can play an important role in breast cancer prevention for the general population. Women who have an alteration in the BRCA genes have an increased risk of breast cancer and therefore may have different experiences engaging with lifestyle behaviours for cancer prevention in comparison to the general population. We are conducting this study to understand the views of women with alterations in the BRCA genes towards lifestyle advice for cancer prevention.

What does taking part involve?

If you decide to take part, a member of the research team will discuss this information leaflet and consent form with you. You will be given a copy of your signed consent form and this leaflet to keep.

We will arrange a time and location for a focus group discussion with a member of the research team. Before you attend the focus group, we will phone you to collect further information such as age, county of residence, educational level, marital status and the age

when you learned of your BRCA gene alteration. We will offer three focus groups – two will be hosted online using a Trinity College Dublin licensed version of Microsoft Teams, and one will be hosted in-person at the Trinity Centre for Health Sciences at St James's Hospital. You may attend whichever focus group location and time works best for you. The focus group will be audio recorded. During the focus group you will be asked questions about physical activity and diet in relation to current cancer research recommendations.

The topics we will talk about include:

- What do you know about BRCA genes and cancer risk?
- Your thoughts on cancer prevention advice (like diet and exercise).
- Your lifestyle habits and challenges.
- What support do you think would help in the future?

After the focus group we will transcribe (write out) the discussion. You may contact the lead researcher at any point within the first month after the focus group to review the transcript. At this point the transcript will be pseudonymised (coded).

What are the possible benefits of taking part?

This study may not directly benefit you. However, your input could help improve advice and support for people with BRCA1/2 gene alterations in the future.

Are there any possible disadvantages or risks from taking part?

We do not expect any risks, but talking about cancer might feel emotional. At all times, the well-being of participants takes priority over research activities. In the event of the focus group triggering an emotional event, one of the focus group facilitators will invite you to speak with them separately either in a breakout room (for online focus groups) or in a separate room (for the in-person focus group). The facilitator will work with you and may advise you to contact confidential support from The Irish Cancer Society, by contacting 1800 200 700 or see cancer.ie for more information.

Data Breach: we take many measures to ensure the confidentiality of all data and the risk to you of a breach of confidentiality is considered very low.

If you are harmed in any way, the researchers on this study are covered by insurance through Trinity College Dublin. This insurance will cover you in the unlikely event that you injured as a result of taking part in this study.

What will happen to the results of the study?

The results of the study will be reported in medical journals and disclosed at medical conferences. No information which reveals your identity will be disclosed.

Some quotations from the focus group may be used in reports. However, no information which reveals your identity will be disclosed.

Part 2 - Data Protection

What information about me (personal data) will be used for this study

For this study we will need some general information about you, which we will ask you to share with us (age, county of residence, educational level, marital status/dependants and the age when you learned of your BRCA gene alteration). We will conduct a focus group, and we will record this and write up the audio into words (a transcript).

Who will access my personal data?

Only the Lead researcher (OC) will be able to identify you. They will keep the master file which links your identity to the research data. The lead researcher will replace your name with a code on all research data. The study supervisor(s) may require access to the research data to ensure academic rigour.

How is the information kept confidential and secure?

Your privacy is important to us. We take many steps to make sure that we protect your confidentiality. We replace your name with a code at the time of the focus group to ensure your confidentiality. All research data is held securely on TCD SharePoint with restricted access to the research team listed above. The lead researcher and co-investigators are governed by a professional code of ethics to maintain your confidentiality.

Confidentiality may be breached in circumstances in which the research team has a strong belief or evidence exists that there is a serious risk of harm or danger to you or another individual. Disclosure may also be required as part of a professional code, legal process, or Garda investigation. In such instances, information may be disclosed to significant others or appropriate third parties without permission from you being sought. Where possible, a full explanation will be given to you regarding the necessary procedures and the intended actions that may need to be taken.

How long will my personal data be needed??

The audio recording of the focus group will be retained until it has been transcribed and the content verified (approx. 1month after focus groups) after which it will be securely deleted

The transcript will be retained until the lead research Ms Orla Crowley has completed her master's thesis, and the thesis has been corrected and approved (approximately quarter 2 of 2026).

Consent forms will be scanned to TCD SharePoint and hardcopies shredded immediately. Online copies scanned to TCD SharePoint will be kept in a locked file for a period of 12 months.

A separate password protected file on TCD SharePoint will be made to store participants contact details and a third password protected file will be made to store pseudonymised demographics and kept until quarter 2 2026. After that point, the link between you and your personal data will be securely deleted.

What is the lawful (legal) basis to use my personal data?

We will only use your personal data for this research project which we hope will improve overall health care . This is in line with Article 6, 1 e and 9, 2 J of the GDPR. We will also ask for your consent as a requirement of Irish law (Health Research Regulations), but we do not rely on this as our legal basis under GDPR.

What are my rights under Data Protection law?

You are entitled to:

- object to our use of your personal data or any further use.
- request access to your personal data and to receive a copy of it.
- request inaccurate personal data be corrected or deleted.
- request restriction of our use of your personal data.
- request deletion of your personal data.

By law you can exercise the above rights in relation to your personal data, unless the request would make it impossible or very difficult to conduct the research. For example, if the study is about to be published then we may not be able to delete data as it would impact on the results.

You can exercise these rights by contacting your study research team or the Trinity College Data Protection Officer, Secretary's Office, Trinity College Dublin, Dublin 2, Ireland. Email: dataprotection@tcd.ie. Website: https://www.tcd.ie/dataprotection/

Part 3 - Approval, Organising and Funding

Has this study been approved by a research ethics committee?

Yes, this study has been approved by Research Ethics Committee (REC). Approval was granted on (INSERT DATE). An annual report will be provided to the REC and on completion of the study.

Who is organising and funding this study?

This study is being undertaken by Orla Crowley as part of her Masters project. This study is being completed as part of a The Trinity St James's Cancer Institute (TSJCI) and has been funded through the Cancer Research Stimulus Awards (CREST awards).

Will I be paid for taking part?

No, we are not paying you to take part in the study.

Part 4 - Future Research

Will my personal data be used in future studies?

No, your personal data will not be used in future studies.

Part 5 - Further Information

What happens if I change my mind?

Your participation in this study is voluntary and you can change your mind even if the study has started.

