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**Participant Information Sheet**

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**Study Title:** Exploiting Image-based Risk Stratification in Early Prostate Cancer to Discriminate Progressors from non-Progressors (RECONCILE)

## This is the Participant Information Sheet for a Health Research Study called RECONCILE Image-Based Risk Stratification in Early Prostate Cancer

We are inviting you to take part in this study because you, together with your responsible clinician, have decided to manage your prostate cancer with active surveillance in the first instance. Active surveillance of prostate cancer, alongside surgery and radiotherapy, is a standard option for management of disease which is confined to the prostate. As reported in U.K. National Guidelines that were updated in 2019, current evidence does not show a difference in the number of deaths from prostate cancer among people managed with active surveillance, prostatectomy or radical radiotherapy during 10 years of follow up.

Before you decide whether or not to participate in this study it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully and take time to decide whether or not you wish to participate in the study. Please do discuss the study with your GP, friends, relatives or others if you wish.

Do not hesitate to contact the RECONCILE research team here at UCLH if you have any questions or wish to discuss the study in more detail.

**PART 1** tells you the purpose of this study and what will happen if you choose to take part.
**PART 2** gives you more detailed information about the conduct of the study.

If you agree to participate in this study we will ask you to donate blood, urine and prostate tissue (up to 3 to 5 additional prostate tissue samples) at the beginning of the study and again one year after enrolment. We will also perform a high quality MRI scan of your prostate at each of these time points. We will check your PSA blood test every three months during the year that you are enrolled in the RECONCILE study. Aside from the donation of a small number of additional prostate tissue samples, your care will not deviate from current active surveillance national standards.

For those already participating in the PLiS study we will ask you to donate a semen sample to RECONCILE at one year. This will enable us to analyse your semen for potential markers associated with prostate cancer.

If at any time there is evidence to suggest that your cancer has progressed or spread we will contact you and inform you of this, as would happen in normal care. The analysis of your donated research samples will not be used to direct your prostate cancer management within the timeframe of the study. We will arrange all the necessary standard of care NHS tests to evaluate any change to the status of your cancer. You will exit or be withdrawn from the study if active surveillance is no longer appropriate for the management of your cancer. You will be offered all available NHS treatment options that are appropriate for your cancer.

If at any time you wish to pursue an alternative management strategy for your prostate cancer that has been recommended by your responsible clinician, i.e. something other than active surveillance, you are free to do so and you can be withdrawn from the study at any time. This will not affect your care.

There may be no direct benefit to you by taking part in this study but your participation will help with our understanding of prostate cancer diagnosis, progression and risk in order to better inform the care of future patients.

Please ask questions if there is anything that is not clear or if you would like any more information.

You are free to decide whether or not to take part in this research. Please remember that your medical care will not be affected if you decide to not take part in this study.

**PART 1**

**What is the purpose of the study?**

Prostate cancer is the most common cancer in men. At the moment we do not fully understand:

- How prostate cancer develops
- Why some prostate cancers grow and others do not
- Which cancers are better served with early treatment or surveillance

The purpose of this study is to carry out very detailed testing of prostate tissue, blood and urine (as well as semen for those already enrolled in the PLiS study) in order to identify markers associated with prostate cancers that are progressing and therefore require treatment. This testing will take place at two time points: at enrolment to the RECONCILE study and one year later. A high quality MRI scan of the prostate will also be performed at each of these time points. These two time points are necessary to compare data and identify important changes in tissue markers over time.

Markers of prostate cancer identified in the donated tissue samples will be correlated with the physical appearance of the cancer on each MRI scan. Markers which are associated with cancers that grow more quickly and more slowly will be identified.

We do not currently have a good way, other than observing over time, to tell the difference between cancers that will progress and those that will not cause any problems. The information gathered within RECONCILE will enable us to predict more accurately how prostate cancers behave. This means that in the future we will be able to offer bespoke treatment for prostate cancer based upon how likely, and how quickly, it is to grow. Patients with prostate cancer which is not likely to progress will therefore be spared the side effects associated with biopsy and invasive treatments, whereas those with cancer that is likely to grow and progress will be offered treatment at an earlier stage.

