## The psychosocial impact of undergoing prostate cancer screening for men with *BRCA1/2* mutations

Bancroft EK1,2\*, Saya S2,1\*, Page EC2,1, Myhill K1,2, Thomas S1,2, Pope J2,1, Chamberlain A2,1,

Hart R3, Glover W3, Cook J4, [Sheffield], Helfand B5, Selkirk T5, Davidson R6, [Glasgow], Eccles DM7,8, [Southampton], Gadea N9, Brewer C10, Barwell J11,12, Salinas M13, Greenhalgh L14, Tischkowitz M15, Henderson A16, Evans DG17, Buys S18, IMPACT Study Steering Committee+, IMPACT Collaborators+, Eeles RA2,1, Aaronson NK19.

## 1. Oncogenetics Team, The Royal Marsden NHS Foundation Trust, London, UK

## 2. Oncogenetics Team, The Institute of Cancer Research, London, UK

## 3. Clinical Genetics Unit, Birmingham Women's Hospital, Birmingham, UK

## 4. Sheffield Clinical Genetics Service, Sheffield Children's Hospital, Sheffield, UK

5. The John and Carol Walter Center for Urological Health, North Shore University Health System, Evanston, IL, USA

6. Duncan Guthrie Institute of Medical Genetics, Yorkhill NHS Trust, Glasgow, UK

7. Wessex Clinical Genetics Service, Princess Anne Hospital, Southampton, UK

8. Faculty of Medicine, University of Southampton, University Hospital Southampton NHS FT, UK

9. High Risk and Cancer Prevention Clinic, Vall d'Hebron University Hospital, Barcelona, Spain

10. Clinical Genetics Department, Royal Devon and Exeter Hospital, Exeter, UK

11. Department of Genetics, University of Leicester, Leicester, UK

12. Clinical Genetics, University Hospitals Leicester, Leicester, UK

13. Hereditary Cancer Program, Catalan Institute of Oncology (ICO-IDIBELL, CIBERONC), L’Hospitalet de Llobregat, Barcelona, Spain

14. Cheshire and Mersey Clinical Genetics Service, Liverpool Women’s Hospital, UK

15. Clinical Genetics, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

16. Northern Genetics Service, Newcastle upon Tyne Hospitals, Newcastle, UK

17. Manchester Centre for Genomic Medicine, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK

18. Huntsman Cancer Institute, The University of Utah, Salt Lake City, UT, USA

19. Division of Psychosocial Research & Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

\* Joint first authorship position

+ Full listing supplied in Appendix 1 Corresponding Author:

Elizabeth Bancroft

TheInstitute of Cancer Research

123 Old Brompton Rd

SW7 3RP

London, UK

Tel: 0207 808 2136

Fax: 0208 722 4110

email: elizabeth.bancroft@rmh.nhs.uk

## ABSTRACT

**Objectives:** To report the baseline results of a longitudinal psychosocial study that forms part of the IMPACT study, a multi-national investigation of targeted prostate cancer (PCa) screening among men with a known pathogenic germline mutation in the *BRCA1* or *BRCA2* genes.

**Patients and methods:** Men enrolled in the IMPACT study were invited to complete a questionnaire at collaborating sites prior to each annual screening visit. The questionnaire included sociodemographics and the following measures: Hospital Anxiety and Depression Scale (HADS), Impact of Event Scale (IES), Short Form 36 (SF36), Memorial Anxiety Scale for PCa (MAX-PC), Cancer Worry Scale (CWS), risk perception and knowledge. The results of the baseline questionnaire are presented.

**Results:** 432 men completed questionnaires: 98 and 160 had mutations in *BRCA1/BRCA2* genes, respectively, and 174 were controls (familial mutation negative). Participants’ perception of PCa risk was influenced by genetic status. Knowledge levels were high and unrelated to genetic status. Mean scores for HADS and SF36 were within reported general population norms and mean IES scores were within normal range.

IES mean intrusion and avoidance scores were significantly higher in *BRCA1/2* carriers than controls and higher in men with increased PCa risk perception. At the multivariate level, risk perception contributed more significantly to variance in IES scores than genetic status.

**Conclusion:** This is the first study to report the psychosocial profile of men with *BRCA1/2* mutations undergoing PCa screening. No clinically concerning levels of general or cancer-specific distress or poor quality of life were detected in the cohort as a whole. A small subset of participants reported higher levels of distress, suggesting the need for health care professionals to identify these risk factors and offer additional information and support to men seeking PCa screening.

**Keywords:** Prostate Cancer, *BRCA1, BRCA2*, Genetic Screening, Psychosocial, Quality of Life

##

## INTRODUCTION

## Prostate Cancer (PCa) is the most common cancer in men in the UK, with 40,000 new cases per year, 10,000 deaths and a lifetime risk of 1 in 8 [1]. Men with germline *BRCA1* or *BRCA2* gene mutations are known to be at an increased risk of PCa. This is estimated to be 1.8-3.75-fold 2.5-8.6-fold increased risk by age 65 for *BRCA1* and *BRCA2* carriers, respectively [2-3]. Whilst there is some debate about whether there is a true increased risk of PCa for *BRCA1* carriers, there is solid evidence that *BRCA2* carriers present at a younger age and with aggressive disease [4-5]. Therefore prostate screening and early detection could have an important role in reducing the disease burden, particularly in *BRCA2* carriers [6].