You do not have to give a reason for changing your mind. This will not affect your medical care/treatment in any way. If you would like to withdraw from the study, please contact the research team who can organise this for you. If you choose to withdraw from the study once it has started you can do so by leaving the focus group or exiting the team's call.

We will discuss with if you are happy for us to continue to use information about you (personal data) which has already been collected. If you do not consent to your personal data being retained for this study, we will delete any information that could identify you.

Please note that we will not be able to remove personal data which has been shared or pooled for use in publication before your request for deletion.

Who should I contact for information or concerns?

If you have any questions, contact:

Lead Researcher: Ms. Orla Crowley at ocrowley@tcd.ie

If you have any questions in relation to your rights under data protection law, you can contact the Data Protection Officer, Trinity College Dublin: Data Protection Officer, Secretary's Office, Trinity College Dublin, Dublin 2, Ireland. Email: dataprotection@tcd.ie. Website: https://www.tcd.ie/dataprotection/.

Under GDPR, if you are not satisfied with how your data is being processed, you have the right to raise a concern with the Office of the Data Protection Commission, 21 Fitzwilliam Square South, Dublin 2, Ireland. Website: www.dataprotection.ie

Part 6 - Next Steps

If you would like to take part in this study, we will ask you to contact the research team, and you will be asked to sign the Consent Form on the next page.

Thanks

Thank you for taking the time to read this Participant Information Leaflet.

You will be given a copy of this Leaflet and the signed Consent Form to keep. Please retain these in case they are needed for future reference.

Appendix 6- Interview guide

Interview Introduction

1. **Introduce yourself and the study** – Briefly explain the purpose of the research, emphasising the focus on understanding lifestyle factors in relation to cancer prevention –

"Hello everyone, my name is Orla Crowley and I'm here to facilitate today's discussion. Emer Guinan is my supervisor, and she is also present to observe and take notes today. This focus group is part of a research study aimed at understanding how lifestyle factors relate to cancer prevention, specifically for women with BRCA1/BRCA2 pathogenic gene variants. We're interested in learning about your experiences, knowledge, and thoughts on how lifestyle choices might impact cancer risk for people with these pathogenic gene variants. This conversation will help us understand what lifestyle practices you consider important and how they align with current cancer prevention guidelines. Anything discussed today will not impact on any of your future treatment and neither myself or Emer are actively involved in your medical care, any specific questions you might have in relation to your medical care can be discussed directly with the nurses at your family risk clinic "

2. **Ethical considerations** –explain how the data will be used and obtain consent for recording the interview.

"Before we start, I'd like to mention that today's discussion will be recorded to help with our analysis. Your responses will be kept confidential, and any personal identifying information will be removed. This research will be used for study purposes only. Your participation is voluntary, and you can choose to stop at any time. If anyone is uncomfortable and wishes to not participate you are free to leave!'

Interview Guide Topics:

1. **Knowledge and Understanding of BRCA Genes and Cancer Risk:**
    - "To start, can you share what you know about BRCA genes, and the cancer risks associated with them?"
    - "Has having a BRCA pathogenic gene variant influenced your lifestyle choices?"
    - "What do you think about the role of lifestyle factors—such as diet and exercise-in modifying cancer risk for people with BRCA1/BRCA2 Pathogenic gene variants?"
        - further prompt - 'Do you feel following a healthy lifestyle has any impact of cancer prevention'

2. **Awareness and Interpretation of WCRF Cancer Prevention Recommendations:**
    - "How many of you are familiar with the World Cancer Research Fund's cancer prevention guidelines?" – if they don't know them at this stage inform them of the recommendations.

- "What specific recommendations from these guidelines do you think are most important for women with BRCA1/BRCA2 pathogenic gene variants?"

3. **Lifestyle Habits and Practices:**
    - "Let's talk about diet. What do you believe a typical healthy diet looks like?"
        - Follow-up: "Are there any specific foods/food groups or supplements you personally avoid or include for health reasons?"
    - "How about physical activity? What would you consider a physically active lifestyle?"
        - Follow-up: "How often do you think people should engage in physical activities like walking, sports, or more formal exercise?"
    - "Do you drink alcohol? What do you consider a reasonable amount of alcohol consumption?"
        - Follow-up: "Has the idea of cancer prevention ever made you think about reducing alcohol? Why or why not?"
    - "Do any of you smoke/vape or have you ever smoked/vaped ?"
        - Follow-up: " What do you believe the impact of smoking/vaping is?"
    - "Are there any other health practices or routines you follow specifically because of your BRCA+ gene test result?"
        - Follow-up: "How did you decide to include these habits or routines in your lifestyle?"
4. **Motivations and Barriers**
    - "What motivates you to follow or not follow a healthy lifestyle / cancer prevention recommendation?"
    - "What challenges or barriers have you encountered in trying to follow the World Cancer Research Fund guidelines?"
        - Follow-up: "Are there specific social, financial, or personal obstacles that make it more difficult to follow these guidelines?"
5. **Outlook and Recommendations for Support**
    - "What kind of information or support would you find most useful in managing your cancer risk?"
        - Follow-up: "Are there any areas—such as diet, exercise, or mental health—where you feel like you could use more guidance?"
    - "If you could design a lifestyle support program specifically for women with pathogenic gene variants in BRCA1/BRCA2 genes, what would it look like?"
        - Follow-up: "How would you prefer to receive this information—through workshops, online resources, or one-on-one counselling?"

Closing

- Before we finish, does anyone have any additional thoughts on lifestyle factors and cancer prevention in relation to BRCA pathogenic gene variants?"
- "Is there anything we didn’t discuss today that you think is important for us to understand about your experience or perspective?"

Appendix 7 - Field notes

Supervisor notes from focus groups

Group1 :

25/04/15 Focus Group Notes

Attended by three ladies.

One lady had connection problems – falling in and out of the conversation.

First focus group – texted Orla to say to probe into their responses. Doing this more from their diet responses onwards

Show that you are listening – pick up on their responses – let them talk .

A little bit of engagement between the two ladies

Lady with connection issues jumped back in again around 20 minutes in.

Moving through the questions a little quick

Settled into the group setting much more after the first half hour

Appendix 8- Ethical approval

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Orla Crowley,
Discipline of Physiotherapy,
Trinity Centre for Health
Sciences, St James's
Hospital, Dublin 8.

20th February 2025

Ref: 250106
Title: Understanding the views of women with BRCA1/BRCA2 pathogenic gene varient s on lifestyle choices for cancer prevention.

