



UK Genetic Prostate Cancer Study (UKGPCS) Newsletter

ICR
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of Cancer Research

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AN UPDATE FOR PATIENTS, THEIR FAMILIES, DOCTORS AND NURSES

An update from Professor Ros Eeles



2011 was another productive year for UKGPCS. We have found more genetic variants that predispose to prostate cancer, which we will be able to use in the development of a genetic risk profile.

Our current studies are:

- (1) To try to determine the overall spectrum of genetic variants that predispose to prostate cancer.
- (2) To try to identify if genetic variants interact with environmental factors that contribute to increased prostate cancer risk.
- (3) To use the information from our genetic and environmental studies to develop targeted prostate screening programmes.
- (4) To investigate how genetic variants might impact on cancer care.

We should like to say a very big thank you to all those men and hospital teams who are helping with this research.

A Patient's Perspective: My 2011 Journey

My name is Chris, aged 72 and I live with my wife Kay in Worcester Park, Surrey. I reckon that from birth everyone starts their own personal journey through life. I want to relate to a journey of mine that started on the 4th January last year. Kay had suggested that I ask my Doctor if I could have a PSA test in addition to my routine blood test. Kay was anxious because she had lost her cousin Keith to prostate cancer at the age of 54. He showed no signs of illness, until it was too late to save him.

My GP agreed to the PSA test and it came back 12.1. My prostate was found to be enlarged but I had no signs of illness. Within two weeks I had various tests and the five days waiting for the results was undoubtedly the most anxious time of my journey. Fortunately, the news was good. The cancer was localised to the prostate and treatment was to consist of hormone therapy starting immediately and Radiotherapy was in June.

On the 18th May, I attended the Royal Marsden Hospital at Sutton. The whole process of Radiotherapy was explained to me, which I started on 29th June and ended on 26th July. I was then approached by a Genetics nurse from the UK Genetic Prostate Cancer Study asking if I would be interested in joining the study which I agreed to do.

The Genetics nurse gave me forms to complete outlining my family's cancer history. Because my parents parted company when I was 3 years old, I contacted one of my half-sisters about our father. She confirmed that he had had successful surgery for breast cancer at the age of 50. I now understand that this fact

would increase the probability of me having prostate cancer, because there is a gene common to both the breast and the prostate. In turn, we have a son who is aged 39. We were recommended to encourage him to have a PSA test, especially as this cancer can be more aggressive if found in a younger person.

On the 31st October, I attended the Royal Marsden Hospital for a final assessment of all my treatment. After an examination it was confirmed that my prostate is excellent and that my PSA is 0.16 which is fantastic. I am probably deluding myself, but I would like to think that by walking and cycling for most of the year, having a daily glass of cranberry juice since June, and taking a daily teaspoonful of manuka honey 15+ during radiotherapy and a month afterwards, all helped me to feel well for most of the time.

Looking back over the last ten months, it has been a roller coaster of emotions with some setbacks. Naturally, there have been a few occasions when I have felt alone on my journey. However, for the vast majority of time I have had phenomenal support from my GP Centre, large teams at the hospitals attended, my family, friends, neighbours, and patients and their carers. It was a privilege to have met so many wonderful people on this journey. Many of the conversations with patients included stories of their personal journeys.



The Royal Marsden Hospital is a very special place. I think this is largely because all the patients have cancer, of one sort or another, which in effect means we are all on the same journey and have the same aim to get well again soon. There was a great comradeship between the staff, patients and carers to pull together to make the treatment a success.

All the hospital's staff showed professionalism, kindness, and understanding, and smiled when introducing themselves and subsequently provided positive support. I found their whole approach so refreshing and I know that many other patients felt the same.

If you have a story to share with us please contact the UKGPCS team on 0208 722 4395

Tony Rose – My Story



The Royal Marsden and The Institute.