## There is no international consensus on general population screening for PCa using the PSA test, with studies reporting conflicting effects on mortality from the disease [7,8]. Additionally, PCa treatments have significant long term side-effects that can impact on masculine identity, physical and psychosocial symptoms and health-related quality of life (HRQoL). Thus research is needed to identify targeted screening tools that can improve the benefit to harm ratio for PCa screening.

## The limited number of studies of screening in men with a family history (FH) of PCa have generally supported the use of screening in this population [9-12]. To our knowledge, no studies, to date, have prospectively evaluated a PCa screening programme for *BRCA1/2* mutation carriers. The IMPACT study (Identification of Men with a genetic predisposition to ProstAte Cancer: Targeted Screening in men at higher genetic risk and controls) is an international, multicentre study evaluating the role of targeted PSA screening in men with *BRCA1/2* mutations [6].

## Evidence supports that genetic testing for mutations in *BRCA1* and *BRCA2* does not have a significant long-term psychological impact on most people tested [13,14]. Studies of men undergoing prostate screening suggest that a minority experience some anxiety, usually while waiting for results [15-17]. Risk factors for anxiety include having a FH of PCa, symptoms or abnormal genetic test results [15-17]. We are not aware of any studies that have reported on the psychological impact of undergoing prostate screening in men with *BRCA1/2* mutations. As *BRCA1/2* mutations confer an increased risk, and a heightened perception of risk of PCa may be associated with psychological distress [18], we may see higher levels of anxiety in this population. However, risk perception has been shown not to reflect true risk in both men with and without a FH of PCa . It has also been reported that cancer worry is high in men with a FH of PCa, with the number of relatives dying from the disease predicting level of worry [18]. However, a low level of PCa worry has also been reported in men with a close relative with PCa [19].

## Many issues arise when counselling men with *BRCA1/2* mutations, and many factors affect the way in which men react to and use the information about their genetic status and risk of developing cancer [20-22]. Little work, to date, has investigated either the HRQoL impact for a man with a *BRCA1/2* mutation living with an increased risk of PCa, or on those men who have gone on to develop PCa [23]. Several studies have confirmed the feasibility of collecting HRQoL and psychosocial data as part of large PCa screening trials [16,24-28].

## In this paper we report the baseline results of a longitudinal HRQoL investigation carried out as part of the IMPACT study. The specific aims of this study are: (1) to evaluate the baseline psychosocial profile of men in the IMPACT study; and (2) to identify possible predictors of high levels of psychological distress or poor HRQoL.

## PATIENTS AND METHODS

### **Study sample and procedures**

The IMPACT study recruited men from families with *BRCA1* or *BRCA2* mutations to a program of annual PCa screening via a PSA test for a minimum of five years. The IMPACT study opened in 2005 and screening will end in 2019. The full design and methods of the IMPACT study have previously been reported elsewhere [6]. The IMPACT study protocol was approved by the West-Midlands Research and Ethics Committee in the United Kingdom (reference 05/MRE07/25) and subsequently by each participating institution’s local ethics committee.

All men eligible for IMPACT were also eligible for the HRQoL study. Men were eligible for participation if they tested either positive, negative or were at 50% risk of inheriting a *BRCA1/2* mutation and were aged 40-69 years. Men who tested negative for their familial mutation constituted the control group. Men were excluded if they were known to have PCa at enrolment or if they had another cancer with a prognosis of less than five years.

The HRQoL study was added to the IMPACT study protocol in 2009. All sites were invited to participate in this sub-study. Men taking part in IMPACT at participating sites were approached by letter prior to their next scheduled study appointment with an invitation to take part in the HRQoL study. Participants joining the HRQoL study are asked to complete a set of questionnaires annually for 5 years, with each assessment taking place prior to their annual PSA test. Men were sent the questionnaire by post approximately four weeks prior to their appointment and asked to mail it back or bring the completed questionnaire to their appointment. Men were split into two cohorts: (1) Prospective Arm - men who joined the HRQoL study prior to their first PSA screen within the IMPACT study; and (2) Truncated-Prospective Arm - men already enrolled in the IMPACT study before joining the HRQoL study. The total target sample was a minimum of 300 men in each arm. In this analysis, we report on the results of the baseline questionnaires in the prospective cohort.

### **Study measures**

#### Psychological distress

Distress was assessed with several measures, including the Hospital Anxiety and Depression Scale (HADS), the Impact of Event Scale (IES), the Cancer Worry Scale – Revised (CWS-R), and the Memorial Anxiety Scale for PCa (MAX-PC). The HADS contains two sub-scales of seven items each which measure the presence and severity of general anxiety and depression [29]. Each subscale generates a score ranging from 0-21, where a score of higher than 10 indicates clinically relevant levels of anxiety or depression.

The IES is a 15 item scale measuring PCa-specific distress through the frequency of intrusive or avoidant thoughts about PCa [30]. Total scores on the intrusion and avoidance scales range from 0–35 and 0–40, respectively. A higher score indicates more frequent intrusive/avoidant thoughts about risk of cancer; a score of >8.5 indicates clinically relevant levels of distress.

