An Investigation on the Irish Population's Attitudes and Knowledge Towards Genetic Screening for Cancer

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ABSTRACT

Genetic mutations are alterations in DNA that may result in the development of a disease later in life. A BRCA gene is a tumour suppressor gene that helps to prevent the development of some cancers, particularly breast cancer. If a mutation occurs, this gene no longer functions at preventing these cancers. Genetic screening is when a population is tested for a mutation in an attempt to identify a group of people that are positive for the mutation. This can help identify cancer in different populations as well as track their inheritance. This study was conducted online, questioning the Irish populations opinions on how a genetic mutation would alter their life. Topics covered included having children, illness prevention therapies if a mutation were discovered, and what impact would a mutation have on their life. Comparisons were made between genders, and age groups to demonstrate if differences of opinions exist between each group selected was compared with the overall attitude of the population. It was discovered that there was an overall difference of opinion between the different age groups, but in some questions like the ones regarding children, the opinions were similar. In this study, an investigation was conducted regarding the Irish population's attitudes and existing knowledge towards genetic screening and how testing positive for a genetic mutation, specifically in either the BRCA1 or BRCA2 gene, would influence lifestyle choices.

KEYWORDS: BRCA, gene, mutation, cancer, Ireland, genetic screening

INTRODUCTION

BRCA1 and BRCA2 are tumour suppressor genes whose normal function is to prevent the over-proliferation of cells resulting in tumour growth. The BRCA gene's normal functions are to encode the proteins that are responsible for repairing DNA double strands if they become separated. A mutation causes these repairs to occur incorrectly which can cause disease-causing errors in the DNA sequence resulting in the over proliferation of cells and tumour growth (Stoppa-Lyonnet, 2016). BRCA1 and BRCA2 mutations are hereditary which means they are passed from generation to generation in a bloodline and studies have shown that there is a 50% chance the mutation will be passed down to children if the parent has the BRCA mutation. Both men and women can have the BRCA gene mutation and those carrying a mutation in either gene have a significantly higher risk of developing a number of different cancers.

The most commonly associated cancer with BRCA gene mutation is breast cancer, but there is also associations of ovarian cancer and prostate cancer with mutated BRCA genes. According to extensive studies, 72% of women who inherit a mutated BRCA1 gene and 69% of women who inherit a mutated

BRCA2 gene will develop breast cancer by the age of 80 (Kuchenbaecker, et al., 2017) and approximately 30% of all breast and ovarian cancers are due to mutations in BRCA1 and BRCA2 genes (Mehrgou & M, 2016). Men with a BRCA mutation are at 20% risk of developing prostate cancer and 7-8% chance of developing breast cancer (Ibrahim, et al., 2018).

It is known that there are certain risk factors that may make a person more susceptible to acquiring cancer. These include gender, weight, alcohol consumption and smoking habits (Feng, et al., 2018). By reducing exposure to carcinogens the risk of developing cancer can be reduced. Nicotine, an active ingredient in cigarettes, is carcinogenic and can result in the production of DNA adducts which can evade cellular repair mechanism allowing for permanent mutations, increased cell proliferation in breast tissue, and induction of migration of cancer cells which enhances tumour progression (Kispert & McHowart, 2017). Simple lifestyle choices such as regular exercise and a healthy, balanced diet can improve overall health and reduce risk of developing disease (Harvie, et al., 2015). Positive lifestyle changes, such as by incorporating physical activity and healthy dietary options into everyday routines, could prevent 25% to 30% of cases of breast cancer.

Preventative therapies are available that can reduce the chances of breast cancer, especially among people who are most at risk. These actions of prevention are only an option once genetic screening is performed for the mutation and following extensive counselling, if required. These therapies include selective oestrogen receptor modulators and neoadjuvant therapies, as well as mastectomy (Slepicka, et al., 2019). Therefore, genetic testing for pathogenic (disease-causing) mutations in these genes is very important. Importantly, knowing which gene is mutated will help determine the correct targeted gene therapy to be used. One such strategy is genetic correction, in which the therapy is molecularly targeted to cancer cells and should leave normal cells unharmed (Obermiller, et al., 2000)

MATERIALS AND METHODS

Survey Design and Distribution

A survey was constructed in Google Forms to determine how the presence of BRCA genes affects lifestyle choices. Questions were included that would gather information about topics including family planning, genetic testing of children, lifestyle, and cancer prevention treatments. The survey was trialled on 20 people so that weaknesses in the survey could be identified before the composition of the finalised survey was established (see Appendix 1).