When my late wife discovered she had terminal breast cancer some 17 years ago, and knowing my hobby was Classic Car Rallying we decided to form a committee of friends down in Brighton to raise money through sponsorship for The Royal Marsden and The Institute of Cancer Research. So I entered my first Monte Carlo Rally which I had always dreamed of since a boy! When we finished my wife and friends organised a Grand Ball at The Grand Hotel in Brighton with the car in the ballroom as 'the star'. Then a fashion show was organised with local retailers and so over the next 7 years this became a regular event. After 5 Monte Carlo Rallies, Balls and fashion shows we raised over £500,000.00 which went towards equipment at both

Unfortunately the next year in 2001 my wife was admitted into The Martletts Hospice in Hove, so that year a close friend took my car on 'The Monte' and brought it back to the hospice so my wife and friends could see it. Sadly the next month my wife passed away. I competed in 2 more 'Montes' and after meeting my present wife who works at The Marsden, I decided to fold the committee up and move to Banstead.

By an ironic chance at the tender age of 71 I have recently been diagnosed with prostate cancer, which I have recently started treatment for at The Marsden.

I would like to think after giving many years to fundraising for The Marsden and The Institute it is my turn to be looked after.

I would like to give my thanks to all the staff in Radiotherapy who made my 7 1/2 weeks bearable as I have now finished my treatment and although initially tired, feel back to strength and have entered my first Rally of 2012 in April in Wales.

Messages from Clinical Fellows:



Dr Chee Goh is a clinical oncologist currently working towards a research degree with Professor Eeles. His research involves correlating genetic markers known to predict risk for prostate cancer, with different treatment outcomes and toxicities using the data collected from men taking part in the UKGPCS. Men are sometimes faced with many treatment options for their prostate cancer and each option has its own set of potential side effects. These side effects in turn can show a large variation in terms of severity and the reasons for this are not always clear. Efforts are now underway to see if genes could hold the answers. Using genetic markers to predict response or tolerance to different treatments could better inform both patients and clinicians to select the best treatment choices, thereby bringing us closer to personalised therapy. The UKGPCS has been invaluable in contributing both sample and treatment data for Chee's studies.

Dr Emma Killick has a background in medical oncology and is working on methods of earlier cancer detection in genetically high risk individuals. The success of this strategy has been demonstrated in familial breast cancer families where a more intensive screening program with mammography and breast MRI has detected cancers at an earlier stage. Emma has been working on a new research study which will evaluate the benefit of whole body MRI in individuals at high cancer risk. Further areas of investigation include protein markers in the serum and urine which may be early predictors of prostate cancer in men carrying a mutated BRCA gene, and analysis of changes to the DNA and the impact of this on cancer risk. Emma is using samples from UKGPCS to investigate whether certain genetic alterations predict the subtype of prostate cancer an individual develops, as determined by the presence of DNA translocations within the tumour. This information may help us tailor the choice of early detection markers to an individual's personal genetic make-up.



Latest Research News

One part of our UKGPCS research involves the known breast cancer susceptibility genes, BRCA1 and BRCA2. These genes were discovered in the early 1990's and alterations (mutations) in them are rare, occurring in less than 0.2% of most of the general population. Studies in families have shown that BRCA mutations predispose women to breast and ovarian cancer; around 5% of women with breast cancer have one of the BRCA mutations and around 10% of women with ovarian cancer are carriers. DNA can break, due to environmental factors and also the normal metabolic processes within our bodies. In normal cells BRCA genes repair DNA breaks, but mutations in the BRCA genes can interfere with their ability to repair DNA, and sometimes the cell will then go on to divide with damaged DNA, eventually resulting in cancer.



Although the BRCA genes are often tested for in families with a history of breast or ovarian cancer, not so much is understood about their role in prostate cancer, so we have used our large resource of UKGPCS samples to determine what proportion of prostate cancer patients might have a BRCA mutation.

Back in 2003 we tested 263 of our samples in men who had developed early-onset prostate cancer at age 55 or younger, and we found that 2% of them carried BRCA2 mutations. We published a further paper on the 263 case samples in 2010, showing that, on average, prostate cancer in the 2% of men who were BRCA2 carriers was more aggressive with a poorer prognosis. This suggests that BRCA2 carriers should not be treated with active surveillance but with more rigorous treatments.

In 2011 we published a paper which confirmed these findings in a larger subset of the UKGPC Study, using samples from 1832 men diagnosed with prostate cancer between the ages of 36 and 88. Nineteen (1.2%) men diagnosed at 65 years or younger were found to have BRCA2 mutations, and no mutations were found in men diagnosed after 65 years of age. The findings suggest that inherited BRCA2 mutations are more closely linked to a younger age of onset than to a family history of prostate cancer.