The CWS-R a six item scale that measures worry about the risk of developing cancer and the frequency and impact of that worry on mood and daily functioning [31,32]. The CWS uses a score of 1 (no worry) to 4 (maximum worry) for each of the six items, giving a summative score between 4 and 24. A high score indicates greater worry, but no clinical cut-offs are available.

The MAX-PC includes three scales assessing PCa anxiety, PSA anxiety, and fear of recurrence. In the current study, we used the PCa anxiety (11 items) and PSA anxiety (3 items) scales [33]. The PCa anxiety scale is scored from 0-33 and the PSA anxiety scale from 0-9, with a higher score indicating higher levels of anxiety.

#### Health-related quality of life (HRQoL)

HRQoL was assessed using the SF-36 Health Survey version 2.0 [34,35]. This questionnaire consists of eight subscales: physical functioning, social functioning, role limitations due to physical, role limitations due to emotional problems, mental health, vitality, pain and general health. Summary scores can also be calculated for two broad areas of subjective wellbeing – physical health and mental health. All scales are linearly converted to a 0-100 scale, with a higher score representing better functioning.

#### Risk Perception

Men were asked to rate their perceived risk of PCa compared with the average man’s risk: lower, the same, slightly increased, moderately increased or strongly increased [36].

#### Knowledge

We developed a “knowledge scale” based on a measure developed by Lerman et al [37] and Wonderlick et al [38]. The 9 true/false items assessed knowledge of inheritance of *BRCA1/2*, the effect of having an altered gene, and risk of PCa. Knowledge scores were created by taking the sum of the correct responses to the 9-items.

The internal consistency reliability, as assessed by Cronbach’s coefficient alpha, was high for all measures used, ranging from 0.79 for the SF-36 General Health scale to 0.96 for the SF-36 Role Physical scale. Fourteen of the 15 scales had an alpha coefficient above 0.80.

### **Statistical analysis**

The dataset contained a small amount of missing data; for all scales except the SF-36, where >75% of a subscale was complete a total score (corrected for the total number of questions) was calculated. Where <75% was completed, data were excluded. For the SF-36 score, scales were excluded when there was <50% of a sub-scale completed, as per the recommendation of the scale’s authors [39]. Ten percent of the data entered were double-checked for coding accuracy and completeness and no errors were identified.

The SPSS 22.0 statistical computer package (SPSS Inc., Chicago) was used to manage and analyse the data. Scores for each questionnaire were calculated in accordance with each scales scoring system. Descriptive statistics, **including means and standard deviations,** were used to summarise the sample characteristics and questionnaire data.

All psychometric scales (HADS, IES, SF-36, MAX-PC and CWS) were skewed towards better scores. Neither log nor square root transformations of these scales produced normal distributions, but given the large sample size within each genetic cohort, parametric tests were utilised. To minimise the potential effect of multiple testing on the Type I error rate, a p value of <0.01 was regarded as statistically significant.

Univariate analysis examined if there were any measurable differences at baseline between *BRCA1* carriers, *BRCA2* carriers and controls on the dependent variables risk perception, HRQoL (SF36), the psychological measures (HADS, IES, MAX-PC) or knowledge. A UK dataset was used as a normative comparator for HRQoL, by randomly selecting individuals matched to our sample on age. Means were then compared using a paired Student’s t-test [34]. Only those aged up to 64 were recruited to this large study and so only men aged 40 to 64 from our sample were used as a comparison.

The impact of other variables on psychosocial outcomes was also explored. Independent variables included demographics (age, employment status and education), prior PSA screening, FH of PCa, time since genetic testing, and co-morbidities coded from clinical interview into a Charlson Co-morbidity Index score [40]. Knowledge of genetics and PCa and risk perception were also included as independent variables, to examine their impact on psychosocial outcomes.

The associations were investigated initially with analysis of variance, Student’s t-tests, chi-squared tests and Pearson’s correlations, as appropriate. For categorical independent variables, strength of association was calculated with Cohen’s *d* for any significant relationship. Subsequently, multivariate linear regression analyses were performed employing all independent variables found to be associated significantly at the univariate level with a psychosocial outcome.

## RESULTS

### **Sample characteristics and response rate**

Of the 65 centres participating in the IMPACT study, 23 agreed to take part in the HRQoL sub-study, including all 19 UK centres, 2 in Spain and 2 in the United States. The main reasons for choosing not to participate as a centre were financial; there was no specific funding to support this sub-study at collaborating sites outside of the UK. A total of 780 men enrolled in the HRQoL study, of whom 476 enrolled prior to their first screening visit (prospective cohort, reported here). This corresponds to 26% of the participants in the IMPACT study taking part in this sub-study. Those who returned their questionnaire >1 month after their initial screening visit or had not returned the study consent form were excluded (n=35), as were 9 men who were untested for their familial mutation, remaining at 50% risk. Thus the data presented are from 432 men, 351 of whom were recruited in the United Kingdom, 50 from the United States and 31 from Spain.

Uptake into the HRQoL sub-study was 85-100% at participating sites. There was no significant difference in the participants’ sociodemographics (employment status or education between the men in this sub-study and those in the parent IMPACT study.