Dear Orla,

Ethical approval for the above research study is now granted by the Faculty of Health Sciences Research Ethics Committee.

Please ensure that you comply with other relevant regulations, including Data Protection and Health and Safety Regulations.

Your sincerely,

Geraldine Foley

Dr Geraldine Foley
Chairperson

Faculty of Health Sciences Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie

Data Protection Impact Assessment (Health Research)

Instruction

Please complete **all six parts** of this document and forward the completed document to researchdpo@tcd.ie

You must title your email **'DATA PROTECTION IMPACT ASSESSMENT'**

You will need to receive feedback on any risks identified, recommendations on the actions or controls needed to address those risk and instruction before you progress with your ethics application.

It is the responsibility of the Research Supervisor / Supervisor / Principal Investigator to ensure that information provided in this document is accurate and of sufficient quality to enable the DPO's office to conduct an effective review.

An incomplete document will be returned without review.

Further information, training, guidance, policies, staff handbook, links and templates is available at https://www.tcd.ie/dataprotection/research/

DPIA Circulation

Name	Date	Reviewed/Consulted
Principle Investigator (PI) Details Orla Crowley		Submitted V.1
DPO Details Evelyn Fox	28.01.25	Reviewed/Advised on V.1 DPIA PIL And ICF
Orla Crowley	12.02.25	Reviewed V.1 to create v.2
Evelyn Fox	06.03.25	Reviewed/Advised on V.2 DPIA, PIL and ICF Orla confirmed that team members are working in an advisory role only

		These team members are working in an advisory role only. Only Orla Crowley, Emer Guinan and Diana Cooke will have access to data all who are full time students or staff of TCD.

Part 1 - Submission Information

RDPO Reference Number		
Title of study	Understanding the views of women with BRCA1/BRCA2 pathogenic gene variants on lifestyle choices for Cancer prevention.	
Trinity College School	School of Medicine	
Date of Submission		
Completed by	Orla Crowley and Dr Emer Guinan	
Supervisor / Principle Investigator (if not Researcher named above)	Dr Emer Guinan	
Email address	Ocrowley@tcd.ie	
Please tick **all** that apply	☐ Student Project ☒ Masters ☐ PhD	☒ Staff Project ☒ Funded ☐ Non-Funded
Description of study	This study aims to explore the views and experiences of women with inherited pathogenic gene variants s (PVs) in the BRCA1 and BRCA2 genes regarding lifestyle factors for cancer prevention, such as diet, exercise, alcohol consumption, and smoking habits. Given the increased risk of breast, ovarian, and other cancers in individuals with BRCA1/BRCA2 PVs, understanding how these women perceive and implement lifestyle modifications based on evidence-based World Cancer Research Fund (WCRF) recommendations is crucial. This qualitative study will collect data using focus group discussions which aims to gain insights into: 1. Awareness and understanding: How well do these women understand the relationship between lifestyle factors and cancer risk, and are they familiar with WCRF's recommendations for cancer prevention? 2.Adherence: To what extent are women with BRCA1/BRCA2 PVs following recommended lifestyle changes, and what factors influence their adherence to these guidelines? 3.Barriers and motivations: What personal, social, or environmental factors prevent them from adopting healthier lifestyle	

	choices, and what motivates them to make or maintain changes in their diet, physical activity, and other behaviours? The study will aim to include 20-25 women, aged 18 and older, who have inherited a BRCA1 or BRCA2 pathogenic gene variants with no prior cancer history. Recruitment will target individuals representing a diverse range of ages, backgrounds, and experiences. The goal is to identify potential gaps in knowledge or areas where interventions may be needed to improve adherence to lifestyle changes that could help reduce cancer risk in this high-risk population. Ultimately, this research aims to provide valuable insights that can help healthcare providers and public health organizations better support women with BRCA1/BRCA2 PVs in making lifestyle changes to potentially reduce cancer risk.

Part 2 - Data Protection Information

1. Provide details of data protection training completed by research team members. Attach certificates of successful module completion	Research Integrity and Impact in an Open Scholarship Era (CA7000) module RIO: Research Integrity and Impact in an Open Scholarship Era Trinity College Data Protection Training (GDPR) Module - Blackboard HSeLanD - Fundamentals of GDPR training Other (provide detail)
2. Are all researchers familiar with the Trinity College Personal Data Breach Procedural Guidelines?	☒ Yes ☐ No
3. Site of data collection	Demographic details will be collected over the phone in advance of focus groups. Data will be entered directly onto the study database stored on TCD SharePoint. Participant name Contact details (address, telephone number) Age County of residence Educational level Marital status/ Dependants Age when they learned of their BRCA gene alteration Focus group data

	Focus group discussions will be held online (x2) and in-person (x1). All will be recorded on TCD Microsoft TEAMS and automatically transcribed. The in-person focus group will take place in the Trinity Centre for Health Sciences at St James's Hospital.
4. What is Trinity's role in respect of the study?	☒ Data controller ☐ Joint data controller ☐ Data processor
5. If Trinity College is a joint data controller, provide detail of the other joint controllers and their Data Protection Officer contact details	TCD is the sole data controller. Orla Crowley is the lead researcher and will collect and manage all data. Dr Emer Guinan is the MSc supervisor and will have access to data for academic oversight. Ms Diana Cooke will code pseudonymised transcripts generated from the focus groups. The other members of the research team are: Dr Jenny Groake, University of Galway. Dr Karen Cadoo, St James Hospital. Ms Kelly Coghlan-Lynch, St James Hospital. Dr Niamh Coleman, St James Hospital. Ms Elizabeth Connolly, St James Hospital. Dr Sarah McGarrigle, St James Hospital. Ms Yvonne Hanhauser, St James Hospital. These team members are working with the team in a scientific and advisory capacity. They have supported protocol development and will support interpretation and dissemination of aggregated results. They will have no access to personal data collected as part of this study.
6. Number of individual participants, or anticipated numbers	25
7. Type of participant (i.e. students, staff, patients, healthcare workers etc.)	Women diagnosed as carriers of a pathogenic gene variant in the BRCA1 or BRCA2 genes who are over the age of 18 years and have no history of cancer.