RESULTS

In total, there were 300 participant responses. A total of 300 responses were gathered, 252 of these were from female participants (84%) and 48 responses were from male participants (16%). Regarding age of participants 60% of the responses were between the ages of 18 and 25, and the remaining 40% were aged 26 or older.

Figure 1 shows the male and female responses received to the question posed regarding children – whether to tell them that one had tested positive for the BRCA gene, whether to test them for the gene having tested positive, or indeed, whether to have children at all.

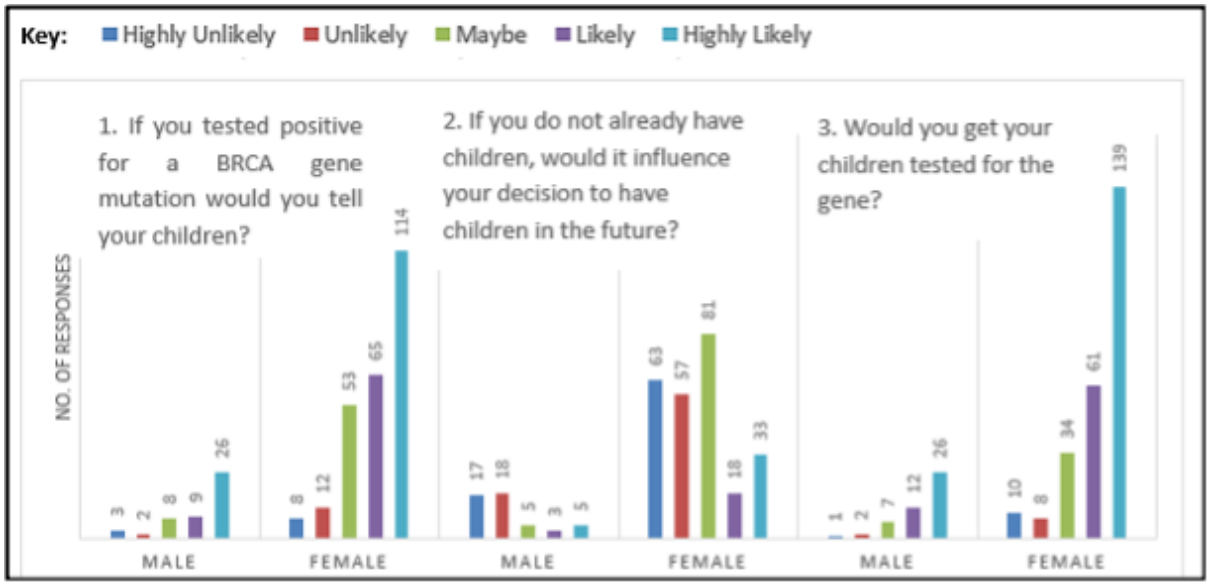

Figure 1. Survey participants' views of the anticipated effect of testing positive for the BRCA gene on their decisions of whether to have children, or, if having children, whether to inform them about the gene

Results of investigating for differences in attitudes by age of the views of the anticipated effect of testing positive on choices regarding children are shown in figure 2. Results show major respondent age-related differences to the question about whether or not to have children.

