2. Literature Review

2.1 Factors influencing risk

Incidence of breast cancer is amongst the highest of any form of malignant cancer (Ries, Eisner, & Kasary, 2002 as cited in King, Marks, Mandell, 2003). Although familial history of breast cancer is not a perquisite for developing the disease it has been understood for some time that the incidence in certain families is far higher than in the general population. Mutations in tumour suppressor genes BRCA1 (Hall et al., 1990; Miki et al., 1994) and BRCA2 (Wooster et al., 1994, 1995) have subsequently been associated with increased incidence of breast cancer. Ford et al. (1998) studied the penetrance of BRCA1 and BRCA2 genes amongst 237 families with high incidence of breast cancer. Their results indicated that BRCA1 was associated with the disease in 52% of the families, BRCA2 in 32% of the families and not associated with either gene for 16%. Although the 16% without either gene indicates that there may be other genetic factors which predispose some individuals, their findings indicate that BRCA1 and BRCA2 are strongly associated with increased risk of developing breast cancer. Several similar studies have been carried out which quote variations in the percentage risk of developing breast cancer, Antoniou et al. (2003) carried out a meta analysis of data from 22 studies into risk of breast cancer amongst BRCA1 and BRCA2 carriers, concluding that the average cumulative risk for BRCA1 carriers to 70 years of age is 65% for BRCA1 (30% – 87%) and 45% (28% – 84%) for BRCA2. It is noted in several studies (Anglian Breast Cancer Study Group, 2000; Antoniou et al., 2003; Mann et al., 2006) that the risk of developing breast cancer for BRCA1 and BRCA2 carriers is significantly modified by their associated family history, being higher for those

who have a strong family history of breast cancer. This suggests other genetic factors may have a part to play, such as those suggested by Rebbeck et al. (1999a) and Runnebaum et al. (2001). Despite reported differences in the quantitative risk value, all studies agree that the risk of developing breast cancer for individuals carrying BRCA1 or BRCA2 mutations is significantly higher than for individuals who do not carry the mutation.

Amongst the general population breast cancer has been linked to a number of non genetic factors. Weight gain (Harvie et al., 2005), physical activity level (Thune & Furberg, 2001), weight distribution (Harvie, Hooper, & Howell, 2003) and dietary fat intake (Bingham et al., 2003) have all been reported to affect the incidence of breast cancer. There is also evidence that the risk of developing breast cancer is modified by several non genetic factors for BRCA1 and BRCA2 carriers as well as for the general population. Antoniou et al. (2003) and Evans et al. (2008) both report evidence that the risk of developing breast cancer is rising with time for BRCA1 and BRCA2 carriers, Evans et al. (2008) report that the risk of breast cancer by age forty rises from 8% in those born before 1930 to 22% for those born later. King and The New York Breast Cancer Study Group (2004) also reports a significant increase in risk for later born cohorts. Tryggvadottir et al. (2006) investigated this trend by studying women with BRCA2 mutations in Iceland and found an increase in incidence of breast cancer from 18.6% to 71.9% between 1920 and 2002. These significant increases in risk amongst a genetically homogeneous group imply that external factors, such as environment, behaviour and lifestyle, which have changed significantly over this period, may influence the risk of developing breast cancer for this group.

Incidence of breast cancer for BRCA1 carrier's peaks around 45 years of age (Narod et al., 1995) which is much earlier than in the general population where risk continues to rise with age. This has lead to speculation that interactions between BRCA1 and 2 mutations and hormone levels may be involved in the increased incidence of breast cancer in carriers. A number of studies have shown that changes in incidence of breast cancer are related to changes in exposure to various reproductive hormones. Eisen et al. (2005) and Rebbeck et al. (1999b) found that oophorectomy had a protective effect for BRCA1 carriers, reducing risk of developing breast cancer by 47% and 61% respectively in the two studies. The anti-oestrogenic drug Tamoxifen has also been studied in relation to BRCA1 and BRCA2 breast cancer incidence, Foulkes et al. (2002) reported a protective effect for BRCA1. King et al. (2001) reported a possible protective effect for BRCA2 but from a small sample size. Narod et al. (2000) reported a significant protective effect for contralateral breast cancer in both BRCA1 and BRCA2 carriers and that this effect was additive to the protective effect of oophorectomy. Further studies are needed to determine if this implied reduction in risk is also present for primary breast cancers in BRCA1 and BRCA2 carriers. Hormonal changes during pregnancy have also been linked with increased risk of breast cancer for BRCA1 and BRCA2 carriers, Johannson, Loman, Borg, and Olsson (1998) report that pregnancy increases the risk of developing early onset breast cancer for both BRCA1 and BRCA2. Jernström et al. (2004) also reported that breast feeding for greater than one year reduced the risk of developing breast cancer, again this was significant for BRCA1 only but the study noted that the sample size for BRCA2 was smaller, which may have limited the statistical power of the study to recognise weaker trends. Oral contraceptives which affect