	As carriers of the BRCA 1 or BRCA 2 pathogenic gene variant , these women have an elevated risk of developing certain cancer types but are otherwise healthy.
8. Is the study considered as health research?	☒ Yes ☐ No
9. List the personal data and /or special category data that will be processed for the study For example: Name, email address, interview recordings, transcripts, video recordings, health records, ethnicity, political beliefs, religion	Participant name Contact details (address, telephone number) Age County of residence Educational level Marital status/Dependants Age when they learned of their BRCA gene alteration Focus group data
10. How often will you need to collect data?	Demographic data will be collected during a pre-focus group phone call. Focus group data will be collected during one focus group per participant.
11. Describe where and how the data will be processed / stored and if data will be shared internally For example: Cloud software (Trinity College Microsoft OneDrive, Teams, SharePoint), server in a data centre in Ireland, desktop / laptop of researcher (personal, College-issued), external hard drive / USB drive, paper files stored in secure room in hospital / office etc.	Orla Crowley the lead investigator will have responsibility for data collation, data quality, storage and backup. All data will be stored securely on TCD SharePoint with access restricted to the lead investigator Orla Crowley and supervisor Dr Emer Guinan. Additionally, Diana Cooke will have access to pseudonymised focus group transcripts for analysis. Participant ID An excel file listing participant IDs to participant names will be stored on password protected file on TCD SharePoint with access restricted to Orla Crowley only. This file will be deleted in when the Ms Orla Crowley's thesis is fully examined and approved (Quarter2 2026). Backups are managed by TCD IT Services via Office 365 within the EU. Written Consent Written consent will be collected on paper forms. These forms will be scanned and uploaded to a password protected file on TCD SharePoint in a file

	separate to data files. Paper copies will be destroyed immediately after scanning. Consent forms will be stored until Ms Orla Crowley's thesis is fully examined and approved (Quarter2 2026). Backups are managed by TCD IT Services via Office 365 within the EU. Participant contact details (phone number, address) An excel file listing participant contact details will be stored on password protected file on TCD SharePoint with access restricted to Orla Crowley only. This file will be pseudonymised. This file will be deleted in December 2025. Backups are managed by TCD IT Services via Office 365 within the EU. Study Database Contains the following demographic details: age, county of residence, educational level, marital status and the age when you learned of your BRCA gene alteration. All study data will be stored on the Trinity network drive (MS SharePoint) and access restricted to lead investigator Orla Crowley and supervisor Dr Emer Guinan. This file will use the pseudonymised study codes only. This file will be deleted in when the Ms Orla Crowley's thesis is fully examined and approved (Quarter2 2026). Backups are managed by TCD IT Services via Office 365 within the EU. Audio Recordings Focus group discussions will be recorded and transcribed on Microsoft Teams on the TCD network drive. Focus group transcription will be reviewed for accuracy and pseudonymised within one month of the focus group being completed. At that point the recording will be deleted, and the focus group analysed. Pseudonymised transcripts will be stored in a Word file on TCD SharePoint. Access will be granted to Ms Diana Cooke through her TCD account. These files will be deleted in when the Ms Orla Crowley's thesis is fully examined and approved (Quarter2 2026).

12. Provide a general description of the security measures in place to keep data secure. For example: Multi factor authentication, use of passwords, use of VPN, device encryption, vendor ISO certification, anti-virus used, use of secure file transfers such as HEAnet, detail on how data is backed up etc.	During the research, all materials produced from this study will be stored on an excel file on TCD SharePoint accessible to the lead researcher and supervisor only. On completion of the study, the key file containing identifiers will be destroyed. This will occur after the lead researchers' MSc thesis has been corrected and results finalised (expected in quarter 2 2026) Hard copy data (consent forms) will be scanned and uploaded to a password protected file on TCD SharePoint in a file separate to data files. Paper copies will be destroyed immediately after scanning. Soft copy personal data will be stored on TCD provided systems i.e. Microsoft Office 365 which requires two factor authentication, a unique user ID and strong password. The researcher will comply with the TCD policies and procedures. In addition, information stored on TCD provided SharePoint requires permission from the site owner to access files/folders. Virtual Private Network (VPN) is installed on the laptop and will be used. Where research data is retained on TCD provided SharePoint, permissions will be granted by the site owner Dr Emer Guinan. Electronic copies of data are automatically backed up by IT systems. Up to date anti-virus software is in place. The master key to the code to participant's identity will be retained securely and separate to the other research data under the control of the PI. The master key file will not contain the contact details of the participants.
13. Is the data shared with any third-party organisation, including commercial entities?	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail. For example: the type of data being shared (description of the data), the reason for sharing, the format of the data that will be shared (i.e., whether identifiable, coded, or anonymous), the security measures in place to protect the data in transit and on receipt etc. Specify if the third party is a data controller, data processor or joint controller(s).	

Include data flowcharts if possible.	
14. Will the data be transferred outside of the UK & EEA?	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail on which country. Please name the organisation you are transferring to.	
15. How long will the data be retained in an identifiable or coded format?	The file linking participant IDs to names and hospital number will be deleted in quarter 2 2026. The study database will be destroyed in quarter 2 2026. Scanned copies of consent forms will be stored on TCD SharePoint. These will be deleted by Dr Emer Guinan in quarter 2 2026.

Part 3 - Screening

The specific criteria listed below are those which are considered by the Data Protection Commission to represent a higher risk to individuals' data protection and privacy rights.

Please mark 'Yes' or 'No' for each of the following as listed.

Does your research involve any of the following:

1. The use of sensitive or special categories of data. For example, data concerning a person's health, genetic data, biometric data, ethnicity, political opinions, data concerning a natural person's sex life or sexual orientation, data relating to criminal convictions.	☒ Yes ☐ No
If you have answered 'Yes' to the previous question, provide further detail. Yes, health data will be collected. Specifically, participants will be asked to self-report their age, county of residence, educational level, marital status and the age when you learned of your BRCA gene alteration.	
2. The secondary use of personal data e.g. information being taken from medical records or another database for use in a research project.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
3. The use of data concerning vulnerable individuals. For example, children (anyone under 18 years), employees, patients, people with an intellectual disability, the elderly, the mentally ill, asylum seekers, or in any case where a	☐ Yes ☒ No