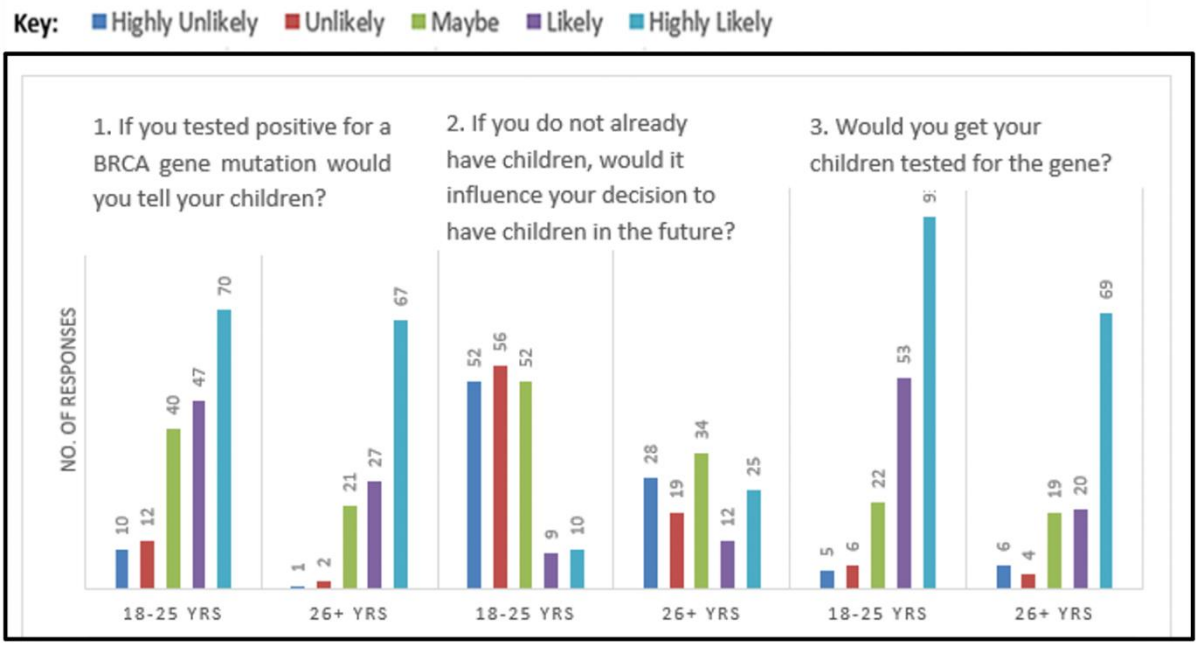

Figure 2. Investigation for age-related differences in response to considerations relating to children after respondents putatively test positive for the BRCA gene

Respondents were asked to consider whether they would opt for a mastectomy after testing positive for the BRCA gene. Figure 3 shows that there is a greater difference between age-groups (18-25y vs >25y) than between male and female respondents.