We are asking patients who are undergoing prostate biopsies and MRI as part of their normal prostate cancer surveillance to kindly allow us to take additional biopsies for this study. We will also ask consenting participants to donate some blood and urine (and semen if already enrolled within the PLiS study) so that we can look at whether anything in these samples can help us develop better ways of understanding how prostate cancer behaves. We will also request your consent to access relevant parts of your medical records after you have exited the study.

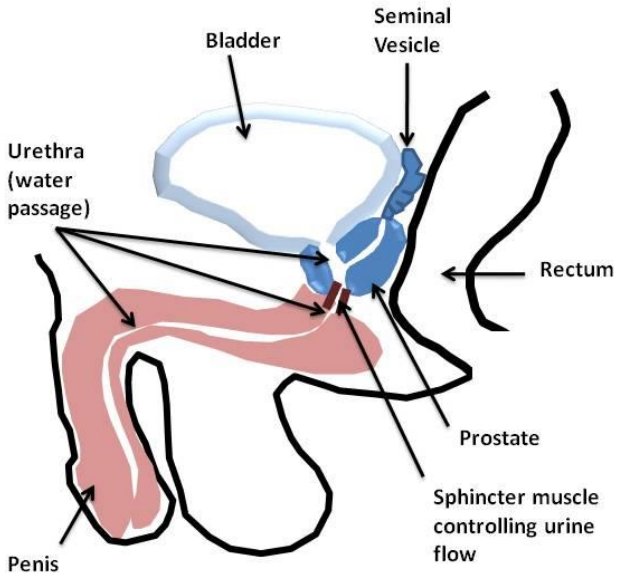
At the end of the study, you will continue standard NHS prostate cancer care at UCLH. This will be active surveillance or active treatment as decided with your Doctor.

*Figure 2 on page 13 of this document provides an overview of the study timeline.*

## What is the prostate?

The prostate is a male gland that sits just below the bladder (See Figure 1). The prostate produces fluid that forms part of the semen and helps nourish sperm. When you empty your bladder, urine flows through a tube (the urethra) that passes through the prostate before reaching the penis.

**Figure 1: Location of the prostate**




## What is a biopsy and how does it diagnose prostate cancer?

We diagnose prostate cancer using an MRI scan and biopsy. MRI shows us where the abnormal areas in the prostate are and these areas are targeted in a procedure that uses needles to take tissue samples (biopsies). The samples obtained are looked at under a microscope to see whether or not cancer is present. An abnormal MRI scan does not mean that cancer is present.

## What is active surveillance?

Active surveillance is a safe strategy to monitor small prostate tumours that are confined to the prostate and considered to be of low and intermediate risk of progression. It provides a period of observation to assess how your cancer behaves. If surveillance detects that your cancer may be growing you will undergo all the necessary tests e.g. re-biopsy and repeat MRI to reassess the tumour.

## What happens if there are signs that my prostate cancer is progressing during the study?

Prostate cancer is a slow growing cancer. Often the first sign that a prostate tumour is progressing, or growing, is a rise in your PSA blood test level. If this is detected during your

period of active surveillance within RECONCILE you will be treated in exactly the same way as an NHS patient who is not enrolled in the study. This means that you will undergo an MRI scan if there is a confirmed and significant PSA rise. You will receive all necessary standard of care NHS investigations and offered all appropriate treatment options for your cancer.

If these investigations indicate progression of your cancer, and you require a further prostate biopsy to confirm this, you will exit the study at this point. This is earlier than the planned one year time point for study completion. We will ask you to donate further research samples (prostate tissue, blood, urine for all patients as well as semen if enrolled in the PLiS study) at this point. Your care will then continue within a standard NHS prostate cancer clinic.

Please remember that you can withdraw from the study at any time without giving any explanation. This will not affect the care that you receive as an NHS prostate cancer patient.

### Why have we invited you to take part in this study?

We have approached you and provided you with this information sheet because you have decided to pursue active surveillance for the management of your prostate cancer following the advice of your doctor. You may have been approached at one of the time points below:

- Following referral to UCLH from another U.K. hospital for the management of your cancer.
- After receiving the results of your recent prostate biopsy performed at UCLH.

You will only be invited to take part in the study if you decide to pursue active surveillance for the monitoring of your prostate cancer following the advice of your doctor.