power imbalance in the relationship between the position of the participant and the researcher can be identified.	
If you have answered 'Yes' to the previous question, provide further detail.	
4. Topics that could be considered particularly intrusive or sensitive in nature.	☒ Yes ☐ No
If you have answered 'Yes' to the previous question, provide further detail. We will be discussion cancer risk with people at an elevated risk of cancer. Their elevated risk is genetic so they may have personal experiences of their family experiencing or dying from cancer. We need to be sensitive to that fact during the focus group discussions.	
5. Data processing on a large scale, either as a specific number or as a proportion of the relevant population, or due to the range of different data items needed, or due to the duration or longitudinal effect of the research, or where it occurs over a large geographical area.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
6. Matching, linking, cross referencing or combining two or more separate datasets. For example, enriching datasets by using additional data sources to provide further information regarding the individuals in a research study.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
7. Systematic monitoring, i.e., data processing to observe, monitor or control individuals, including data collected through systematic monitoring of a publicly accessible area. For example, collecting patient-related data at hospital level to understand bed occupancy, CCTV, GPS tracking etc.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
8. Evaluation or scoring, including profiling individuals. For example, predicting outcomes in individuals based on their economic situation or performance at work, behaviours, health, preferences etc.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
9. Automated decision-making which results in legal or similar significant effect. For example, a recruitment aptitude test which uses pre-programmed algorithms and criteria leading to the exclusion or discrimination of individuals etc.	☐ Yes ☒ No

If you have answered 'Yes' to the previous question, provide further detail.	
10. Innovative use or application of new technological or organisational solutions. For example, machine learning, artificial intelligence, sentiment analysis etc.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	
11. Use of biometric data (fingerprint and face recognition, gait analysis) to uniquely identify an individual.	☐ Yes ☒ No
If you have answered 'Yes' to the previous question, provide further detail.	

Part 4 - GDPR Principles

In order to evidence that you have considered each of the GDPR Principles please respond to each of the questions listed below:

4.1 - Transparency of Processing
There are no exemptions under GDPR to transparency obligations towards participants

Please attach your Participant Information Leaflet and Consent Form and any Invitation Letter, Privacy Notices, Privacy Policies, Data Protection Statements etc. that you have drafted.

Please use the TCD provided Participant Information Leaflet and Consent Form templates available **here.** These have been drafted to comply with the requirements of the GDPR and the Health Research Regulations ('HRR').

1. Are you using the Trinity College Dublin approved templates? Please note that any use of templates which are out of date or not approved by the DPO's office will delay your application.	☒ Yes ☐ No
If you have answered 'No', please outline why you are using a different template. For further details on information that should be provided to participants please see Article 13 GDPR	
2. Is your Participant Information Leaflet (PIL) And Informed Consent Form (ICF) tailored to your audience in easy-to-read language? Please note that all PILs and ICFs should be tailored to their audience (i.e. patient, healthcare worker, child) and any adult PILs should be drafted to the reading age of a 12-year-old.	☒ Yes ☐ No
Provide detail	

4.2 - Data Minimisation

1. Do you need all of the personal data listed in Part 2 for your research project or could some variables be removed without compromising your project?
Yes, the researcher has carefully considered the personal data to be collected for this research and all the personal data listed in Part 2 above is required to accurately describe the demographic characteristics of the sample and to meet the aims and objectives of the research study.

4.3 - Purpose Limitation

1. What is the purpose of your research project? Please consider this from the perspective of the participant – What are you doing with their data and why.
There is considerable evidence that certain lifestyle factors including maintaining a healthy body weight, exercising and making certain dietary choices, can alter the risk of a breast cancer developing in the general population. The impact of these factors in women who already have an elevated risk due to carrying BRCA1/2 genes is unknown however cancer prevention strategies such as maintaining a healthy lifestyle are important aspects of counselling this group. However, given that this group have an elevated cancer risk and are highly likely to bring family experiences of cancer to their decision making, how they perceive this lifestyle advice may be very different. We want to explore that through focus group discussion so that we can plan interventions/future programmes that are more effective at tailoring this advice to the concerns of this cohort.

4.4 - Data Quality

1. How are you ensuring that information obtained from other organisations is accurate? (if applicable)	☒ N/A or Provide detail
2. How will the data you collect be kept accurate, consistent and up to date?	Demographic data will be entered immediately into the database and is kept to a minimum which will reduce the risk of error. Focus groups will be automatically transcribed by TCD Microsoft TEAMS and verified before pseudonymisation.
3. What controls do you have to determine when the data has been altered, disclosed or erased, and by whom?	The research database will only be accessible on TCD systems by Orla Crowley and Emer Guinan. An access log will be maintained to document if data is altered or erased.

4.5 - Lawful and Fair Processing

Lawful Basis for processing Ordinary Personal Data

Please tick which Article 6 GDPR lawful (legal) basis applies to your research project.

Consent (required by parent/guardian if children under the age of 18 are taking part)	☐
Public interest or exercise of official authority **(Recommended for University research)**	☒
Legitimate interests (if collaborating with a company)	☐

Condition for processing Special Category Data (Sensitive Personal Data)
If you are also processing special category personal data then, in addition to the Article 6 lawful basis, you must also satisfy one of the conditions as set out under Article 9 GDPR. Please tick which condition applies.

Explicit Consent (required by parent/guardian if children under the age of 18 are taking part)	☐
Information that has been already made public by data subject	☐
Archiving purposes in the public interest/ Scientific or Historical Research purposes / Statistical purposes (Recommended for University research)	☒

4.6 - Data Storage and Data Security
In addition to the information that you have provided in Parts 1 to 3 above, please provide further detail on the following:

1. When will the key to re-identify participants be deleted? (where applicable) Please consider that data should be stored as long as necessary but as short as possible. If data is to be kept longer, there should be periodic review to ensure it is still necessary.	An excel file listing participant IDs to participant names will be stored on password protected file on TCD SharePoint with access restricted to Orla Crowley only. This file will be deleted in when the Ms Orla Crowley's thesis is fully examined and approved (Quarter2 2026). Backups are managed by TCD IT Services via Office 365 within the EU.