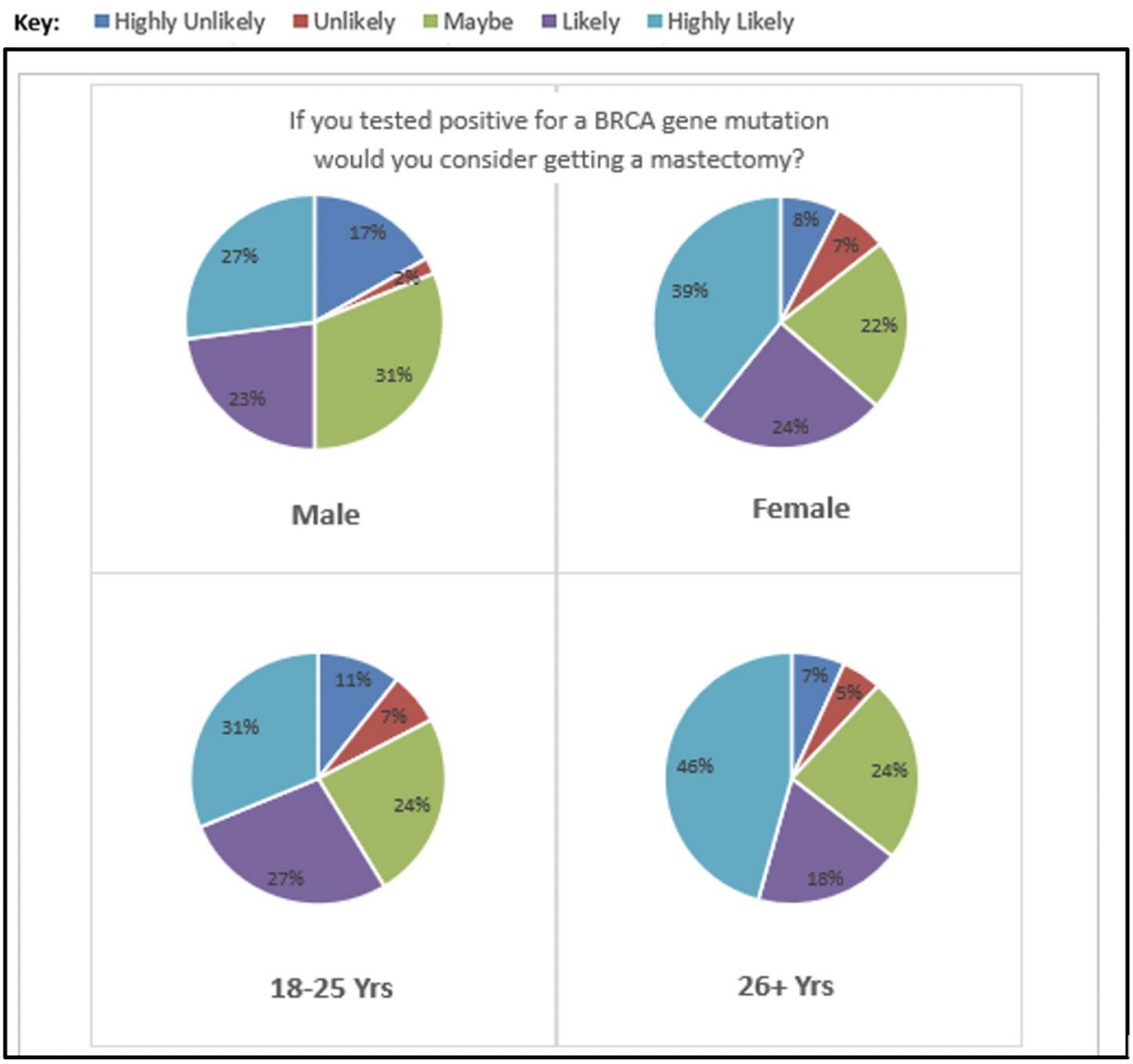

Figure 3. Opinion of respondents when asked whether they would opt for a mastectomy after testing positive for the BRCA gene.

The survey results indicated differences in opinion between different groups when asked about prevention therapies as shown in figure 4. There are differences in opinion between the two age-groups and between male and female respondents.