Ninety-eight men (22.7%) carried a mutation in the *BRCA1* gene, 160 (37.0%) carried a mutation in the *BRCA2* gene and 174 (40.3%) were controls. The median time from undergoing genetic testing to joining the IMPACT study was 7.2 months (range 0 months – 15.4 years); 47.4% of men joined within 6 months of testing, and 39.6% of men had had at least one PSA measurement before they joined the IMPACT study.

The sociodemographics and family cancer history of the cohort are shown in Table 1. The mean age of men when they completed the baseline questionnaire was 53.1 years. The majority were Caucasian (98.9%), in higher managerial or professional occupations (55.3%), and well-educated, with 37.7% having college degrees or postgraduate qualifications.

### **Risk perception and knowledge**

Participants’ perception of their lifetime risk of PCa was influenced significantly by their carrier status (p<0.001) (Table 2). *BRCA2* carriers were more likely to rate their risk of PCa as moderately or strongly increased compared to the general population than the control group.

Knowledge scores were not impacted by the genetic status of the participant, time since genetic testing or education level. FH of PCa, education level, time since genetic testing and age were not significantly associated with any of the outcome variables.

### **SF-36**

Overall physical functioning SF36 scores did not differ significantly from the normative sample (IMPACT sample aged 40-64 mean: 48.1; matched norm sample mean: 47.5, p=0.52). The overall mental functioning SF36 score was significantly better in our cohort compared with the normative sample, but the effect size was small and both mean values were close to the standardised mean of 50 (IMPACT sample 40-64 mean: 52.0; matched norm sample mean: 49.8, p=0.008, Cohen’s *d*=0.21). Means also did not differ significantly across genetic groups.

### **HADS**

The overall mean anxiety and depression scores for the HADS scale were 4.9 and 2.8, respectively, which were not higher than previously reported general population norms [41]. The means across different genetic risk groups also did not differ significantly (Table 2; anxiety: p=0.99; depression: p=0.75).

None of the independent variables showed a significant association with either the anxiety or depression scores. Those with higher risk perception had slightly higher scores on the anxiety and depression scales (Table 3, p=0.02 and p=0.03 respectively), though not significantly so.

### **IES, CWS, MAX-PC**

At the univariate level, the mean intrusion and avoidance scores on the IES scale were significantly higher in both *BRCA1* and *BRCA2* carriers compared with controls (Table 2, intrusion: p=0.001; avoidance: p<0.0001) and higher in those who perceived their PCa risk as moderately or strongly increased (Table 3, intrusion: p<0.001; avoidance: p=0.001). However, at the multivariate level, risk perception contributed more significantly to the variation in IES scores than genetic status (Table 4).

A similar pattern was seen for the cancer worry score. Scores were generally low and univariately associated with genetic status (Table 2, CWS: p=0.004) and risk perception (Table 3, CWS: p<0.001). Again, risk perception was more highly associated with higher cancer worry than genetic status in the multivariate model (Table 4).

PCa anxiety scores (MAX-PC) were only associated with risk perception ( p <0.001) and so a multivariate analysis was not undertaken.

**DISCUSSION**

This study investigated the baseline HRQoL and psychosocial profiles of men taking part in the IMPACT study, prior to their first screening appointment. The results indicate that participants, in general, do not have clinically concerning levels of general or cancer-specific distress or poor HRQoL. A small subset of participants has higher levels of distress, but perception of risk contributed more to explaining the variance in distress level than did genetic status.General population screening studies in the UK and European series have reported similar findings; that PCa screening does not have a detrimental effect on measures of HRQoL and psychological health [28,42,43].

It was reassuring that participants’ perceptions of PCa risk were influenced by carrier status, largely reflecting what would have been communicated during genetic counselling [2,3]. As expected, *BRCA2* mutation carriers had the highest perceived risk of PCa, most frequently classifying risk as ‘slightly’ or ‘moderately’ increased, and controls most frequently classifying risk as the ‘same’ as the general population.

Knowledge levels were high across the cohorts, irrespective of genetic status, education level and time since testing, demonstrating that men retained accurate information about inheritance of *BRCA* mutations and cancer risk. The knowledge questionnaire was designed specifically for this study, but was adapted from that used in other studies [37,38]. These studies reported knowledge levels to be around 50% in women at risk of breast cancer prior to genetic testing. The high levels of knowledge reported in our cohort could reflect their participation in the IMPACT study, where they recently revisited their risk status in making a decision to undergo screening. However, men were asked to complete these questionnaires prior to their first meeting with the study team, and so they may not have had a detailed discussion about risk of PCa since being informed about their genetic status. The sociodemographics of the cohort indicate that the participants were highly educated, which has been found to be associated positively with an individual’s ability to learn information communicated during genetic counselling [44].

HRQoL assessments did not detect any clinically relevant differences in either physical or mental health when compared with general population samples, both matched and unmatched by age [34]. Our results support those of the Finnish European Randomised Screening for Prostate Cancer study cohort in which HRQoL was also assessed with the SF36 [43]. As in our cohort, HRQoL scores were observed to be higher than in the general Finnish population [43], but not at clinically significant levels; this was hypothesised to be because the men were generally healthy and well educated. However the Finnish cohort was not age-matched, which may have conferred some bias.