So BRCA mutations are still relatively rare in prostate cancer, but in our latest finding their incidence is around 6x higher in men with prostate cancer than in the general population. If you take part in UKGPCS we ask if there are any cancers in your family in your male or female relatives, and this is partly to see if there are many cases of breast or ovarian cancers, which could suggest that a BRCA mutation is present. If you are at all concerned about your family history of cancer, in the first instance you should talk to your GP who can refer you to your local genetics service. BRCA testing is currently usually only carried out on individuals with a strong family history of breast or ovarian cancer, but a genetics service will be able to give you any advice that you need about your family risk of cancer and whether testing would be relevant to you or your relatives.

For men who find that they do have BRCA1/2 alterations, clinical trials are underway looking at a new treatment option; Poly (ADP-ribose) polymerase or PARP inhibitor drugs preferentially target cancers which have BRCA mutations. They work by targeting the cancer cells with broken DNA and killing these cells while leaving normal cells undamaged.

Our research suggests that it would help if we could test all prostate cancer patients diagnosed aged 65 or younger for BRCA mutations, as part of their cancer care pathway. This can only happen once diagnostic testing becomes faster and cheaper, but the technology to make diagnosis and treatment more personalised is improving rapidly and so we hope that the developments in cancer genetics will make this a reality.

All of our research publications can be found online at our website www.icr.ac.uk/ukgps, just click on the links to open each publication

The PROFILE Study — Recruitment Continues.....

Aim of study: The PROFILE study aims to investigate whether our current knowledge of genetics of prostate cancer can be used to develop a targeted screening programme for men with a strong family history of the disease.

Prostate cancer risk: PROFILE arises from many years of research into prostate cancer risk factors, including the discovery of 46 genetic variants that are known to raise the risk of prostate cancer. In addition to this it has been recognised that a family history of prostate cancer substantially increases men's chances of developing the disease.

Recruitment eligibility: To take part in PROFILE men have to be aged between 40 - 69 and have a family history of prostate cancer but not have had prostate cancer themselves. For the purposes of the study, family history is considered to be positive if a man is related to someone who has been diagnosed with prostate cancer under 70 or if several family members have been diagnosed with prostate cancer.

Screening for participants: Men who enrol on the study give a blood sample from which DNA is extracted. They are offered a one-off prostate biopsy where samples of tissue taken from the prostate are examined to check for cancer. In addition to this they are offered a 6 monthly PSA (prostate specific antigen) test. Some men are also offered an MRI scan of the prostate.

Recruiting: PROFILE has been running since October 2010 and currently has 80 participants. Our target is to enrol 100 participants.

Outcome: We hope to eventually develop a genetic profiling test for the general population that can be used in an accessible and effective prostate screening programme.

PROFILE is using the genetic variants found so far in UKGPCS—if you or any family relatives would like more information please contact Elizabeth Bancroft (or) Natalie Taylor on Tele no: 020 7808 2136/020 8661 3643
or Email: elizabeth.bancroft@rmh.nhs.uk or natalie.taylor@rmh.nhs.uk

Staff News

There have been some changes in the Data Team since the last newsletter.

Michelle Guy, Study Co-Ordinator, returned to the study following the birth of her second daughter.

The team said a sad farewell to Amanda Hall in January 2011. Amanda worked on the study for 7 years, the team are really grateful for her hard work over the years and wish her the best of luck for the future in her new career of critical care nursing.

Amanda was replaced by Angela Morgan who is now the new UKGPCS Research Nurse. Angela moved into uro-oncology research nursing in 2008, following a career background in community and urological surgical nursing. Angela joined the UKGPCS team in April 2011. She says "I am really excited to be involved with such an important study for men".

We would like to thank the organisations supporting our work:



And many thanks to our generous donors

Chris Jones in memory of his father Tony Jones, Anne and Stuart Cliff, The Ronald and Rita McAulay Foundation, Mr Tony Maxse, Mr Hugh Knowles, Liz, Chris, Tim and Sarah Powell, Mrs Rogers, Mr J and Mrs F A Lavington and The Annabel Evans Memorial Fund

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