2. Are you using any software or applications to collect or analyse data?	☒ Yes ☐ No If yes, provide detail: ☒ MS Teams ☐ Zoom ☐ SurveyMonkey ☐ Qualtrics ☐ SPSS ☐ Python ☐ Other – provide detail NVIVO available through TCD systems
3. What access controls do you have in place to safeguard project data? (role or location) • If role-based access, provide information on the role(s) that can access data • If location-based access, what physical security measures are in place? (e.g. locked doors, swiped access, locked cabinets) • Indicate how events are logged and how long this log is kept	During the research, all data and documentation will be stored on the Trinity network drive (MS SharePoint) and access restricted to the lead investigator and supervisor. Data analysis will be completed on TCD systems (TCD SharePoint, TCD NVIVO license for qualitative analysis). No paper-based forms will be used. Demographic data will be immediately entered onto the study database on TCD SharePoint. Written consent will be collected on paper forms. These forms will be scanned and uploaded to a password protected file on TCD SharePoint in a file separate to data files. Paper copies will be destroyed immediately after scanning.

4.7 Data Subject Rights

Participants have rights in relation to their personal data. These are set out under Chapter 3 of the GDPR

1. How will you action requests from individuals (or someone acting on their behalf) for access / amendment / restriction to the use of their personal data?	Any requests received from a data subject to exercise their rights will be forwarded without delay to the DPO. Personal data will only be used for this research project. If participants require access to their data they are advised to contact the lead investigator Orla Crowley. They may access focus group transcripts up to 1 month after the focus group. This is explicitly stated on the PIL.

	Data can be accessed through Subject Access Request (SAR).
2. Do you have a procedure in place if an individual wishes to withdraw their consent to take part in the study, and wishes no further use of their personal data?	The following statement is included on the PIL: Your participation in this study is voluntary and you can change your mind even if the study has started. You do not have to give a reason for changing your mind. This will not affect your medical care/treatment in any way. If you would like to withdraw from the study, please contact the research team who can organise this for you. We will discuss with if you are happy for us to continue to use information about you (personal data) which has already been collected. If you do not consent to your personal data being retained for this study, we will delete any information that could identify you. Please note that we will not be able to remove personal data which has been shared or pooled for use in publication before your request for deletion.
3. Are there any limitations on participants rights? For example, their right to withdraw might be restricted if you are about to publish. Are any restrictions clear to participants from your information leaflet?	The following statement is included on the PIL: Please note that we will not be able to remove personal data which has been shared or pooled for use in publication before your request for deletion. The following is also stated The research data, i.e., coded transcripts, will be retained for a period of 12 months from the date of focus groups, until quarter 2 2026 approximately. Consent forms will be scanned to TCD SharePoint and hardcopies shredded immediately. Online copies scanned to TCD SharePoint will be kept in a locked file for a period of 12 months. A separate password protected file on TCD SharePoint will be made to store participants contact details and a third password protected file will be made to store pseudonymised demographics and kept until quarter 2 2026. After that point, the link between you and your personal data will be securely deleted.

Part 5 - Data Protection Checklist for Health Research

As your project relates to health research, then you must comply with the requirements of the Health Research Regulations 2018 (as amended).

If you intend to seek a Public Interest Waiver from the Health Research Consent Declaration Committee (HRCDC) please review the guidance notes which are available to download from the HRCDC website before proceeding further.

Any submission to the HRCDC must be reviewed in advance by the RDPO at researchdpo@tcd.ie

Please complete the Y/N boxes below and provide detail as appropriate

Checklist – Have you completed the following?		**Detail**
Obtain ethical approval for the health research by a research ethics committee Regulation 3 (b) (i);	Y	Trinity College Dublin Faculty of Health Sciences REC Meetings scheduled on 28 January 2025
Identify and document the data controller, joint controllers and data processors Regulation 3 (b) (ii) (iii) (iv);	Y	Trinity College Dublin is the data controller
Ensure relevant contractual arrangements are in place. Regulation 3 (b) (iii), Article 26 GDPR and Article 28 GDPR.	′/N	Not applicable
Identify and document funding bodies or any other organisation that supports the project. Regulation 3 (b) (v);	Y	This study is being completed as part of a The Trinity St James's Cancer Institute (TSJCI) and has been funded through the **C**ancer Research Stimulus Awards (CREST awards).
Identify third parties with whom data will be shared even if pseudonymised and/or anonymised. Regulation 3 (b) (vi);	′/N	All study data will be stored on the Trinity network drive (MS SharePoint) and access restricted to lead investigator Orla Crowley and supervisor Dr Emer Guinan. Diana Cooke will have access to pseudonymised transcripts only.

Ensure all members of the research team have completed data protection training Regulation 3 (b) (vii) and Article 32 GDPR	Y	As per Part 2 above (training)
Ensure you only use the minimum data necessary to carry out the research. Regulation 3 (c) (iii) and Article 5 (1) (c) of the GDPR ;	Y	As Per Part 2 above (Data Minimisation)
Implement controls to limit the access to the personal data and controls to log whether and by whom the data has been consulted, altered, disclosed or erased and by whom. Regulation 3 (c) (iv); and (v) and Article 28 GDPR	Y	As per Part 2 above (Data Security) and Part II.
Implement security measures to protect the personal data Regulation 3 (vi)and (viii) and Article 32 GDPR	Y	As per Part 2 above (Data Security) and Part II.
Arrangements to anonymise, archive or destroyed when the research has been completed. Regulation 3 (c) (vii) and Article 5 (1) (e)	Y	See Part 2 (Data Storage)
Ensure arrangements in place to ensure data is processed in a transparent manner Regulation 3 (d) and Article 5 (1) (a) GDPR	Y	See PIL and ICF and Section A. (Transparency)
Obtain explicit consent for the processing of personal data for the health research, recorded and retained by the controller, and a copy of which is provided to the data subject prior to the commencement of the health research in accordance with international best practice on the ethical conduct of health research (which includes informed consent, transparency and independent ethical oversight) for the processing of his or her personal data for the purpose of specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof. Regulation 3 (e) as amended	Y	As per Section A (Purpose Limitation) and in line with PIL And ICF

Part 6 - Processing Risks

Describe the source of risk and nature of potential impact on individuals as well as implemented or suggested solutions / mitigating actions.

Include associated Compliance and Corporate risks as necessary. It is common to use a RAG matrix rating system for assessing risk. RAG stands for red, amber, green. To achieve a RAG rating, each risk first needs . likelihood and impact score. Each risk will be RAG rated by taking the likelihood and impact scores and using the matrix below.