### Do I have to take part?

No. It is up to you to decide whether or not to take part. If you decide to take part we will ask you to sign a consent form and give you a copy of the Patient Information Sheet to keep. You will have adequate time to decide whether to take part (normally at least 24 hours) and you are free to withdraw at any time without giving a reason and without affecting any future care you receive.

### What are the alternatives?

If you choose not to take part in the study, you will not need to provide additional urine and blood samples and you will have the standard number of biopsies during your active surveillance. You will continue to be monitored with active surveillance in an NHS clinic with all appropriate NHS treatment options available to you.

### Can I change my mind?

Yes, you can decide at any time not to have any of the procedures and withdraw from the study.

## What will happen to me if I take part in the study?

***At enrolment:***

Once you have discussed the study with the research team we will ask you to sign a consent form. This initial discussion may be over the telephone. We will note your consent in your medical records and ask you to sign a paper consent form. The consent form can be signed in person during a hospital visit or remotely at your home and returned to us by post or email. Consent can also be taken over the telephone if this is more convenient. Please see Figure 2 on page 13 for an overview of the study.

You may be consented at the time of your prostate MRI scan. Prostate MRI scans involve inserting a cannula (a small, flexible plastic tube) into a vein and injecting a contrast chemical to boost the signals we see from the prostate. This is exactly the same procedure as an NHS MRI scan that you would receive for the monitoring of your prostate cancer in a non-research setting. Either here or at your next visit you will receive some questionnaires about your condition to complete in your own time.

At the next visit to the hospital, which would likely be at the time of your targeted transperineal prostate biopsy, we will collect urine and blood samples. We will ask you to donate a minimum of 50ml of blood (approximately 4 tablespoons), up to a maximum volume of 100ml (7 tablespoons) and around 50ml (approximately 4 tablespoons) of urine.

The targeted biopsy will be similar to the biopsy that you had for diagnosis and will usually be performed under local anaesthetic or sedation. These are confirmatory biopsies directed towards the abnormality identified on your MRI scan, and its surrounding tissue, to ensure your suitability to continue active surveillance. At the time of this confirmatory biopsy we will take some additional samples (up to a maximum of 3) for research. The risk of collecting these additional biopsies is low and we will explain them in detail below. This visit will last about half a day.

Images from your MRI scan and scanned images of your prostate biopsy tissue will be uploaded to the study database. About two weeks after this visit you will be given the results of the scan and biopsy by a doctor, either in person or by telephone if you request so.

***At three, six and nine months after enrolment:***

At three, six and nine months after your biopsy you will come in for a short visit (no more than an hour) and we will take some blood for a prostate specific antigen (PSA) test. This test is standard practice for people on active surveillance. A rise in PSA is often the first indicator that a cancer is growing.

***At one year after enrolment:***

One year after your original high quality MRI and biopsy we will repeat both of these tests and collect a second set of blood and urine samples. The MRI, biopsy, urine and blood collection will be performed in exactly the same way as your initial tests. You will also be

given the same questionnaires that your received at baseline to complete. Patients enrolled in the PLiS study will be asked to donate a semen sample at this point.

If at any point in the trial a confirmed PSA result suggests any growth or progression of your cancer you will be informed and follow a standard NHS prostate cancer pathway for re-investigation of your disease.

We will also require your permission to use identifiable information such as your name, address, date of birth and NHS number so that we can collect healthcare information on you from national records, such as the Office for National Statistics, NHS Digital, Public Health England, and other applicable NHS information system, or national database. The information we receive will be related to both your prostate and general healthcare (for example: cancer diagnosis, prostate cancer treatment details). Rigorous safeguards are in place so that we send, receive, store and handle your data safely and securely. For this you will not have to attend the hospital but we do need your permission to receive and hold this information on you securely.

We will collect healthcare information on you during the study and three years after your prostate biopsy. Further funding will be explored for life-long collection of this data.

### What will happen to the samples taken for research purposes?

Analyses on samples (including stored images from your MRI scan and biopsy) will be performed by UCL.