In terms of general distress, scores were within previously reported population norms [41] and no differences were observed between carriers and controls. For cancer-specific distress, a significant difference was found between *BRCA* carriers and controls for both the IES and CWS. However the differences were small and mean scores remained below clinically relevant levels for the IES. Importantly, at the multivariate level, risk perception was found to have a stronger association with distress levels than genetic status itself.

There was no significant association observed between anxiety and having a FH of PCa, supporting previous reports [15,24,28,42,45]. Men reporting higher PCa risk perception were found to have consistently higher scores across all psychological distress scales (general and cancer-specific). Similar results were reported by Taylor et al [24]. However, the effect size was small across all scales and no group had a mean distress score that reached clinically significant levels, where such thresholds were available [30,41]. Therefore, it is fair to conclude that, whilst having a modest impact on men’s distress levels, a high perceived PCa risk is not associated strongly with clinically significant levels of distress in this cohort.

A number of studies have reported that anxiety surrounding cancer screening affects a small number of people who are predisposed to anxiety, and that this anxiety continues throughout participation in cancer screening [16,27,28,42,46]. Our data support this finding, with a small proportion of men reporting clinically significant levels of distress. It will be important to compare these baseline levels with subsequent screening rounds in IMPACT and to include previous high PSA results as a covariate, as both the European and American screening studies report high levels of anxiety in men with previously elevated PSA levels [26,27]. Identifying men with a predisposition to high levels of psychological distress could facilitate providing timely support to manage this distress and potentially increase adherence with screening recommendations.

We did not observe a significant association between distress and age. While this supports several earlier studies [16,42], one study reported an inverse relationship between age and distress levels [27].

It is important to consider whether we would have observed different results if all men in the IMPACT study had been included in this psychosocial sub-study. However we found no difference in sociodemographics between the men in the sub-study and those in the IMPACT study as a whole. It could be that those more predisposed to anxiety may be inclined not to join the psychosocial sub-study; however no evidence of this has been found by others [28].

We obtained a very high uptake level for the psychosocial sub-study, with at least 85% opting in at participating sites. Uptake was also found to be high in the ERSPC Swedish cohort, with 84-94% of men with abnormal PSA levels completing a questionnaire measuring anxiety levels [27]. This high participation rate is likely due to the embedding of this psychosocial study into an existing screening study, and therefore inviting participants who are already highly motivated to contribute to research.

A strength of the present study is the use of a number of different, standardized psychological measures that offer extensive insight into the psychosocial profile of the participants and that allow comparison of the results with a number of other PCa screening studies that have used the same or similar measures.

We would note that our sample was restricted to men who have previously engaged with health services by undergoing genetic testing and who responded positively to an invitation to take part in a research study. In addition, there was limited variability in ethnicity and other sociodemographics, which may limit to some degree the generalisablity of the findings.

The data presented represent a snapshot of men’s psychosocial profiles when they joined the IMPACT study. Follow-up data will inform whether the PCa screening process has an impact on HRQoL or distress over time.

**CONCLUSIONS AND CLINICAL IMPLICATIONS**

To the best of our knowledge, this is the first study to report the psychosocial and HRQoL profile of men with *BRCA1/2* mutations taking part in a PCa screening study. Uptake into the study was very high, and participants had very high levels of knowledge about genetics and PCa. As a whole, the cohort did not demonstrate any clinically concerning levels of general or cancer-specific distress or poor HRQoL. A small subset of participants reported higher levels of distress, but perception of risk was more strongly associated with distress levels than was genetic status. It is important for health care professionals to be aware of these predictors of distress so that men with potential for heightened distress can be identified and adequate counselling and support can be offered. Follow-up data will determine whether these factors have an impact on adherence with screening and whether men experiencing abnormal PSA results experience more distress.

**ACKNOWLEDGEMENTS**

This research is coordinated by The Institute of Cancer Research, London, UK and is supported by grants from Cancer Research UK (Grant references (C5047/A21332, C5047/A13232 and C5047/A17528) and The Ronald and Rita McAulay Foundation. We acknowledge support from the National Institute for Health Research (NIHR) to the Biomedical Research Centres at The Institute of Cancer Research and Royal Marsden Foundation NHS Trust, at Central Manchester Foundation Trust and the Oxford Biomedical Research Centre Program. The Institute of Cancer Research is the Sponsor of the IMPACT study. We thank Mr and Mrs Jack Baker for support for the study in NorthShore University HealthSystem, Evanston, Illinois.

**CONFLICTS OF INTEREST**

Prof Rosalind Eeles – Janssen: provided medical education support to GU ASCO Feb 2013. Succinct Communications: received an honorarium and expenses for attending and speaking at UK Cancer Convention Oct 2013

The authors have no other conflict of interest to declare**REFERENCES**

[1] Cancer Research UK. Cancer Research UK CancerStats. Available at: http://info.cancerresearchuk.org/cancerstats [Accessed 01/04/2015]

[2] Leongamornlert D, Mahmud N, Tymrakiewicz M, et al. Germline BRCA1 mutations increase prostate cancer risk. *Br J Cancer* 2012; 106: 1697-701.

[3] Kote-Jarai Z, Leongamornlert D, Saunders E, et al. BRCA2 is a moderate penetrance gene contributing to young-onset prostate cancer: implications for genetic testing in prostate cancer patients. *Br J Cancer* 2011; 105(8): 1230-4.

