

**PARTICIPANT INFORMATION SHEET & INFORMED CONSENT FORM**

**D**etermining feasibility of **R**andomization to

high vs. ad libitum water **In**take in Polycystic **K**idney Disease:

THE **DRINK** RANDOMISED FEASIBILTY TRIAL

You are being invited to take part in a research trial. Before deciding whether to take part, you need to understand why this research is being done and what it involves. Please take time to read the following information carefully and talk to others about the trial if you wish. Please ask us if anything is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

Section 1 tells you the purpose of this trial and what will happen to you if you take part.

Section 2 gives you more detailed information about the conduct of the trial.

**Section 1: Purpose of the trial and what will happen**

**1. What is the purpose of the trial?**

We are studying a condition called autosomal dominant polycystic kidney disease (ADPKD). People who are affected by this condition develop many cysts in their kidneys. A cyst is a fluid filled sac. These cysts are non-cancerous, but over the years they grow in size and number causing health problems. By the age of 30-50 years most people with the condition will have high blood pressure and chronic kidney disease. Half of those affected will have kidney failure that needs either dialysis or a kidney transplant by the age of 60 years. It is common and affects approximately 1 in every 800 people in the United Kingdom.

Polycystic kidney disease is an inherited condition with an autosomal dominant pattern of inheritance. This means there is a faulty gene that can be passed on from a parent to their child and that a parent has a 50% chance of passing on this gene to each of their children.

Vasopressin is a hormone produced by the brain. Its role is to maintain the body’s water balance. In states of dehydration it acts on the kidneys to conserve water and produce concentrated urine. If the body is well hydrated, the body stops making vasopressin and dilute urine is produced.

Research has shown that in polycystic kidney disease, the vasopressin hormone acts in an abnormal way. It drives the cysts to grow, so there are many more cysts and causes more fluid to collect inside them so they grow even bigger. Your kidneys should be around 10cm long. In this condition vasopressin can cause them to grow to more than 40cm long. This causes a lot of pain and discomfort, kidney damage and squashes other organs in the abdomen.

The main way to prevent polycystic kidney disease getting worse over the years is to stop the vasopressin hormone. We think that by getting people with ADPKD to drink large quantities of water, they can produce dilute enough urine to stop the body making vasopressin. By switching off the vasopressin signal in the body, we think we should be able to slow down the progression of the kidney damage in ADPKD in the long term (Figure 1).

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Figure 1: Effect of high water intake on vasopressin

So far research to test this has been done in rats with polycystic kidney disease and the results have been very exciting. It has shown that by giving rats lots of water (more than 3 times what they would normally drink everyday) their kidney function stays stable and their cysts do not grow.

We would like to carry out a large trial (with lots of people over a long period of time) to test whether drinking large amounts of water beyond thirst levels can stop the cysts growing and the condition getting worse. However, we do not know whether such a study will be possible. It may be difficult for some people to drink the necessary amount of water, and patients may prefer not to take part in a study. We also do not yet know enough about high water intake in ADPKD to know how safe it is.

Therefore, we need a feasibility study. A feasibility study like this one tests whether a larger long term study would be possible or not. The study will be a “miniature” version of a potential future large trial.

**2 What is the drug being tested?**

The study does not test a drug. Instead, the study compares high fluid intake to “drinking as usual”.

**3 Why have I been invited?**

 You have been invited to participate in this trial because you have autosomal dominant polycystic kidney disease.

We plan to include 50 participants with polycystic kidney disease, mainly from Addenbrookes hospital. However, we will be inviting participants from across the United Kingdom to take part.

**4 Do I have to take part?**

 Participating in this trial is completely voluntary. If you decide to participate you will be asked to sign an Informed Consent Form, however you are still free to change your mind and leave the trial at any time without giving a reason. If you chose not to participate or to leave the trial, your future medical treatment and normal standard of care will not be affected in any way.

1. **What will happen to me if I take part?**

If you agree to participate in the trial, you will be asked to sign the Informed Consent Form at the end of this document. You will be given a copy of this to take away and refer to later.