We will use your blood, urine, (semen where applicable) and tissue specimens to extract DNA and RNA (genetic material), proteins, immunological markers and other chemicals. We will use molecular tests such as DNA and RNA sequencing to check how cancerous samples differ from normal samples. If you have any cancerous cells, we may keep some of them for growing in the laboratory to test how changes in the DNA and the RNA influence the behaviour of cancer cells.

DNA testing will be performed on the samples you provide. It is therefore possible that the research could produce findings of clinical significance for you or your relatives. Some tests on the samples you donate (blood, urine, semen, tissue) could suggest that genetically you or a family member may be more likely to develop certain diseases. In such situations we will inform you and your GP, but as these tests are performed in a research setting any results would need to be repeated using additional existing tests.

Once we have completed the analyses which are planned to answer our research questions, we will store any remaining samples or substances extracted from them securely for future research so that we can repeat any tests on them if necessary and evaluate new academic tests for prostate cancer care. Your samples would be considered a gift from you and no personal results from these tests or studies will be provided to you.

## What are the possible benefits to me and for others like me in taking part in this study?

The study may not benefit you directly. However, it could mean that, in the future we are better able to predict the aggressiveness of prostate cancers and therefore provide better treatment options.

## What are the possible disadvantages and unwanted side effects of the study?

If you do decide to take part in this study there are certain risks associated with some of the trial procedures. We will monitor you for these side effects and offer you any treatment that may be required. In this trial there will be two biopsies over the course of one year which carry the possibility of the side effects detailed in the table below. The table below gives the side-effects that could occur with biopsies under normal practice. As we are only taking a few additional research biopsies these risks will not be significantly higher than the rates we quote in the table. However, there may be small increases in the risk of temporary bleeding in the urine and sperm as well as a small increase in the amount of bruising of the skin. There is no evidence that having multiple biopsies raises your chances of prostate cancer spreading.

| **Side effect** | **Prostate Biopsy** | |
|---|---|---|
| | **Proportion of patients** | **Duration** |
| Pain/Discomfort in back passage | Almost all | Temporary for 1-2 days |
| Burning when passing urine | Almost all | Self-resolving, 1-3 days |
| Bloody Urine | Almost all | Self-resolving, 1-7 days |
| Bloody Sperm | Almost all | Lasting up to 3 months |
| Poor erections | 1-2 in 100 | Temporary for 1-6 weeks |
| Infection of skin/urine | 1-2 in 100 | 7 days with treatment with antibiotics |
| Infection of skin/urine needing admission and intravenous antibiotics | Less than 1 in 500 | 7-14 days with treatment with antibiotics. Rarely up to 28 days of antibiotics after leaving hospital. |
| Difficulty passing urine requiring catheter placement for up to a week. A catheter is a soft plastic tube placed into the bladder to drain urine. | 1 in 100 | 3-7 days |
| Bruising of skin | Almost all | Self-resolving, 7-14 days |
| Bruising spread to scrotum | 1 in 100 | Self-resolving, 7-28 days |

On very rare occasions patients experience a few side effects from the contrast used in the MRI scan such as nausea or headache.

The main risks of blood tests are discomfort and bruising at the site where the needle goes in. These complications are usually minor and go away shortly after the tests are done.

**What data will be collected and how will it be used?**

University College London (UCL) is the sponsor for this study and is based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about you for 20 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting the RECONCILE trial coordinator at: situ.reconcile@ucl.ac.uk

UCLH NHS Trust will collect information from you and your medical records for this research study in accordance with our instructions.

UCLH will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCLH will pass these details to UCL along with the information collected from you and your medical records. The only people in UCL who will have access to information that identifies you will be people who need to contact you to process or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

UCLH will keep identifiable information about you from this study for 20 years after the study has finished.

**This completes Part 1 of the information sheet. If you are considering participating in the study, please continue to read the additional information in Part 2 before making your decision.**

**PART 2**

## What if new information becomes available?

Sometimes, during the course of a research project, new information becomes available about the procedures that are being studied. If you are in the study and this happens, your study doctor will tell you about it and discuss with you whether you want to, or should, continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign a consent form that includes new information. If any relevant new information becomes available after you have had all of your procedures, it will not affect you as you will no longer be in the study.