[4] Castro E, Goh C, Olmos D, et al. Germline BRCA mutations are associated with higher risk of nodal involvement, distant metastasis, and poor survival outcomes in prostate cancer. *J Clin Oncol* 2013; 31: 1748-57.

[5] Gallagher DJ, Gaudet MM, Pal P, et al. Germline BRCA mutations denote a clinicopathologic subset of prostate cancer. *Clin Cancer Res* 2010; 16: 2115-21.

[6] Bancroft EK, Page EC, Castro E, et al. Targeted prostate cancer screening in BRCA1 and BRCA2 mutation carriers: results from the initial screening round of the IMPACT study. *Eur Urol* 2014; 66(3): 489-99.

[7] Andriole GL, Crawford ED, Grubb RL, 3rd, et al. Prostate cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial: mortality results after 13 years of follow-up. *J Natl Cancer Inst* 2012; 104: 125-32.

[8] Schroder FH, Hugosson J, Roobol MJ, et al. Prostate-cancer mortality at 11 years of follow-up. *N Engl J Med* 2012; 366: 981-90.

[9] Catalona WJ, Antenor JA, Roehl KA, Moul JW. Screening for prostate cancer in high risk populations. *J Urol* 2002; 168: 1980-3; discussion 3-4.

[10] Kiemeney LA, Broeders MJ, Pelger M, et al. Screening for prostate cancer in Dutch hereditary prostate cancer families. *Int J Cancer* 2008; 122: 871-6.

[11] Makinen T, Tammela TL, Stenman UH, et al. Family history and prostate cancer screening with prostate-specific antigen. *J Clin Oncol* 2002; 20: 2658-63.

[12] Uzzo RG, Pinover WH, Horwitz EM, et al. Free prostate-specific antigen improves prostate cancer detection in a high-risk population of men with a normal total PSA and digital rectal examination. *Urology* 2003; 61: 754-9.

[13] Foster C, Watson M, Eeles R, et al. Predictive genetic testing for BRCA1/2 in a UK clinical cohort: three-year follow-up. *Br J Cancer* 2007; 96: 718–724.

[14] Meiser B. Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psycho-Oncology* 2005; 14: 1060–1074.

[15] Sweetman J, Watson M, Norman A, et al. Feasibility of familial PSA screening: psychosocial issues and screening adherence. *Br J Cancer* 2006; 94: 507–512.

[16] Brindle LA, Oliver SE, Dedman D, et al. Measuring the psychosocial impact of population-based prostate-specific antigen testing for prostate cancer in the UK. *BJUI Int* 2006; 98: 777–782.

[17] Bancroft EK, Castro E, Bancroft G et al. The psychological impact of undergoing genetic-risk profiling in men with a family history of prostate cancer. *Psycho-onc* 2015; 24(11): 1492-9.

[18] Bratt O, Damber JE, Emanuelsson M, et al. Risk perception, screening practice and interest in genetic testing among unaffected men in families with hereditary prostate cancer. *Eur J Cancer* 2000; 36: 235–241.

[19] Cormier L, Guillemin F, Valeri A, et al. Impact of prostate cancer screening on health related quality of life in at-risk families. *Urology* 2001; 59: 901–906.

[20] Strømsvik N, Raheim M, Gjengedal E.. Cancer worry among Norwegian male BRCA 1/2 mutation carriers. *Familial Cancer* 2011; 10: 597-603.

[21] Hallowell N, Ardern-Jones A, Eeles Ret al . Communication about genetic testing in families of male BRCA1/2 carriers and non-carriers: patterns, priorities and problems. *Clinical Genetics* 2005; 67(6): 492-502.

[22] Hallowell N, Arden-Jones A, Eeles R et al. Guilt, blame and responsibility: men's understanding of their role in the transmission of BRCA1/2 mutations within their family. *Sociology of Health and Illness* 2006; 28 (7): 969-88.

[23] Moynihan C, Bancroft EK, Mitra A et al. Ambiguity in a masculine world: Being a BRCA1/2 mutation carrier and a man with prostate cancer. Psychooncology. 2017 Aug 15. [Epub ahead of print]

[24] Taylor KL, Di Placido J, Redd WH, Faccenda K, Greer L, Perlmutter A. Demographics, family histories, and psychological characteristics of prostate carcinoma screening participants. *Cancer* 1999;85(6): 1305-12.

[25] Taylor KL, Shelby R, Kerner J, Redd W, Lynch J. Impact of undergoing prostate carcinoma screening on prostate carcinoma-related knowledge and distress. *Cancer* 2002;95(5): 1037-44.

[26] Taylor KL, Shelby R, Gelmann E, McGuire C. Quality of life and trial adherence among participants in the prostate, lung, colorectal, and ovarian cancer screening trial. *J Natl Cancer Inst* 2004; 96(14): 1083-94.

[27] Carlsson S, Aus G, Wessman C, Hugosson J. Anxiety associated with prostate cancer screening with special reference to men with a positive screening test (elevated PSA) - Results from a prospective, population-based, randomised study. *Eur J Cancer* 2007; 43(14): 2109-16.