 This is a **randomised control feasibility trial**. This means;

Randomised: As we sometimes don’t know which way of treating patients is best we need to compare different treatments. We divide people into groups and give each group a different treatment. You will be allocated one of the treatments for this trial in a random way (by chance), much like flipping a coin. You will have a 50% chance of being prescribed large amounts of water beyond thirst.

Feasibility: this is a study done on a smaller scale before a larger scale trial. It is designed to answer one question “is a large trial possible”.

**What does taking part involve?**

Step 1:

During your routine clinic appointment a member of the research team will introduce the trial to you and provide you with this information leaflet to take away and read. Alternatively you may be sent information in the post.

Step 2:

You will be invited to attend for a screening clinic visit.

Step 3: Screening Visit

The screening visit has two parts.

1) Consent: a member of the trial team will discuss the trial information again. There will be another opportunity to ask any questions you may have. If you are happy to proceed you will be asked to sign a consent form.

2) Screening assessment:

* Medical review: During this visit the research doctor will ask you about your medical history and look at your medication list. A member of the team will also ask you about your dietary habits. We will also examine your heart, lungs and abdomen.
* Blood test: A blood sample will be taken, roughly 30 mls (2 tablespoons). This is mainly to check the function of you kidneys, salt levels in the blood and how concentrated your blood is.
* Radioisotope test: within our study, there will be an optional sub-study which you will be invited to take part in. **You can take part in the main study without taking part in the sub-study.**
	+ The sub-study will involve having a more specialised test called the EDTA-GFR test. This is a test designed to measure kidney function accurately. You will need to come to the nuclear medicine department and have several blood tests on the day. There is a separate information sheet which you will be given (Radioisotope Sub-study Patient Information Sheet Version 1) that describes the sub-study in detail.
* Urine tests: We will also collect a urine sample 50mls (3 tablespoons). You will also be given two large bottles to take away for 24 hour urine collections. For each of these you will start in the morning by throwing away the first urine sample, then collecting all the urine passed throughout the day and night, including your first urine the next morning. You will need two of these, they don't have to be done one after the other. You will need to hand these in at your next clinic visit.

The purpose of the screening visit is to make sure that it will be safe for you to take part in the trial. This visit will take 1 hour.

Step 4: First trial visit (Week 0)

This will be the first visit in the active part of the trial. Again you will have a medical review, blood tests and urine tests as before. You will only have to collect one 24 hour urine sample. If you are in the group that needs to drink large quantities of water (beyond thirst) you will receive an individual prescription based on your urine tests that tells you how much fluid you must drink daily to keep your urine dilute.

As part of the trial we will want you to test your own urine at home. This is a very simple test. You will be shown how to test your urine and record the result. The study team will be available by phone to help if you have any questions.

You will be given urine strips to take home with you. Twice a week on Monday and Thursday you will receive a text message in the morning (between 9am – 12 pm) reminding you that you will need to test your urine between 4-8pm later that day (Diagram). Once you have tested your urine you will need to wait 60 seconds before matching the colour on the test strip with the corresponding chart on the bottle. You will then need to record the number that that colour corresponds to into a smartphone application or online via the trial website, or you can phone in the result.





Step 5: Active Trial period

You will have 5 clinic visits during the study. Each visit will take 30 minutes. At these visits you will have a medical and dietary review, blood and urine tests, and be asked to complete a questionnaire. Your test results will be used to determine whether you are drinking the right amount of fluid. This trial itself will take 8 weeks. At the end of 8 weeks, you can go back to your normal drinking habits, as you prefer.

Step 6: End of trial Visit (Week 12)

You will be asked to attend one final visit roughly 4 weeks after the 8 week visit. This final visit is the end of the trial. Again you will have a medical review, blood and urine tests. No further follow-up is needed after this. But if you have any further questions or concerns we will make sure you have our contact details.

Once all of the results have been put together and analysed, if you are interested we would be happy to forward you on a summary/conclusion through your preferred method of communication.

Tests and Assessments Schedule

|  |  |  |  |
| --- | --- | --- | --- |
|  | Screening | Treatment | End of trial |
|  | Week 0 | Week 2 | Week 4 | Week 8 | Week 12 |
| Medical Review | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| Dietary assessment | ✔ | ✔ |  | ✔ |  | ✔ |
| Blood sample | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| Radioisotope Test (Sub-study only) \* |  | ✔\* | ✔\* | ✔\* |  |  |
| Urine sample | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| 24 hour urine collection | ✔ |  | ✔ |  | ✔ | ✔ |
| Questionnaires | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| Total time for visit | 1 HOURS | 30mins | 30 mins | 30 mins | 30mins | 30 mins |

\* Note if you are involved in the radioisotope sub-study each appointment will take around 5 hours.