Should your cancer show progression you will be offered full re-classification of your cancer in line with standard of care NHS diagnostic procedures. You will be offered all available NHS treatment options for the management of your cancer and you will be withdrawn from the study if active surveillance is no longer appropriate or you choose an alternative management approach. The study team will ensure your care continues in an appropriate NHS prostate cancer clinic. As described earlier, you can withdraw from the study at any time.

## What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions, contact details are at the end of the document. If you remain unhappy and wish to complain formally, you can do this via the hospital's Patient Advisory Liaison Service (PALS). If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions, contact details are at the end of the document. If you remain unhappy and wish to complain formally, you can do this via the hospital's Patient Advisory Liaison Service (PALS).

PALS Ground Floor Atrium
University College Hospital
235 Euston Road
London NW1 2BU

Tel: 020 3447 3042

http://www.nhs.uk/chq/pages/1082.aspx?CategoryID=68 Email: uclh.pals@nhs.net

In the unlikely event that you are injured by taking part, compensation may be available. If you are harmed due to the negligence of someone treating you, then you may have grounds for legal action for compensation. NHS Trusts are responsible for clinical negligence and other negligent harm to individuals that are under their care and covered under the NHS Indemnity Scheme.

## What happens when the study stops?

Once you have completed the study the results of the tests we have conducted will be provided to your GP and consultant urologist looking after your prostate cancer. They will determine your ongoing care as active surveillance within RECONCILE is in line with standard of care NHS prostate cancer surveillance guidelines.

The type of ongoing care you receive will depend on your individual circumstances which your doctor will discuss with you. If at any point during the study you lose the capacity to give informed consent then you will be withdrawn from the study. Any tissue or data that has been previously collected with your consent would be retained and used in the study.

We may ask for your consent to check your health status prospectively through national UK NHS databases on a long term basis.

## What will happen to the results of the research study?

The results of this study will be published in scientific or medical journals and may be presented at scientific or medical meetings. Please be assured it will not be possible to identify you in any report or publication.

We will summarise the results for participants once they are available. Your study team will send you a copy of the results upon request. This study has been placed on an internet directory of clinical trials (www.clinicaltrials.gov) and the result, once available will be posted here.

## Who is organising and funding the research?

RECONCILE is organised by UCL (Co-Chief Investigators: Mr Clement Orczyk and Professor Mark Emberton). The research is funded by the J P Moulton Charitable Foundation.

## Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect participants' safety, rights, wellbeing and dignity. RECONCILE has been reviewed and approved by London Stanmore Research Ethics Committee.

## What happens now?

You will have some time to think about the study and make your decision. A member of the study team will be happy to answer any questions. You may wish to discuss it with your family or friends. Once you have reached your decision please let the study team know.

You will be asked to sign a consent form either at home ( returned to us by post or email) or during a visit to the hospital. You may also provide consent over the telephone. You will be given a copy of the consent form to keep together with this information sheet. If at any time

you have any questions about the study you should contact a member of the study team or the study doctor.

## Contact details

If at any time you have any questions about the study you should contact your local study team:

Local study team's contact details:

RECONCILE STUDY GROUP
SITU
Third Floor
Charles Bell House
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W1W 7JN

**Tel:** +44 (0)20 7679 9280
**Fax:** +44 (0)20 7679 9280
**Email:** uclh.reconcile@nhs.net

**Miss Teresa Marsden** (Study Doctor, University College London Hospitals)
**Tel**: +44 (0)20 7679 4466
**Email**: teresa.marsden2@nhs.net

You may also contact Mr Clement Orczyk or Professor Mark Emberton (Urology Consultants and Study Chief Investigators) via their office:
**Tel**: +44 (0)20 33479194

In an emergency it is best to contact your GP or go to your local casualty department or dial 999 for an ambulance.

If you would like some independent advice, you can contact either of the following:
Macmillan Cancer Support is a useful source for further information. They can provide information on prostate health care and clinical trials. You can find this at www.macmillan.org.uk

Alternatively, you can call them on 0808 808 0000 (Freephone), and they will send you information leaflets in the post free of charge.

**We will give you a copy of this information and a copy of the signed consent form to keep.**
**Thank you for taking the time to read the information about the study.**

**Figure 2: Study Overview**