[28] Essink-Bot ML, de Koning HJ, Nijs HGT, Kirkels WJ, van der Maas PJ, Schroder FH. Short-term effects of population-based screening for prostate cancer on health-related quality of life. *J Natl Cancer Inst* 1998; 90: 925–31

[29] Zigmund AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavia* 1983; 67: 361–370.

[30] Horowitz M. Stress response syndromes and their treatment. In Goldberger L. & Breznitz S. (Eds) Handbook of stress: Theoretical and clinical aspects pp.711–732. New York: Free Press 1982.

[31] Lerman C, Trock B, Rimer BK, Boyce A, Jepson C, Engstrom PF. Psychological and behavioural implications of abnormal mammograms. *Ann Intern Med* 1991; 114: 657–661.

[32] Watson M, Lloyd S, Davidson J, et al. The impact of genetic counselling on risk perception and mental health in women with a family history of breast cancer. *Br J Cancer* 1999; 79: 868–874.

[33] Dale W, Hemmerich J, Meltzer D. Extending the validity of the Memorial Anxiety Scale for Prostate Cancer (MAX-PC) at the time of prostate biopsy in a racially-mixed population. *Psychooncology* 2007; 16(5): 493-8.

[34] Jenkinson C, Stewart-Brown S, Petersen S, Paice C. Assessment of the SF-36 version 2 in the United Kingdom. J Epidemiol Community Health 1999; 53(1): 46-50.

[35] Ware J, Sherbourne C: The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473.

[36] Lerman C, Lustbader E, Rimer B, et al. Effects of individualized breast cancer risk counseling: a randomized trial. *J Natl Cancer Inst* 1995; 87: 286–292.

[37] Lerman C, Narod S, Schulman K . BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. *JAMA* 1996; 275(24): 1885-1892.

[38] Wonderlick AL, Fine BA. Knowledge of Breast Cancer Genetics Among Breast Cancer Patients and First-Degree Relatives of Affected Individuals. *J Gen Couns 1997;* 6(2): 111-130.

[39] Maruish ME, DeRosa MA. A guide to the integration of certified Short Form survey scoring and data quality evaluation capabilities. Lincoln, RI: QualityMetric Incorporated; 2009.

[40] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *Journal of Clinical Epidemiology* 1994; 47(11): 1245-1251

[41] Breeman S, Cotton S, Fielding S, Jones GT. Normative data for the Hospital Anxiety and Depression Scale. *Qual Life Res* 2015; 24(2): 391-8.

[42] Macefield RC, Lane JA, Metcalfe C et al. Do the risk factors of age, family history of prostate cancer or a higher prostate specific antigen level raise anxiety at prostate biopsy? *Eur J Cancer* 2009; 45: 2569–73.

[43] Vasarainen H, Malmi H, Määttänen L et al. Effects of prostate cancer screening on health-related quality of life: results of the Finnish arm of the European randomized screening trial (ERSPC). *Acta Oncol* 2013 ; 52(8): 1615-21.

[44] Portnoy DB, Roter D, Erby LH. The role of numeracy on client knowledge in BRCA genetic counselling. *Patient Educ Couns* 2010; 81(1): 131-6.

[45] Bratt O, Emanuelsson M, Grönberg H. Psychological aspects of

screening in families with hereditary prostate cancer. *Scandinavian Journal of*

*Urology and Nephrology* 2003; 37(1): 5-9.

[46] Brunton M, Jordan C, Campbell I. Anxiety before, during, and after participation in a population-based screening mammography programme in Waikato Province, New Zealand. *N Z Med J.* 2005; 118(1209): U1299.

Table 1: Sociodemographics of the cohort

|  |  |  |
| --- | --- | --- |
|  | **N** | **%** |
| *Age* | Mean: 53.1; Median: 53.0 | SD: 8.5 |
| *Education* | **415** | **96.1** |
| Pre-high school | 108 | 25.0 |
| High school or technical | 144 | 33.3 |
| Degree or postgraduate | 163 | 37.7 |
| *Employment* | **429** | **99.3** |
| In active paid work | 328 | 75.9 |
| Retired | 82 | 19.0 |
| Unemployed | 19 | 4.4 |
| *Family history of prostate cancer* | **432** | **100** |
| None | 293 | 67.8 |
| In ≥1 first degree relative | 139 | 32.2 |
| *Time since genetic testing* | **424** | **98.1** |
| 0-3 months prior to enrolment | 125 | 28.9 |
| 3-6 months | 76 | 17.6 |
| 6-12 months | 48 | 11.1 |
| 12-24 months | 49 | 11.3 |
| 2-5 years | 76 | 17.6 |
| >5 years | 50 | 11.6 |

Table 2: Descriptive statistics and summary of group comparisons for the psychosocial variables

