

## APPENDIX C

### **Identification of Men with a genetic predisposition to Prostate Cancer: Targeted screening in BRCA1/2 mutation carriers and controls –**

#### **Patient Information Sheet (Version 2 – 08/04/05)**

##### **Invitation to participate and description of the project**

We would like to invite you to take part in a research study. Research has shown that men who have an alteration in the Breast Cancer 1 (*BRCA1*) or Breast Cancer 2 (*BRCA2*) genes are at a higher risk of developing prostate cancer. This study aims to look at methods of early detection of prostate cancer in men at a higher risk and compare this with a control group. You will have been invited into this study either because you have been found to have an alteration in *BRCA1* or *BRCA2* after a genetic test in a genetics centre, or because you are acting as 'a control'. Men in the control group have had a genetic test for an alteration known to be present within their family and this test has been negative. Having a control group will enable us to compare the measurements that we will take in this study in people who have an increased risk of prostate cancer (those with the genetic alteration) and those who are currently thought to have the same risk as the general population (the controls).

This study is being carried out at many centres all over the UK and Europe. The results of this study will help us to develop a programme of early detection for prostate cancer in men with these gene alterations.

Before you decide it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others and your GP, if you wish. Please ask us if anything is not clear or if you would like to have more information and take time to decide whether or not you wish to take part. Thank you for reading this.

##### **What are the aims of this study?**

Prostate cancer is the second most common cancer in men in the UK (after lung cancer) with 1 in 14 developing prostate cancer within their lifetime. Studies have indicated that men with *BRCA1* or *BRCA2* gene alterations are more susceptible to prostate cancer than men without an alteration. The most recent data suggest that men with the *BRCA1* gene have up to 2 times the risk of developing prostate cancer (although the risk could be lower than this), and men with the *BRCA2* gene have up to 5 times the risk of developing prostate cancer in their lifetime (although the risk could be higher than this). One of the aims of this study is to determine exactly what the risk of prostate cancer is for these men.

##### **Why am I invited to take part?**

You are being invited to take part either because you have an alteration in the *BRCA1* or *BRCA2* gene, or because you have been found not to carry the *BRCA1* or *BRCA2* gene fault in your family and will act as a control.

##### **What will happen to me if I take part?**

If you decide to take part an appointment will be made to meet with the research team in order to discuss the study in detail and ask any questions before you agree to take part. If you already attend a genetics clinic the appointment can coincide with your regular outpatient appointments. Any additional visits can be arranged at a time that is convenient for you, alternatively we can arrange to visit you at home. For men participating as controls, and

therefore not attending a clinic, arrangements can be made locally to collect these samples as convenient. All travel expenses incurred as a result of taking part in this study will be reimbursed

Once you have definitely decided you want to take part you will be asked to sign a consent form and to complete a short questionnaire about your health. We would like to collect information from you about any urinary / prostate problems or procedures, such as bladder or bowel tests, that you may have had in the few months before entering into the study as these can affect the measurements.

You will be asked to give a blood and a urine sample once a year for 5 years. The blood sample will be taken, using a needle, from a vein in the arm and you will be asked not to eat 4 hours before the sample is taken. You will be provided with a container in which you will be asked to provide a urine sample. These procedures should take approximately thirty minutes of your time. We would also like to keep in touch with you for 5 years following the study so that we can follow-up what happens to you.

***Please refrain from ejaculation (having sex) for 24 hours before the blood sample is taken.***

#### **Prostate Specific Antigen (PSA) testing for Prostate Cancer**

Part of the blood test will be used to measure your Prostate Specific Antigen (PSA) level. This is currently the best tool for early detection of prostate cancer. PSA is a protein naturally produced by the cells of the prostate gland and is released into the bloodstream. When the prostate gland enlarges, PSA levels in the blood tend to rise. There are many reasons why your PSA level may be raised for example aging, urine infections, infection of the prostate gland, inflammation of the prostate gland and prostate cancer. If you are found to have a raised PSA level then you will be asked if you will undergo a biopsy (small tissue sample) of the prostate gland.