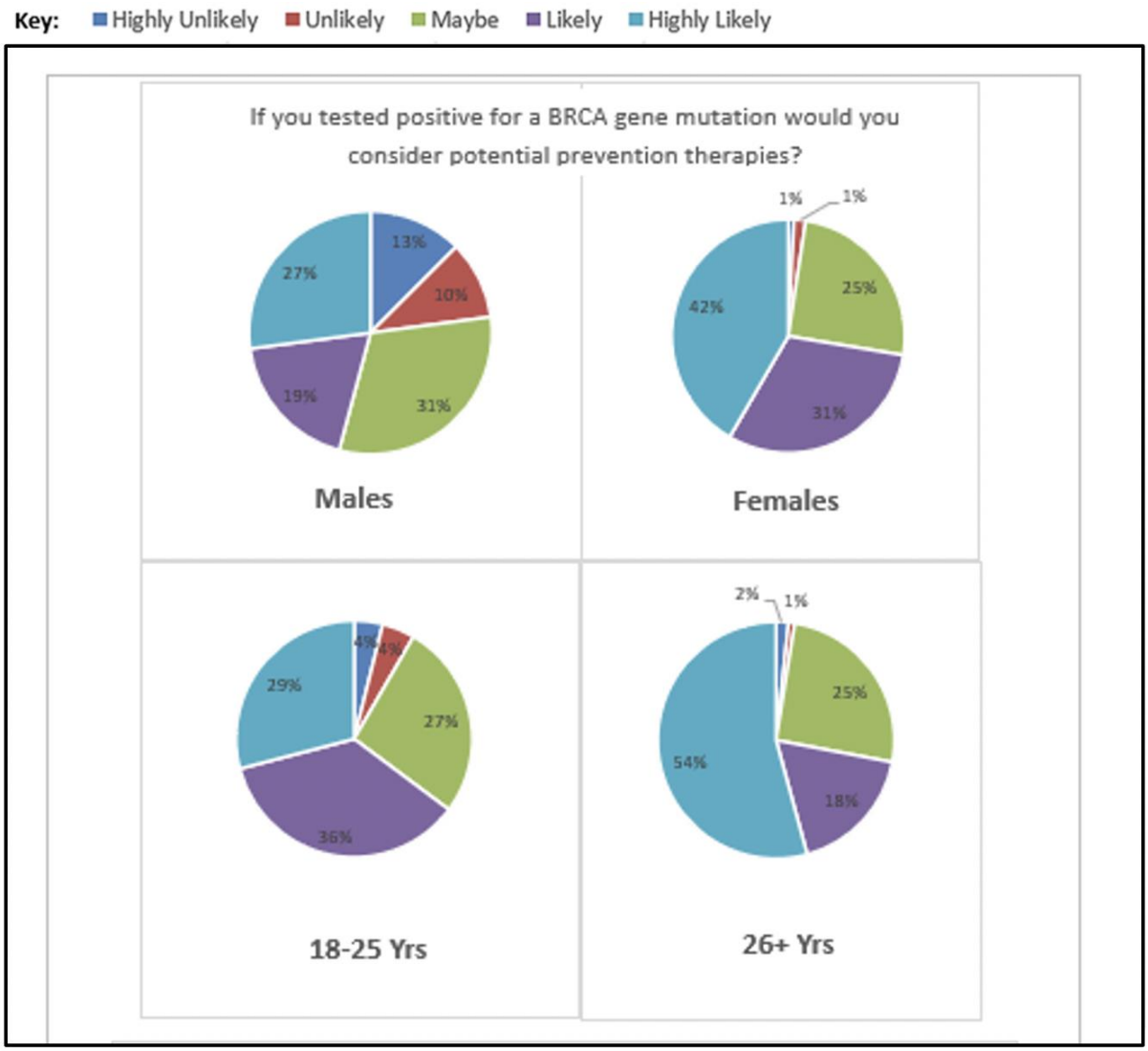

Figure 4. Opinion of survey participants when asked whether they would consider availing of prevention therapies after testing positive for the BRCA gene

In response to the question posed as to whether having tested positive for the BRCA gene would affect their life positively or negatively, in each category of respondent (male, female, those 18-25 and those over 25) the majority of the respondents were accounted for by the combined total of undecided/slightly negative impact categories see Figure 5.