Impact	Likelihood				
	1 - Rare	2 - Unlikely	3 - Possible	4 - Likely	5 – Highly Likely
1 - Negligible	1	2	3	4	5
2 - Minor	2	4	6	8	10
3 - Moderate	3	6	9	12	15
4 - Major	4	8	12	16	20
5 - Critical	5	10	15	20	25

Risks to individuals - Examples

- Hacking of computers where study data is stored.
- The context in which information is used or disclosed can change over time, leading to it being used for different purposes without people's knowledge.
- Incorrect or overuse of individuals' data.
- Lack of transparency, fairness or lawfulness of processing activities.
- Failure to explain effectively how data would be used.
- New surveillance methods may be an unjustified intrusion on their privacy.
- Measures taken against individuals as a result of collecting information about them might be seen as intrusive.
- Personal data being used for automated decision making may be seen as excessively intrusive.
- The sharing and merging of datasets can allow organisations to collect a much wider set of information than individuals might expect.
- Identifiers might be collected and linked which prevent people from using a service anonymously.
- Vulnerable people may be particularly concerned about the risks of identification or the disclosure of information.
- Collecting information and linking identifiers might mean that an organisation is no longer using information which is safely anonymised.
- Anonymisation techniques chosen may turn out to be ineffective.
- Use of technology capable of making visual or audio recording may be unacceptably intrusive.
- Information, which is collected and stored unnecessarily, or is not properly managed so that duplicate records are created, presents a greater security risk.

- If a retention period is not established information might be used for longer than necessary.

Compliance risks

- Non-compliance with the common law duty of confidentiality.
- Non-compliance with the Data Protection Acts 1988- 2018/ General Data Protection Regulation (GDPR), Privacy and Electronic Communications Regulations (PECR).

Associated organisation / corporate risks

- Non-compliance with the data protection or other legislation can lead to sanctions, fines and reputational damage.
- Failure to adequately conduct a DPIA where appropriate can itself be a breach of the GDPR.
- Data breaches regarding privacy and personal data are likely to cause reputational risk to the University.
- Problems which are only identified after the study has commenced are more likely to require expensive fixes.
- The use of biometric information or potentially intrusive tracking technologies may cause increased concern and cause people to avoid engaging with Trinity College.
- Public distrust about how information is used can damage Trinity's reputation and lead to a reluctance on the part of individuals to trust us, and to take part in our research projects.
- Data losses which damage individuals could lead to claims for compensation.
- Problems with data protection in the research project design identified late in the design process, or after completion, may be expensive and cumbersome to fix.
- Unnecessary processing and retention of information can also leave you at risk of non-compliance with the GDPR.
- Any harm caused to individuals by reason of mishandling of personal data may lead to claims for compensation against the University.

Different projects carry different risks, and these should be considered. The above examples are a guide, not an exhaustive list.

Processing Risks - Table

Describe the source of risk and nature of potential impact on individuals as well as implemented or suggested solutions / mitigating actions.

Delete examples if not appropriate to your project and include any other risks that you have identified that are not included as examples.

Use the RAG matrix above to help calculate the risk.

Risk detail	**Risk likelihood (1 – 5)**	**Risk severity (1 – 5)**	**Risk score (1 – 25)**	**Solutions / Mitigating Actions**	**Solutions / Mitigating actions implemented?**	**Residual risk (Unchanged / Reduced / Eliminated)**	**New score**
Breach of data held electronically by “hackers	4	. 4	16	All files will be stored on TCD SharePoint in password protected files with access restricted to team members who require it in line with TCD policies. Access to TCD provided systems requires two factor authentication, a unique user ID and strong password. Access to TCD provided SharePoint also requires permission from the site owner to access files. The PI will comply with TCD policies and procedures. The master key to the codes to identify participants will be stored securely and separately to other research data and will not include either the participant’s MRN or contact details.	Yes	Reduced	. 8
Data may be kept longer than required in the absence of appropriate policies.	3	4	12	The research data will be retained until quarter 2 2026. At that point, the link between participants and their personal data will be securely deleted. Consent form will be retained until quarter 2 2026.	Yes	Reduced	4

				At this point, we anticipate that Orla Crowley's thesis will be submitted, examined and approved and therefore further access to the data will not be required.			
Information, which is collected and stored unnecessarily, or is not properly managed, so that duplicate records are created, presents a greater security risk.	3	4	12	Data containing patient identifiers will be Stored on a password protected file on TCD Sharepoint. Written consent will be collected on paper forms. These forms will be scanned and uploaded to a password protected file on TCD Sharepoint in a file separate to data files. Paper copies will be destroyed immediately after scanning. Consent forms will be stored for 1 year and not shared with anyone. Demographic data will be immediately entered to the study database which will be an excel file stored on TCD Sharepoint.	Yes	Reduced	6
Non-compliance with the common law duty of confidentiality.	3	4	12	Information and consent forms will explicitly inform participants that their data will be kept confidential but will emphasise the statutory limitations of confidentiality. Confidentiality may be breached in circumstances in which the research team has a strong belief or evidence exists that there is a serious risk of harm or danger to either the participant or another person. Disclosure may be required as part of a legal process or Garda investigation. In such instances, information may be disclosed to significant others or appropriate third parties without permission being sought from the participant. Where possible, a full explanation will be given to the participant regarding the necessary procedures and also the intended actions that may need to be taken.	Yes	Reduced	6

The context in which information is used or disclosed can change over time, leading to it being used for different purposes without participant's knowledge.	2	4	8	Participant's data will only be used for the purpose of this study as outlined in the PIL. PIL will make participants aware of how data is processed.	Yes	Reduced	4
Inappropriate disclosure of personal data internally within your organisation due to a lack of appropriate controls being in place.	3	4	15	Access is restricted to designated staff only which include lead researcher Orla Crowley and research supervisor DR Emer Guinan. Diana Cooke will have access to pseudonymised transcripts only. Only TCD approved systems will be used for sharing of information internally.	Yes	Reduced	4
Accidental loss of electronic equipment by organisation's personnel may lead to risk of disclosure of personal information to third parties.	**3**	**5**	**15**	**Data containing patient identifiers will be processed in a password protected file on TCD SharePoint.** **Written consent will be collected on paper forms. These forms will be scanned and uploaded to a password protected file on TCD SharePoint in a file separate to data files. Paper copies will be destroyed immediately after scanning. Consent forms will be stored until quarter 2 2026 and not shared with anyone. Demographic data will be immediately entered to the study database which will be an excel file stored on TCD SharePoint.**	**Yes**	**Reduced**	**8**
Vulnerable individuals or individuals about whom sensitive data is kept might be affected to a very high degree by inappropriate disclosure of personal data.	**3**	**5**	**15**	All computers storing data will be encrypted. Access is restricted to designated staff only. Access is via 2FA. Key code is kept separately to research data to mitigate any inappropriate disclosure. Access is restricted to lead research Orla Crowley and research supervisor Dr Emer Guinan.	**Yes**	**Reduced**	**8**
Personal data being used in a manner not anticipated by data subjects due to an evolution in the nature of the project.	**2**	**4**	**8**	PIL will ensure that individuals are fully informed about how their information will be used. Personal date will not be used for any other purpose other than those stated in the PIL	**Yes**	**Reduced**	**6**