There is a lot of controversy amongst experts about whether the PSA test is helpful in diagnosing prostate cancer. Approximately two out of three men with a raised PSA level will not have prostate cancer. The PSA test can also miss prostate cancer. Please take time to read the “PSA Testing for Prostate Cancer” leaflet enclosed which discusses the pros and cons of having a PSA test.

**If you are found to have a raised PSA level then a biopsy of your prostate gland will be recommended and you will be referred to a Specialist doctor, called a Urologist, who will discuss this procedure with you.**

#### **Biopsy of the prostate gland – what will this involve?**

A biopsy of the prostate gland is a more accurate test for prostate cancer than PSA but is more invasive than a blood test. A biopsy will only be recommended if you are found to have a raised PSA level. The doctor can feel your prostate gland by inserting a finger into your rectum (back passage). A specially shaped lubricated ultrasound probe which is a little larger than a man's finger is placed into the rectum. The probe uses ultrasound waves to produce an image of the prostate and the doctor will use the ultrasound to guide a needle through the wall of the rectum to take a tissue sample. Ten samples will be taken and looked at by a specialist doctor using a microscope to look for prostate cancer. With your permission we would like to take a further two tissue samples for research. Unfortunately, even if there is a cancer in the prostate gland it may not be picked up on biopsy. Your PSA level will be taken again the following year and the biopsy will need to be repeated if the PSA level starts to rise by a certain amount.

The procedure will be carried out in the out-patient clinic by a specialist doctor and local anaesthetic will be injected beforehand. It takes about 45 minutes and most men describe it as uncomfortable and some describe it as painful. You will be given a short course of antibiotics immediately before and after the biopsy to reduce the risk of infection and you will need to drink a lot of water for the next 24 hours. After the scan and biopsy you may notice blood in your urine which should clear within two to three days, but may continue for up to ten days or two weeks. You may also notice blood from your back passage which should settle within one to two days. Finally you may see blood in the semen which may last for several weeks. Please read the following table carefully as you need to be aware of the potential limitations and complications of having a biopsy:

<b>Potential limitation and complications of having a prostate biopsy</b>	
Discomfort	Most men describe the biopsy as an uncomfortable experience and some describe it as painful
Anxiety	The biopsy procedure can cause significant anxiety. It is possible that you may be told your biopsy result is suspicious of cancer but never be found to have a cancer. This is called a “false positive” result and can cause you to feel very anxious.
A cancer may be missed	Up to 20% of cancers may be missed at biopsy. This is termed a “false negative” result.
Infection	There is a 3% chance that an infection will occur following the biopsy and antibiotics will be given before and after the procedure to reduce this risk
Bleeding	Approximately one third of men will experience some bleeding when passing water, opening their bowels or after sex following the biopsy

**What will happen if I am found to have prostate cancer on the biopsy?**

If you are found to have prostate cancer you will discuss all of the treatment options with a specialist. The best way to treat early prostate cancer is not known and there is no proof that treating early prostate cancers helps men to live any longer than simply having regular check-ups. However, treating some cancers while they are still small may stop them from spreading and causing problems. Many prostate cancers grow very slowly, and the side effects of treatment may be worse than the effects of early prostate cancer, so it can be difficult to decide whether or not to have treatment. All of your options will be discussed with a specialist and tailored to suit your specific needs.

There are three main treatment options for treating prostate cancer.