**6. What will I have to do?**

During the trial you will need to attend extra clinic visits (in addition to your usual clinic follow up). You will also have regular blood samples taken and provide urine collections. If you are in the high water intake group, you will receive an individual daily water prescription. This means you will need to drink that amount of water *throughout* the day. In order to make it easier to achieve, you should have a moderate intake of salt and protein. Therefore, a member of the team will go through your diet and give you some advice.

Additionally, you will need to monitor your own urine at home twice a week as explained previously. Once you test your urine you should record your result into a specific smartphone application or online, or telephone the study team. You will be shown how to do this in clinic.



Although high water intake is unlikely to be harmful to an unborn baby or nursing infant, we would advise that if you are pregnant or breastfeeding you will not be able to take part. Female participants who do become pregnant whilst taking part in the trial should let a member of the

research team know at their next visit. No additional methods of contraception are required to participate in the trial.

You should tell the trial team if you feel unwell or different in anyway. If you have any major concerns or are feeling very unwell please contact your trial doctor immediately using the contact numbers at the end of this information sheet.

You should discuss your participation in this trial with any insurance provider you have (e.g. travel insurance, protection insurance, life insurance, income protection, critical illness cover and private medical insurance) and seek advice if necessary, as failure to notify them may affect or invalidate your cover.

1. **What are the side effects of high water intake?**

Drinking water is generally safe and encouraged. Taking large quantities can rarely (less than 1% of patients) cause the following side effects:

* Low salt levels in the blood
* Accumulation of fluid in the body – if fluid accumulates on the lung this can potentially be life threatening if not treated quickly
* High blood pressure
1. **What are the possible disadvantages and risks of taking part?**

Throughout the trial, you will be monitored regularly by a trained research team.

Side effects

If you are in the water intake group, you may find you have to go to the toilet frequently, including getting up at night, to pass urine.

Clinic Visits

You will be required to attend extra visits to the hospital (6 in total).

Blood tests

You will need you to have regular blood tests. A blood sample is taken by inserting a needle into a vein in your arm. This can sometimes lead to bruising and discomfort, or to a little bleeding, at the site where the needle is inserted.

Urine sample

The 24 hour urine collections can be cumbersome to collect.

1. **What are the possible benefits of taking part?**

There is no guarantee that you will benefit from taking part in this trial. You may experience relief in your symptoms or an improvement in your disease. However information collected as part of your participation in this trial may benefit patients with polycystic kidney disease in the future.

1.  **What are the alternatives for treatment?**

There are currently no standard treatments for polycystic kidney disease.

Blood pressure control

Blood pressure control is important for any patient with chronic kidney disease, and this is also true of polycystic kidney disease.

Tolvaptan

There is a new medication that has recently been introduced in the United Kingdom called Tolvaptan. This medication acts by blocking the effects of the vasopressin hormone. Only a small number of patients are currently eligible for treatment with tolvaptan. If you are eligible for treatment with tolvaptan, taking part in this short study will not prevent you from going onto tolvaptan after the study is complete.

Your study doctor will be able to answer any questions you might have over tolvaptan.

1. **What happens when the trial stops?**

Once the trial stops you can go back to your normal drinking habits. We will aim to see you once more in clinic, roughly 4 weeks after the trial ends. You will be reviewed by a member of the research team, and a final set of blood and urine samples will be taken. If there are any problems with these we will contact you to let you know and update your GP.

**12. Expenses & Payment?**

 You will not receive any payment for participating in this trial, however we can reimburse any reasonable travel and parking costs.

**Section 2: Trial Conduct**

**13. What if new information becomes available?**

Sometimes during the course of a trial, new information becomes available which might affect your decision to continue participating in this trial. Your trial doctor will contact you to discuss the new information and whether you wish to continue participating in the trial. If you still wish to continue on the trial, you will be asked to sign a new Informed Consent Form.