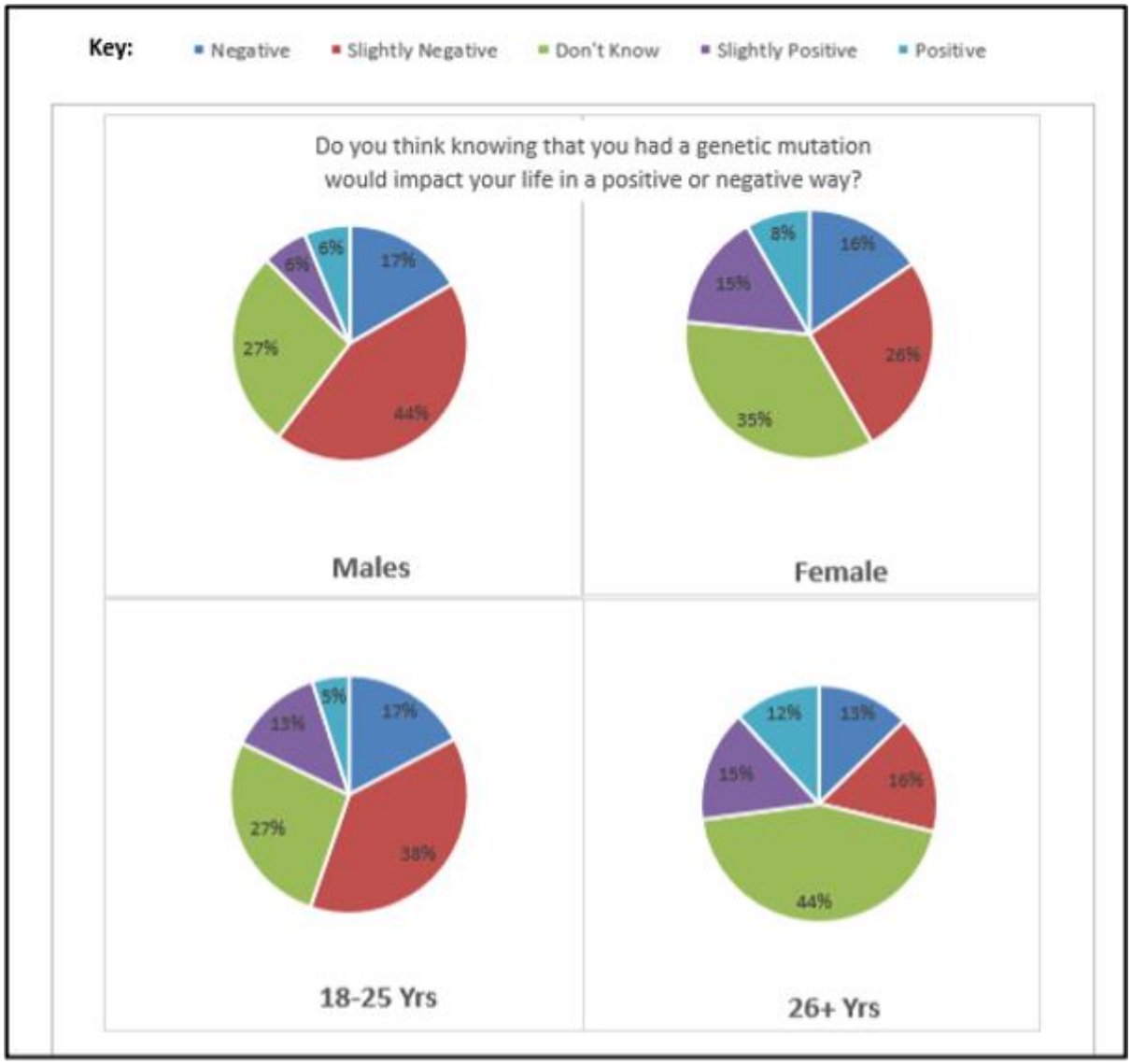

Figure 5. Survey respondents' opinion on whether they considered that having tested positive for the BRCA gene would impact their lives in a positive or a negative way

DISCUSSION

BRCA1 and BRCA2 are two genes that normally play a role in preventing tumour growth. However, in some people these genes are mutated. When mutated, they can increase chances of developing breast cancer. In females, it is estimated that the presence of a BRCA gene mutation increases their chances of developing breast cancer by 70% (Kotsopoulos, 2018). When males carry a BRCA gene mutation, it is estimated that they are up to 10% more likely to get breast cancer (breatcancer.org, 2019). However, those carrying the mutation may never develop breast cancer. The carrier of the mutated gene has a 50% chance of passing the gene mutation to one of their children (Rauscher, et al., 2019). There are also a number of risk factors that may increase the likelihood of developing illnesses such as cancer, including smoking or drinking alcohol.

Breast cancer can occur in both males and females. Breast cancer in females is quite common, with 1 in 9 women in Ireland affected by breast cancer at some stage in their lives (Breast Cancer Ireland, 2020). In comparison, a significantly lower number of males are affected by breast cancer in their lives, estimated at 1 in 1000 (Salman, 2017). Approximately 3,000 women are diagnosed with breast cancer

in Ireland annually while approximately only 25 men are diagnosed with breast cancer every year in Ireland (Irish Cancer Society, 2020).

In this study, the aim was to analyse how the diagnosis of a mutated BRCA gene mutation could affect aspects of life, and their opinions regarding certain topics. The aspects investigated in this study included family planning, treatment options to prevent the development of breast cancer and the impact of diagnosis of mutated gene. There have been no Irish studies conducted on the subject, but some similar studies have been carried out in the United States. The profile of the survey responses chosen were Irish nationals over the age of 18. Three hundred people participated in this survey, of which 252 (84%) were female and 48 (16%) were male.