- **Radiotherapy:** This involves either (1) a course of radiotherapy treatment (usually daily over 6-7 weeks) as an outpatient or (2) insertion of radioactive seeds (brachytherapy) into the prostate gland as an inpatient. The aim is to cure, although there are possible side-effects of both treatments. Following radiotherapy treatment impotence (erection problems) may be suffered by between 2 and 6 out of every 10 men (20-60%). Up to 1 in every 10 men (10%) may experience diarrhoea or bowel problems, and up to 1 in every 20 men (5%) may experience bladder problems. Brachytherapy is the insertion of radioactive seeds under a general anaesthetic. This involves an overnight stay in hospital. The side-effects may include immediate bladder and bowel problems which fade over time. Impotence may be suffered by up to 1 in 3 men and up to 1 in 100 men may suffer with long-term bladder problems.

- **Surgery:** This involves an operation to remove the prostate gland. The aim is to cure, although again there are possible side-effects. Up to 2 in every 10 men (20%) may experience some bladder problems, and between 2 and 8 out of every 10 men (20-80%) may experience impotence (erection problems) after surgery.
- **Active Monitoring:** This involves regular check-ups to monitor the cancer and check it is not growing. The advantage is that for many men it avoids the side effects of radiotherapy and surgery. If there are any signs that the cancer is developing, treatment would be offered. The disadvantage is that the cancer may grow to a more advanced stage. Some men find the uncertainty difficult to cope with.

There is little known about the progression of prostate cancer in the higher risk group that this study is targeting. Some studies have indicated that prostate cancer may occur at an earlier age in men with the *BRCA1* and *BRCA2* genes.

#### **What else will my blood and urine samples be used for?**

Proteins, hormones and metabolic compounds (substances that the body makes) found in the blood and urine samples will also be studied in the laboratory. The reason for looking at these substances is to help us to understand the effect of the *BRCA1* and *BRCA2* genetic alterations on the working of the body. Part of the blood sample will be used for genetic analysis related to prostate cancer risk. This is research only and has no insurance implications. If any result is found that is of clinical importance to you or your family you will be informed only if it has been agreed beforehand that you would like to know. If you wish to have this taken forward, you would be offered a new analysis in the genetics clinic where a new blood sample will be taken after full counselling.

Through analysis of these results it may be possible to improve health care in men in this high-risk group and may lead to a new diagnostic test for prostate cancer. This study is for five years and results from it may help us to develop a better system to identify early prostate cancer in men who are at an increased risk of the disease.

If the blood test indicates that your PSA level is raised above 3.0ng/ml you will be recommended to have a biopsy of the prostate gland.

#### **What are the possible benefits of taking part?**

There may be no direct benefits to you as an individual. The detection of early prostate cancer that would otherwise never have caused symptoms may result in anxiety and side effects of treatment. Conversely, it is possible that we may find results detecting prostate cancer that would otherwise have remained undetected until it caused symptoms; this could then be treated earlier. The results of this study will help us to develop a better system of identifying prostate cancer in the early stages in men who are at an increased risk of the disease. The results of this research may lead us to develop new detection tests.

#### **What are the possible disadvantages of taking part?**

There is only a small possibility that you may experience bruising around the area where the blood sample has been taken. The possible side-effects of the biopsy are detailed above. Some people may experience anxiety as a result of the blood test and/or biopsy, support is available (see below). We would like to emphasise that as a result of taking part in this study, a raised PSA level may be found that will result in a prostate biopsy with the risks of the side-effects outlined above. At present, in the UK, PSA testing is not routinely offered to men in the general population.

**What support will there be for me if I decide to take part?**

The study research nurse ..... will be your main contact point (telephone: .....). Her/his role is to support you during and after taking part in the study. She will refer you to a nurse specialist or to a psychological counsellor if required.

**Do I have to take part?**

Your participation in the study is entirely voluntary. If you agree to take part and then change your mind and wish to withdraw, you may do so at any time without this decision affecting any current or future medical care you may receive.

Your legal rights are not affected by your giving consent to participate. Any personal information gained from this study, including specimens we may obtain from you will remain strictly confidential. With your permission, we will inform your GP of your participation in this study. Before agreeing to take part in this study you should check that any private medical insurance you have will not be affected by you taking part.