reproductive hormone levels have also been reported to influence the risk of developing breast cancer for BRCA1 carriers. Ursin et al. (1997) found a strong link between oral contraceptive use and increasing risk for BRCA1 carriers although their sample was small for BRCA1 and extremely small for BRCA2. Grabrick et al. (2000) conducted a larger historical cohort study which also reported a strong link between oral contraceptive use and increased incidence of breast cancer in those with a family history. Some researchers have suggested that, although smoking has not been associated with altered risk of developing breast cancer in the general population (Barron, LaVecchia, & Levi, 1990) its anti-oestrogenic effects may alter the risk for BRCA1 and BRCA2 carriers. Brunet et al. (1998) reported a significant reduction in breast cancer risk for smokers in their study of 186 subject pairs, this result suggests that further study in this area is required.

Body weight and energy intake have been cited as factors which may affect the incidence of breast cancer in individuals with BRCA1 and BRCA2 mutations. Silvera, Jain, Howe, Miller, and Rohan (2006) reported a link between increased energy intake and incidence of breast cancer in the general population. Nkondjock, Robidoux, Paredes, Narod, and Ghadirian (2006) found that a high energy intake was associated with an increased risk of breast cancer for BRCA1 and BRCA2 carriers, although their study was relatively small with 89 carriers, the association was found to be independent of exercise and BMI. Kotsopouls et al. (2005) studied BMI, weight and weight gain in 2146 women with BRCA mutations, they concluded that weight loss between age 18 and 30 decreased the risk of developing breast cancer in this population. Although the limited study

by Nkondjock et al. (2006) did not show a link between physical activity and onset of breast cancer for BRCA1 and BRCA2 carriers, there are a number of studies that have indicated a statistically significant link for the general population. A case control study of over 3501 women by Carpenter, Ross, Paganini-Hill, and Bernstein (2003) found that risk of breast cancer was reduced for those taking regular exercise post menarche. In their study of 1008 cases King, Marks, and Mandell (2003) found that the association between, both physical activity and healthy weight as a teenager, and the delayed onset of breast cancer, was significant amongst BRCA1 and BRCA2 carriers. As several of these studies acknowledge it is difficult to isolate the separate effects of exercise and a healthy weight as studies into each are inevitably confounded due to the very clear relationship between these two factors in free living subjects.

Evidence from epidemiological studies has shown that diets including a significant amount of fruit and vegetables can be protective against cancer (Block, Patterson, & Subar, 1992; Willett, 1994). However there have been relatively few studies which investigate the link between diet and breast cancer risk for BRCA1 and BRCA2 carriers. Nkondjock et al. (2006) found that increased energy intake was associated with higher risk but no link for specific nutrients. Although studies by the Collaborative Group on Hormonal Factors in Breast Cancer (2002), and Key et al. (2004) report a raised breast cancer risk due to alcohol consumption for the general population this remains to be studied in BRCA1 and BRCA2 carriers.

2.2 Attitudes to risk modifiers

There have been a number of studies into the health beliefs of individuals with an increased risk of developing breast cancer, either through carrying BRCA1 and BRCA2 mutations or due to a family history of breast cancer. A number of studies have investigated treatment preferences and attitudes towards effectiveness for different treatment options. Attitudes to surgical intervention seems to be consistent. Cappelli et al. (2001), Kram, Peretz, and Sagi (2006) and Wagner et al. (2000) report that prophylactic oophorectomy is a more acceptable prevention measure than prophylactic mastectomy. Metcalf et al. (2007) studied a group of 372 women with BRCA1 or 2 mutations who did not have breast cancer and found that 54% have had an oophorectomy, 21% a mastectomy, and 6% had taken Tamoxifen, whilst 46% had not taken any of these options. These studies seem to indicate that BRCA mutation carriers believe that preventative surgery is likely to reduce risk of developing breast cancer. Attitudes to screening programmes have also been investigated. Spiegel, Hill, and Warner (2009) found that women diagnosed with BRCA mutations felt that screening was an important way to detect breast cancer. De Leeuw, van Vilet, and Ausems (2008) carried out a meta analysis on adherence to screening amongst women at high risk of breast cancer and found that screening increased amongst those with a positive BRCA result.

Few studies have directly compared belief in effectiveness of medical intervention with life style changes, those that have indicate that lifestyle behaviour modifications may not be thought as effective as are medical interventions. Madlensky et al. (2005) used data from the Minnesota Breast

Cancer Family Study to carry out a large cohort study on women who had a relative who had been diagnosed with breast cancer, both blood relative and female relatives who were related through marriage. They found that medical interventions such as preventative surgery or oestrogen altering drug use were associated with the genetic at risk group but no association for changes in diet or exercise. This result was also repeated by Madlensky, Flatt, Bardwell, Rock, and Pierce (2005) who found no difference in reported preventative lifestyle behaviours between breast cancer survivors with a family history of breast cancer and those with no family history. These studies indicate that, although surgical interventions may be thought to have a more direct effect on levels of risk, behaviour changes may be a preferred option.