The trial sponsor or the trial doctor may decide to stop the trial at any time. If that happens we will tell you why the trial has been stopped and arrange for appropriate care and treatment for you.

**14. What if I decide I no longer wish to participate in the trial?**

 You are free to stop participating in this trial at any time without giving a reason and without it affecting your future care or medical treatment. If you decide not to participate any further, no more tests will be performed and you will no longer receive the treatment for this trial. Any information already provided or results from tests already performed on you or your samples will continue to be used in the trial, however no further information will be collected or tests performed. Any samples already provided for the trial can be destroyed if you wish.

The trial doctor may also choose to withdraw you from the trial if they feel it is in your best interests or if you have been unable to comply with the requirements of the trial. Reasons for trial withdrawal could include:

* You have experienced a serious side effect
* You are unable to complete the visits, medication or trial documentation as required
* You become pregnant or plan to become pregnant
* The trial doctor feels you no longer appear to benefit from the treatment.

If you have experienced any serious side effects during the course of the trial which require you to withdraw from the trial, your trial doctor will follow-up with you regarding your progress until the side effect has stabilised or resolved.

1. **What if there is a problem?**

Any complaint about the way you have been dealt with during the trial or any possible harm you might suffer will be addressed. If you have any concerns about any aspect of this trial you should speak to your trial doctor who will do their best to answer your questions.

In the event that something does go wrong and you are harmed by taking part in the research and this is due to someone’s negligence then you may have grounds for a legal action for compensation against Cambridge University Hospitals NHS Foundation Trust (your hospital – for multicentre trials). If your claim is successful your legal costs will be met. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

The NHS does not provide no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm. They are able to consider an ex-gratia payment in the case of a claim.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this trial, you can do this through the NHS complaints procedure.  In the first instance it may be helpful to contact the Patient Advice and Liaison Service (PALS) at your hospital.

1. **Will my taking part in this trial be kept confidential?**

All information collected about you as a result of your participation in the trial will be kept strictly confidential. Your personal and medical information will be kept in a secured file and be treated in the strictest confidence. You may ask to see your personal information at any time and correct any errors if necessary.

Once you have agreed to participate in this trial you will be allocated a unique trial number that will be used on all your trial documentation. This number will be linked to your personal information; however you will only be identified by this unique number.

We will need to inform your GP of your participation in this trial so that any medical decisions made by your GP account for any treatment you are receiving as part of this trial.

Authorised staff, who work for or with the sponsor of the trial, the hospital R&D Department may require access to your personal information and/or medical records to verify the data for this trial and ensure that it is being conducted in accordance with UK law. All information will be treated in the strictest confidence during the review process.

1. **What will happen to my samples?**

We will be collecting two main types of samples from you, these are samples of urine and blood. Once the samples are taken, they are sent to the central Cambridge laboratory so that they can be analysed and give us the result. All the samples will be anonymised. This means they do not have any of your details including name, date of birth or hospital number. However each sample



will be labelled with a unique number that is relevant to our specific trial. Once the samples have been fully analysed they will be destroyed.

1. **What will happen to the results of the trial?**

The results of the trial will be anonymous and you will not be able to be identified from any of the data produced. When the results of this trial are available they may be published in peer reviewed medical journals and used for medical presentations and conferences. They will also be published on the clinicaltrials.gov website, a central registry for all clinical trials conducted in the EU.

If you would like to obtain a copy of the published results please contact your trial doctor directly who will be able to arrange this for you.

1. **Who is organising (sponsoring) and funding the trial?**

This trial is sponsored by Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge.

The trial is jointly being funded by the Polycystic Kidney Disease (PKD) charity, the British Renal Society (BRS), the British Kidney Patient Association and the Addenbrookes Charitable Trust (ACT).

1. **Who has reviewed this trial?**

All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by (name of REC here).

1. **Further information and contact details**

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email: add-tr.drinktrial@nhs.net

Dr Thomas Hiemstra:

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For further information about ADPKD please visit the PKD Charity website:

http://pkdcharity.org.uk

PALS at Addenbrookes Hospital:

Tel: +44(0)1223256170

Email: pals@addenbrookes.nhs.uk

**In the event of an emergency please contact:**

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