**Will I be contacted again?**

If you complete the reply slip saying you would prefer not to take part then you will not be contacted again. If you decide to participate we may wish to re-contact you to discuss your form in more detail, for further information or if a point on the form requires clarification. We would re-contact you if a research finding was relevant to you or your family.

**Will my taking part in the study be kept confidential?**

If you consent to take part in the research an authorised member of staff may inspect your medical records for the purposes of analysing the results. Any information you give us will be kept strictly confidential and no member of your family will be contacted by us, except through yourself. Information is stored on a database adhering to guidelines set out in the Data Protection Act. All specimens obtained from you will be stored using identifying codes that will be known only by the research team.

**What will happen to the results of the study?**

The overall results of the study will be available and research will be presented as research publications - nobody will be identified in these publications.

**Who is organising and funding the research?**

This research is being organised by a team within the Cancer Genetics Unit at the Royal Marsden Hospital headed by Dr Ros Eeles. This study is funded by Cancer Research UK, The Ronald and Rita McAulay Foundation and Dr Eeles' Research Fund.

**Who has reviewed the study?**

The Multi-Centre Research Ethics Committee has reviewed and approved this study. It has also been approved by the Committee for Clinical Research at the Royal Marsden Foundation NHS Trust and your regional Ethics Committee.

**We would like to thank you for reading this information sheet.**

If you would like any further information, please do not hesitate to contact:

**\*\* Please insert local contact details**

**Reply Slip – Please return in enclosed Stamped Addressed Envelope to:**

**\*\*Please insert local contact details**

.....

Name: \_\_\_\_\_

Date of Birth: \_\_\_\_\_

**Please delete as appropriate\***

**\* I would like to take part in the IMPACT study. I would like a member of the research team to contact me by telephone with further details of how to take part. The telephone number I can be contacted on is \_\_\_\_\_ and the best time to reach me on this number is \_\_\_\_\_.**

**\* I would prefer not to take part in the IMPACT study**

# PSA Testing for Prostate Cancer

*An information sheet for men considering a PSA Test*

## What is the aim of this leaflet?

Prostate cancer is a serious condition. The PSA test, which can give an early indication that prostate cancer may be present, is now available to men who wish to be tested. However, experts disagree on the usefulness of the PSA test. It is not yet known whether or not PSA testing will save lives from prostate cancer. The aim of this information sheet is to give you balanced information about the PSA test, which we hope will help you decide whether or not having the test is the right thing for you.

You may wish to discuss this information with your doctor or practice nurse.

## What do we know about Prostate Cancer?

Prostate cancer is the second most common cause of cancer deaths in men. Each year in the UK about 22,000 men are diagnosed with prostate cancer and 9,500 die from the disease. Prostate cancer is rare in men below the age of 50 years, and the average age of diagnosis is 75 years. The risk is greater in those with a family history and is also known to be greater in African American men. Prostate cancer is also more common in the West, suggesting that there may be a link with western lifestyle factors, such as diet. The prostate gland lies below the bladder. Prostate cancers range from very fast growing cancers to slow growing cancers. Slow growing cancers are common and may not cause any symptoms or shorten life.

- Prostate cancer is the second most common cause of cancer deaths in men
- Prostate cancer is rare in men under the age of 50 years

## What is a PSA test?

The PSA test is a blood test that measures the level of PSA in your blood. PSA (Prostate Specific Antigen) is a substance made by the prostate gland, which naturally leaks out into the blood stream. A raised PSA can be an early indication of prostate cancer. However, other conditions which are not cancer (e.g. enlargement of the prostate, prostatitis, urinary infection) can also cause a rise in PSA.

Approximately 2 out of 3 men with a raised PSA level will not have prostate cancer. The higher the level of PSA the more likely it is to be cancer.

The PSA test can also miss prostate cancer.