2.3   Theoretical models

A number of theoretical models have been proposed to explain and predict behaviour changes which are related to individual's perception of their health. The Health Belief Model (HBM) proposed and refined by Becker (1974 as cited in Janz & Becker, 1984) and Rosenstock (1974 as cited in McClenahan, Shevlin, Adamson, Bennett & O'Neill, 2007) postulates that health behaviour changes are likely to be motivated by a number of factors; susceptibility, severity, benefits, and barriers. This model has been shown to have some success in predicting behaviour change and intention by a number of studies. Keesling and Friedman (1987) used it to correlate sun protection use and Hingson, Strunin, Berlin, and Heeren (1990) applied the model to use of drugs, alcohol and unprotected sex. Harrison, Mullen, and Green (1992) carried out a meta analysis of the component elements of the model across 16 studies but did not find that any one of the

components was significantly more powerful as a predictor of behaviour. Further refinements to the model were proposed by Rosenstock, Strecher, and Becker (1988) who suggest that inclusion of 'self efficacy' significantly improve the validity of the HBM. This improved model was found to provide a better explanation of behaviour by Nejad, Wertheim, and Greenwood (2005) who studied dieting and fasting behaviour and by McClenahan, Shevlin, Adamson, Bennett, and O'Neill (2007) who studied testicular self examination. Both of these studies compared the HBM with the Theory of Planned Behaviour (TPB). TPB postulates that behaviour can be predicted by three elements; attitude, subjective norm and perceived behavioural control. Attitude refers to the individual's perception of what the result of the behaviour will be. Subjective norm is the perception by the individual of the behaviour expectations of others, perceived behavioural control relates to how much an individual believes they are able to control that behaviour. Nejad et al. (2005) found that attitude was the strongest predictor of behaviour where as McClenahan et al. (2007) found the perceived behavioural control had the strongest correlation to behaviour. From meta analysis and single studies it is clear that theoretical models have had some success in predicting the attitudes and beliefs which are often present in those individuals who make health related behaviour changes. Although there is some variation amongst the studies when analysing which categories of belief are strongest predictors of behaviour change, it would seem that those elements which relate to self efficacy and control as well as those relating to effectiveness of the behaviour change are most closely correlated to actual behaviour change.

2.4 Health beliefs of those with genetic predisposition

There have been a number of empirical studies carried out in an attempt to understand the motivations and beliefs of individuals at an increased risk of breast cancer and how these may relate to behaviour changes they may make. Several studies have been carried out to investigate how individuals at high risk believe lifestyle affects the risk of developing breast cancer. Lemon, Zapka, and Clemow (2004) carried out a telephone based structured interview study of 600 women with a recently diagnosed first degree relative. They reported that, although 31% of respondents felt that control over breast cancer risk is not possible and only 20% felt that it is very possible, the majority of the group perceived that the lifestyle factors of regular exercise, high fat diets, high fibre, fruit and vegetable consumption, alcohol consumption and smoking were activities which affected risk of developing breast cancer. Beagan and Chapman (2004) performed a qualitative in-depth interview study on 30 women who had been diagnosed with breast cancer between 6 months and 15 years previously. They found that there was a significant variation in beliefs about the role of diet in the risk of developing breast cancer. Some participants felt that there was a link between a number of dietary elements and increased risk of developing cancer, others felt that they were not sure of any link and some felt that there was no link between diet and risk of breast cancer. This study also reported that dietary changes carried out were not correlated to whether or not individuals believed that diet and cancer risk were linked. These researchers also used data from this study to compare the attitudes of those who had been diagnosed directly with a cohort who had not been diagnosed with breast cancer (Chapman & Beagan, 2003). They found that there was no significant difference between

the two groups attitude to the link between diet and breast cancer risk. In 2006, Rabin and Pinto carried out a study which used posted questionnaires to investigate the attitudes of 61 cancer survivors and 31 first degree relatives to the causes of breast cancer and health behaviour changes made. They reported that this group believed that genetics (47%), stress (48%) and pollution (42%) were the most likely causes of breast cancer and that diet (27%), exercise (20%), smoking (16%) and alcohol (10%) had a lesser role to play. Spector et al. (2009) carried out an interview based qualitative study into risk perception and lifestyle behaviours amongst women with a family history of breast cancer. They found that relatively few individuals felt that they had control over risk. Although diet, exercise and weight control were frequently cited as risk factors, the group made stronger associations with family history, stress and toxins. Spector's 2007 study based on interviews with 10 BRCA carriers drew similar conclusions, finding that most women believed that there may be a relationship between 'healthy lifestyle' and reduced risk. It should be noted that some of the data presented in this paper uses qualifying statements such as 'might affect' and 'seems like' which indicate that respondents may not be convinced of a direct causal relationship and that these interviews were carried out via telephone restricting non verbal communication. When reviewing studies carried out to investigate attitude to lifestyle as a risk factor it seems clear that both quantitative questionnaire based studies and qualitative in-depth interview studies recognise diet and exercise is felt to be a risk factor. However the qualitative studies seem to indicate that this is not a strong belief held by the group, particularly when compared with the level of conviction expressed towards hereditary factors and even environmental factors such as stress and toxins. It is interesting to note that