Information released in anonymised form might lead to disclosure of personal data if anonymisation techniques chosen to turn out not to be effective.	**3**	**4**	**12**	All study data will be stored on the Trinity network drive (MS SharePoint) and access restricted to lead investigator Orla Crowley and supervisor Dr Emer Guinan. Diana Cooke will have access to pseudonymised transcripts only. This file will use the pseudonymised study codes only. The master key to the code to participant's identity will be retained securely and separate to the other research data under the control of the PI. The master key file will not contain the contact details of the participants	**Yes**	**Reduced**	**8**
Personal data being used for purposes not expected by data subjects due to failure to explain effectively how their data would be used.	**3**	**4**	**12**	PIL will ensure that individuals are fully informed about how their information will be used.	**Yes**	**Reduced**	**8**
Data unnecessary for the project may be collected if appropriate policies not in place, leading to unnecessary risks.	**2**	**4**	**8**	**Only minimal data is collected. All data is necessary for the project and has to be justified in the DPIA.**	**Yes**	**Reduced**	**6**

DPO Feedback

DPO – comments / feedback on information provided
1. Main query is around number of applicants which is unusual for a Masters' project. PI to confirm why so many and what their role is and whether they are all TCD employees. Thanks
06.03.25 RESOLVED. PI response explains this (included for the record) This project is funded by a TSJCI CREST award which promotes collaboration between academics and clinicians. We are using the CREST funds to pay for the fees for Orla's MSc. Therefore, we are in the fortunate position to have a wide team of collaborators working with us and advising on the project,
2.
3.
4.
5.
6.

Disclaimer

This material contained in this template contains general information and guidance only. Please note that this guidance does not constitute legal advice and is provided for general purposes only. Neither is it intended to provide a comprehensive or detailed statement of the law.

No liability whatsoever is accepted by Trinity College Dublin, the University of Dublin for any action taken in reliance on the information contained in this guidance. You should not act, or refrain from acting, on the basis of any information provided in this document. Rather, you should always seek specific legal or other professional advice. Any and all information is subject to change without notice.

Template Version Control

Reference	Date	Author
Version 4.0	November 2023	Trinity College RDPO, DP Executive, DPO

Appendix 10- Consent form

CONSENT FORM

STUDY: Understanding the views of women with BRCA1/BRCA2 pathogenic gene variants on lifestyle choices for cancer prevention.

Recruitment Site: Trinity College Dublin

Principal Investigator Name and Contact details: Ms Orla Crowley – OCROWLEY@TCD.IE / 01 410 3848

There are **three sections** in this form.

Section 1 contains statements of understanding and asks you to tick each if you understand. Please ask any questions you may have when reading each of the statements.

Section 2 asks for your consent for this study. Please select either 'yes' or 'no' to indicate your choice.

Thank you for participating.

The end of this form is for the researchers to complete.

1. General Understanding	**Tick**
I confirm that I have read and understood the Information Leaflet for the above study. The information has been fully explained to me, and I have been able to ask questions, all of which have been answered to my satisfaction.	
I understand that taking part in this study is entirely voluntary. I understand that not taking part will have no negative impact on me.	
I understand that I can leave this study at any time without giving a reason. I understand that leaving this study will not affect my medical care, now or in the future.	
I understand that I will not be paid for taking part in this study or receive any benefits from any products developed as a result of this research study.	
I know how to contact the research team if I need to. (Contact details above)	
By ticking each box above, choosing my options below and signing this document I agree to participate in this study as described in the Participant Information Leaflet.	
2. Consent	
I agree to take part in this research study, having been fully informed of the risks and benefits in the participant information leaflet provided to me.	**Yes** ☐ **No** ☐

I agree to the use of information collected for this study including information and recordings from focus group meetings as described in the participant information leaflet.	**Yes** **No**

_____

Participant Name (Block Capitals) Participant Signature Date

_____

To be completed by the Principal Investigator or nominee.

I, the undersigned, have taken the time to fully explain to the above participant the nature and purpose of this study in a way that they could understand.

I have explained the risks and possible benefits involved. I have invited them to ask questions on any aspect of the study that concerned them.

I have given a copy of the participant information leaflet and consent form to the participant with contact details of the study team.

Researcher name _____

Title and qualifications _____

Signature _____

Date _____

Copies to be created and retained: 1 for Participant and 1 for PI.

Appendix 11- Code book

Theme	Subthemes	Codes
Challenges in Accessing and interpreting information: The BRCA1 and BRCA2 experience	Insufficient medical guidance and need for a liaison figure	Surgical decisions framed by medical preference Government level information Messaging/ framing wording Limited discussions of options Need for liaison person Clearer information from outset Lack of reliable information Mismatch information from medical professionals Lack of pathway
	Absence of BRCA specific resources	General information influence General advice not BRCA specific falling between diagnostic categories desire for group/in person information sessions
	Turning to online support/resources	Self-directed research public awareness Charities Tracker apps Peer support groups Social media Awareness of social media trends Social role
Drivers of Behaviour change	Looking towards the future	Longevity Perceived value of health investment Health planning Surgical planning Fertility/ children as a purpose
	The Challenges with risk reducing surgeries	Risk reducing surgery Cancer risk/prevention Awareness of menopause

		Menopause Consequences of risk reducing surgery Redundancy of risk factors with genetic risk
	Life and Social factors as motivators and barriers	Lack of planning Children Time as a facilitator Competing responsibilities Cost Comorbidities Time constraints Routine
	Balancing control versus inevitability	Control over life Mental health Stress management Grief Family history Guilt re lifestyle choices Behaviour intention gap Risk perception Personal experiences
Additional codes :	Identity changes following risk reducing mastectomy Body image post-surgery Complementary therapies Distrust in food systems/ marketing	