When participants were asked about the topic of family planning and genetic screening there were similarities seen in the responses to certain topics while other areas highlighted differences of opinion. When participants were asked would get their children tested upon finding out they themselves had the mutated BRCA gene, both age groups concurred, answering they would get their children tested. Similarly, as seen in figure 1.1, males and females both answered they would likely get their children tested. The participants were then asked if they tested positive for a BRCA gene mutation would they inform their children. As seen in figure 1.2, the response from both age groups was similar with the majority of participants in the two age categories responding highly likely. Similarly, both males and females responded that they were likely to tell their children if they have a BRCA gene mutation (figure 1.1). This data highlights that regardless of age or gender, people have great interest in the area of genetic screening and are willing to get tested for the benefit of their health and their children's health.

However, there was contrasting opinions recorded in response to other questions regarding family. As seen from figure 1.2, the 26+ year olds are much more likely than the 18-25-year-olds to let the presence of the gene mutation affect their decision to have children in the future. Figure 1.1 showed most males felt the diagnosis would unlikely affect their decision to have children in the future. In comparison, females seemed indecisive about their decision with 32% responding maybe, while only 23% deemed the diagnosis unlikely to affect their decision to have children. This response supports the theory that females may feel more at risk at developing breast cancer than males and this may account for this increased level of indecision in the female cohort.

The differences in opinion between the age groups could be due to the fact that the two groups are at different stages of their lives when it comes to having children. The survey results indicate that 99% of the 18-25-year-old participants did not have children, whereas 88% of the 26+ year olds did have children. This difference of opinion might be accounted by the majority of the 26+ group answered the questions on children from a position of having children, whereas the 18-25-year-olds were answering the questions in a hypothetical sense.

Treatment options are available which can help decrease risk of developing breast cancer. Two different preventative measures were proposed to the participants. The first option was the removal of breast tissue in a mastectomy procedure with the second being the use of prevention therapies, such as selective oestrogen receptor modulators and neoadjuvant therapies

The preferred preventative treatment chosen by all participants was the use of prevention therapies. As seen in figure 3, 65% of 18-25-year-olds and 72% of 26+ year olds were 'likely/highly likely' to utilise this therapy measure. In contrast, only 58% of 18-25-year-olds and 64% of 26+ year olds were 'likely/highly likely' to consider getting a mastectomy. With regards to male and females, figures 2 and 3 again show that preventative therapies are a more popular option than a mastectomy. It was noted that females were more likely than males to consider preventative measures. Due to the low incidence of breast cancer among males (Irish Cancer Society, 2020), they potentially do not feel the need to undergo preventative measures as much as females do.

Prevention therapies are more appealing to participants as it is less invasive and does not require an operative procedure and can in most cases reduce the chances of getting breast cancer by between 44%

and 69%. However, these therapies may sometimes carry side effects (Slepicka, et al., 2019). Undeniably, the removal of breast tissue is a procedure associated with much emotional and physical trauma, so this is a decision not taken lightly. Post-mastectomy can induce many issues including, but not limited to, an effect on self-esteem, distorted self-image, reduced sex drive as well as physical problems such as pain and lymphoedema (Rodriguez, 2009). Therefore, it is unsurprising that participants were less likely to consider such an invasive procedure especially since a diagnosed mutated BRCA gene does not always lead to breast cancer but is only an increased risk factor. However, it must be noted that in BRCA gene mutation carriers, mastectomy is an effective procedure reducing the chances of getting breast cancer by 90% (Thorat & Balasubramanian, 2019). Additionally, advances in technology in the medical field has made many post-surgery options available to improve life post-mastectomy including breast reconstruction, breast prosthesis and mental health support groups and foundations (Rodriguez, 2009).

Participants were asked if they would inform their health insurance provider about the discovery of a mutated BRCA gene, considering that their premium may increase. Most males 31% responded that it was highly unlikely they would inform the insurance company while mast females (29%) were indecisive. However, 28% of females responded that they were highly likely to inform their insurance provider of the diagnosis. Comparing the responses from the different age groups, the older age category was more likely to inform the provider with most of the younger participants indecisive. An article published in the Irish Times suggested that if people felt obliged to inform their insurance provider it may discourage people from genetic testing performed as it may ultimately increase their insurance premium (McConnell, et al., 2000). These findings highlight the need for raised awareness of the benefits of genetic screening in Ireland as the public appear to be more concerned about their insurance rates increasing than recognising the true benefit of genetic screening. Genetic screening can aid the early detection of illnesses and in some cases preventative measures can be used to result in improved health outcomes (FORCE - Facing Our Risk of Cancer Empowered, 2020). Interestingly, many Irish health insurance providers promote genetic testing by assisting customers in financing the tests (VHI Healthcare, 2020).