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Scale*** |  |  | **Overall** | ***BRCA1* carriers** | ***BRCA2* carriers** | **Controls** |  |
|  |  | N | Mean (SD)% above threshold | N | Mean (SD)% above threshold | N | Mean (SD)% above threshold | N | Mean (SD)% above threshold | Cohen’s *d*\* |
| **SF36 Physical Component Summary** | Range | 0-100 | 404 | 47.4 (10.0) | 90 | 46.4 (10.7) | 148 | 47.1 (10.1) | 166 | 48.3 (8.6) |  |
| **SF36 Mental Component Summary** | Range | 0-100 | 404 | 52.4 (10.2) | 90 | 52.1 (11.1) | 148 | 51.2 (10.5) | 166 | 53.7 (9.3) |  |
| **Total Anxiety (HADS)** | Range | 0-21 | 431 | 4.9 (3.6) | 97 | 4.9 (3.5) | 160 | 4.8 (3.8) | 174 | 4.9 (3.4) |  |
| Abnormal threshold | ≥11 | 28 | 6.5% | 6 | 6.2% | 12 | 7.5% | 10 | 5.7% |  |
| **Total Depression (HADS)** | Range | 0-21 | 431 | 2.8 (3.0) | 97 | 2.9 (3.2) | 160 | 2.9 (3.1) | 174 | 2.7 (2.7) |  |
| Abnormal threshold | ≥11 | 9 | 2.1% | 3 | 3.1% | 4 | 2.5% | 2 | 1.1% |  |
| **Total Intrusion (IES)** | Range | 0-35 | 423 | 2.3 (4.9) | 94 | **3.0**† (5.7) | 158 | **3.1**† (5.5) | 171 | **1.3**† (3.5) | -0.02; 0.35; 0.38 |
| Abnormal threshold | ≥19 | 12 | 2.8% | 4 | 4.3% | 6 | 3.8% | 2 | 1.2% |  |
| **Total Avoidance (IES)** | Range | 0-40 | 418 | 4.3 (7.0) | 93 | **6.0**† (8.4) | 156 | **5.1**† (7.4) | 169 | **2.6**† (5.2) | 0.11; 0.48; 0.39 |
| Abnormal threshold | ≥19 | 32 | 7.7% | 12 | 12.9% | 15 | 9.6% | 5 | 3.0% |  |
| **Total MAX-PC** | Range | 0-33 | 420 | 3.5 (5.4) | 94 | 4.1 (5.5) | 156 | 3.9 (6.2) | 170 | 2.8 (4.6) |  |
| **Total Cancer Worry** | Range | 4-24 | 430 | 9.5 (2.5) | 97 | **9.7**† (2.7) | 160 | **9.9**†(2.7) | 173 | **9.1**† (2.0) | -0.09; 0.25; 0.36 |
| **Risk Perception** |  | 423 | N/A | 91 | N/A | 156 | N/A | 171 | N/A |  |
| Moderately or strongly increased | 133 | 31.4% | 31 | **32.3%**‡ | 86 | **55.1%**‡ | 16 | **9.4%**‡ | 0.43§ |
| **Total Knowledge Score** | Range | 0-9 | 404 | 7.1 (1.7) | 92 | 6.9 (1.8) | 151 | 7.2 (1.6) | 161 | 7.1 (1.7) |  |

\*Cohen’s *d* values are listed comparing *BRCA1* carriers with *BRCA2* carriers; *BRCA1* carriers with controls; *BRCA2* carriers with controls; †p<0.01 using an analysis of variance test (ANOVA); ‡p<0.01 using a chi-squared test for independence; §Cramer’s V test for nominal association

Table 3: Means of psychosocial scales according to risk perception categories

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Risk Perception** |  |  |
| **Scale****(mean scores)** | *Up to slightly increased* | *Moderately-Strongly increased* | p | Cohen’s *d* |
| *HADS Anx* | 4.54 | 5.43 | *0.02* |  |
| *HADS Dep* | 2.55 | 3.23 | *0.03* |  |
| *IES Int* | 1.33 | 4.42 | *<0.001* | -0.57 |
| *IES Av* | 3.32 | 6.11 | *0.001* | -0.39 |
| *MAX-PC (PCa)* | 2.62 | 5.32 | *<0.001* | -0.47 |
| *CWS-R* | 8.89 | 10.84 | *<0.001* | -0.76 |

Table 4: Results of linear regression analysis for the Hospital Anxiety and Depression Scale (HADS), Impact of Events (IES) Intrusion (Int) and Avoidance (Av) and Cancer Worry Scale (CWS)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | ***Variables*** | ***B*** | ***SE*** | ***T*** | ***p*** | ***R2*** | ***R2 Change*** |
| ***IES Int*** | *Risk Perception* | 2.92 | 0.55 | 5.32 | <0.001 | 0.087 | 0.087 |
| *BRCA2 status* | 0.42 | 0.58 | 0.72 | 0.47 | 0.087 | 0.000 |
| *BRCA1 status* | 0.98 | 0.62 | 1.59 | 0.11 | 0.092 | 0.006 |
|  |  |  |  |  |  |  |
| ***IES Av*** | *BRCA1 status* | 2.88 | 0.91 | 3.18 | 0.002 | 0.017 | 0.017 |
| *BRCA2 status* | 1.50 | 0.85 | 1.76 | 0.08 | 0.042 | 0.025 |
| *Risk Perception* | 2.18 | 0.81 | 2.70 | 0.007 | 0.058 | 0.017 |
|  |  |  |  |  |  |  |
| ***CWS*** | *Risk Perception* | 1.98 | 0.27 | 7.46 | <0.001 | 0.137 | 0.137 |
| *BRCA2 status* | -0.07 | 0.28 | -0.24 | 0.81 | 0.138 | 0.001 |
| *BRCA1 status* | 0.14 | 0.30 | 0.47 | 0.64 | 0.138 | 0.000 |