attitudes to how lifestyle is related to the cause of breast cancer may be different to attitudes to how these factors may influence the course of breast cancer once diagnosed. Pinto et al. (2002) studied 86 women who had been treated for breast cancer, they reported that the majority believed that exercise (74%) and diet (85%) could change the course of cancer.

It is also important to investigate how attitudes relate to actual behaviour changes. Spector et al. (2009) found that behaviour change was related to belief that behaviour was a risk factor for some individuals but not for others. They also reported that diet was the most often reported behaviour change with exercise being less frequent. Their in-depth interview study revealed that barriers to change can play as significant a role in behaviour change as does perceived benefits or perception of risk factor. Similarly Beagan and Chapman's (2004) in-depth interview study reported that attitude to how diet affects risk is not related to actions to change diet and that diet is shaped by many factors. This contradiction between belief that diet may not affect risk and yet still making diet changes may be explained for these individuals by the results of Maskarinec, Murphy, Shumay, and Kakai (2001) and Salminen, Lagström, Heikkilä, and Salminen (2000) who reported that a health crisis often causes immediate diet change. This is in contrast to Lemon et al. (2004), Quach, Porter, Leventhal, and Kelly (2009) and Rabin and Pinto (2006) who all reported that behaviour changes were positively associated with belief that the behaviour was a risk factor. Significantly these three studies were quantitative in nature and data was collected by mailed questionnaire or pre-structured telephone interviews (Lemon et al. 2004). The use of closed questions, delivered by telephone or by postal

questionnaire, addresses some of the practical issues of efficient data collection and allows these studies to include large sample sizes. However this study design does not include scope for individuals to easily provide responses or information outside that prescribed by the researcher. For example Lemon et al. (2004) asked the question "How possible is it for you to reduce your own risk of breast cancer?" Respondents are restricted to one of 4 pre prescribed answers from "not at all possible" to "very possible" and had no opportunity to accurately describe their belief. Telephone or posted questionnaires also inhibit any communication between researcher and subject which may be provided through interpretation of body language. When studying individual's attitudes and beliefs in relation to complex and multifaceted issues, qualitative research methods have a number of strengths. The use of in depth one to one interviews, allow the subject to express their opinions and feelings in a way that is most appropriate for them and reduces the restrictions imposed by closed questions. It also allows the researcher to accommodate and respond to results or responses which were not expected or foreseen at the beginning of the study. Strength of feeling is also easier to express when individuals are using their own descriptive language and when the researcher has the opportunity to probe further into a subject when the interviewee may initially not give a clear answer. The studies by Beagan and Chapman (2004), Chapman and Beagan (2003), Spector (2007) and Spector et al. (2009) all used qualitative methodology. The important insight into strength of belief, which is provided by these 4 papers, illustrates that the use of qualitative research can provide valuable additional perspective which needs to be considered in conjunction with the findings from more traditional quantitative research. To date there has been very little research published which

has used qualitative techniques to investigate beliefs and behaviours amongst this high risk population group. The combined total number of subjects involved in these studies is 40 of whom only 10 were known to be BRCA carriers. We believe that it is important that further qualitative research is carried out amongst this group to gain further insights and increase the generalisability of findings for this population. We hope that by completing this qualitative in depth interview study involving 20 BRCA carrier subjects we will have added to current understanding and provided useful information to inform future qualitative and quantitative research.

2.5   Summary of relevant published work

From the literature it would seem that there is considerable evidence that certain behavioural factors can influence the risk of developing cancer for BRCA carriers. However the evidence from both theoretical and empirical analysis indicate that the relationship between attitudes and beliefs relating to diet, exercise, breast cancer, and behavioural change is complex and may include influences and factors outside of those normally described in theoretical models of health behaviour. This may be particularly true of diet related changes.

2.6   Key interview objectives

This interview study aimed to explore health beliefs and the reasons for these amongst BRCA carriers.

The key objectives of the interviews were:

o   To explore women's perceptions of their breast cancer risk and behaviours targeted at reducing that risk.

o   To explore experiences of family history of cancer as well as perceived control over personal risk and potential interest in diet prevention strategies and studies.