In a study published in the International Journal of Biological Sciences, it was stated that the modern western diet, particularly the excess consumption of saturated fats, is associated with mortality and poor prognosis in breast cancer patients. This study also reported that increased breast cancer risk is associated with high alcohol intake and smoking at an early age (Sun, et al., 2017). Participants were asked if they would consider lifestyle changes to improve their overall health and help reduce risk of disease development. Most participants indicated they would take steps to improve their lifestyle such as exercise, diet, smoking and alcohol consumption. However, there was as a small number of participants answered that they were unwilling to change their current lifestyle and would not improve their smoking/drinking habits. Overall, the investigation of lifestyle factors was positive as it highlights that the vast majority of the public would be more conscientious of their life choices upon a gene mutation diagnosis.

Finally, participants were asked the impact the diagnosis of a mutated BRCA gene would have on a persons' outlook on life. The 18-25 year-olds consider the presence of a BRCA gene mutation would have a negative impact on their life. While the majority of the 26+ age group answered that they did not know what effect it would have on their life. This may indicate that the older age group may be able to see both the positives and negatives of having a BRCA gene mutation.

Interestingly, a greater number of males would consider the presence of a BRCA gene mutation to have a negative impact on their lives in comparison to females, as seen in figure 4. Only a small number of participants would consider the diagnosis to have a positive effect, 12% of males and 23% of females. There was a significant negative response from the male participants about the diagnosis and although the opinions of participants cannot be presumed, it could be suggested that this response is to male stigmatization surrounding breast cancer. A research investigation conducted by the National Centre for Biotechnology Information (NCBI) in 2018 titled 'Men With a "Woman's Disease": Stigmatization of Male Breast Cancer Patients—A Mixed Methods Analysis (Dorak & Karpuzoglu, 2012) analysed

how male patients felt following a diagnosed with breast cancer and their journey during cancer treatment. In the study, the patients were asked a series of questions regarding their diagnosis and cancer treatment. A significant 26% of the participants responded that they had experienced sexual stigmatization during their treatment because of their gender. Some doctors refused to treat the patients because they were male and other participants even recalled being called by a female pronoun in a waiting room due to gender presumption that 'only' females can develop breast cancer.

It was important to investigate how the participants felt about the potential diagnosis of a mutated BRCA gene in this survey. Firstly, the findings highlighted that the participants had a more pessimistic view on the diagnosis and failed to recognise the positive aspect of the situation. This further reiterates that the public is not sufficiently informed about genetic screening and that people fail to recognise that the diagnosis of a mutated gene although upsetting can save lives. It is important to stress that having the mutated gene does not guarantee someone will ever develop breast cancer in their lifetime. Confirmation of the mutation allows preventative steps to be taken to stop disease development as seen in mastectomy where breast cancer development risk is reduced by 90% (Thorat & Balasubramanian, 2019). Identifying the mutation gives the person the choice as to whether they wish to act upon the diagnosis or not. For those who do not avail of a genetic test, they remain unaware of their options.

With regards family planning, the diagnosis of a mutated BRCA gene allows people to discuss with their partner the risk of gene inheritance and make informed decisions about starting a family. Someone who has not had a genetic screening test is unaware of any genetic mutations they may carry and the potential risk posed if they decide to have children, especially if this mutation is potentially life threatening.

Lastly, it could be said that having the knowledge of a mutated BRCA gene may reap benefits for the person as it can make them more conscientious of their health by encouraging the person to improve their diet and participate in active exercise. Not availing of genetic screening may lead to a lack of utilisation of preventative measures and lack of positive steps to improve their health.

One major limitation in this study is the lack of diversity with the participants. The survey was circulated through social media platforms and because of this, the population was quite limited. The survey should be circulated more widely using multiple different platforms to gather data from as many different subgroups of people.

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