- A PSA test involves a blood test
- If the level of PSA in the blood is raised, this may indicate that prostate cancer is present.
- However, many men with a raised PSA will not have prostate cancer
- The PSA test can also miss prostate cancer

## What happens after the PSA test?

As a rough guide there are three main options after a PSA test:

### PSA level is not raised

- Unlikely to have cancer.
- No further action.

### PSA slightly raised

- Probably not cancer, but you might need further tests.

### PSA definitely raised

- Your GP will refer you to see a specialist for further tests to find out if prostate cancer is the cause.

### If the PSA level is raised, what further tests would be carried out?

If your PSA is definitely raised, a prostate biopsy is required to determine if cancer is present. This involves taking samples from the prostate through the back passage (bottom). Most men find this an uncomfortable experience, and some describe it as painful. Sometimes complications or infection may occur. Approximately 2 out of 3 men who have a prostate biopsy will not have prostate cancer. However, biopsies can miss some cancers and worry about prostate cancer may remain even after a clear result.

- While a raised PSA level in the blood may indicate cancer, a prostate biopsy is still required to determine if cancer is present
- About 2 out of 3 of men who have a biopsy will not have prostate cancer

### If early prostate cancer is detected, what treatments are used?

There are three main options for treating early prostate cancer which are summarised below:

- **Radiotherapy:** This involves a course of radiotherapy treatment on the prostate gland at an outpatient clinic. The aim is to cure, although there are possible side effects. Impotence (erection problems) may be suffered by between 2 and 6 out of every 10 men (25-60%). Up to 1 in every 10 men (10%) may experience diarrhoea or bowel problems, and up to 1 in every 20 men (5%) may experience bladder problems.
- **Surgery:** This involves an operation to remove the prostate gland. The aim is to cure, although again there are possible side effects. Up to 2 in every 10 men (20%) may experience some bladder problems, and between 2 and 8 out of every 10 men (20-80%) may experience impotence (erection problems) after surgery.
- **Active monitoring:** This involves regular check-ups to monitor the cancer and check it is not growing. The advantage is that for many men it avoids the side effects of radiotherapy and surgery. If there are signs that the cancer is developing, treatment would be offered. The disadvantage is that the cancer may grow to a more advanced stage. Some men find the uncertainty difficult to cope with.

### So should I have the PSA test?

#### Benefits of PSA testing

- It may provide reassurance if the test result is normal
- It may find cancer before symptoms develop
- It may detect cancer at an early stage when treatments could be beneficial
- If treatment is successful, the consequences of more advanced cancer is avoided

#### Downside of PSA testing

- It can miss cancer, and provide false reassurance
- It may lead to unnecessary anxiety and medical tests when no cancer is present
- It might detect slow-growing cancer that may never cause any symptoms or shortened lifespan
- The main treatments of prostate cancer have significant side-effects, and there is no certainty that the treatment will be successful

#### Further information

If you have any questions or wish to receive more information about PSA testing and prostate cancer you can discuss it further with your doctor or practice nurse, or look at one of the following sources of information:

#### Useful web-sites on prostate cancer and PSA testing:

<http://www.nelc.org.uk>  
<http://www.cancerscreening.nhs.uk>  
<http://www.dipex.org>

#### Booklet:

Understanding the PSA Test  
Cancer BACUP  
3 Bath Place  
Rivington Street  
London EC2A 3DR  
Cancer BACUP Helpline:  
0808 800 1234

#### Internet:

<http://www.cancerbacup.org.uk>

#### Book:

Understanding Prostate Disorders  
Professor D Kirk  
British Medical Association (BMA)  
ISBN:1-898205-87-6

#### Cancer Research UK web-site:

<http://www.cancerresearchuk.org>  
<http://www.cancerhelp.org.uk>

**Helpline: 0800 226237**

This information sheet was prepared by Jo Brett, Dr Eila Watson, Colleen Bukach, and Dr Joan Austoker, Cancer Research UK Primary Care Education Research Group, University of Oxford.  
The information sheet is based on information initially prepared by Dr Graham Easton.

