Bedfordshire Hospitals NHS Foundation Trust

# Do probiotics aid men with indolent prostate cancer in addition to a phytochemical rich whole foods? A randomised, double-blind, placebo-controlled trial

## Participant Information

You have been invited to take part in a clinical trial by the doctors and the research team at Bedford Hospital, Bedfordshire Hospitals NHS Foundation Trust. Before agreeing to take part, you should know exactly what this will mean for you, and what you are required to do. This information leaflet supports the verbal explanation given to you by your doctor and research nurse or practitioner. This trial has been approved by the National Research Ethics Committee and has been sponsored by Bedfordshire Hospitals NHS Foundation Trust.

**Why have I been invited to take part in this trial?** You have been asked to consider participating in this clinical trial because you have had a diagnosis of prostate cancer and you are being managed by surveillance.

**What is the trial trying to find out?** The purpose of this trial is to find out if an intervention aiming to improve gut health could help men with early prostate cancer, and who are currently being managed with surveillance. More specifically, whether a capsule containing a blend of lactobacillus probiotics, could influence PSA progression, urinary symptoms and erectile function. The most reliable way to find this information is to conduct a randomised trial (1:1) involving the trial supplements and placebo (or dummy supplements). This will be discussed in more detail later on in this leaflet, but you will have a 50% chance of being randomly selected to receive the probiotic supplements and a 50% chance of a placebo (dummy supplement).

There is already some evidence that phytochemical rich supplements can slow PSA progression (Phytochemicals are found naturally in plants which provide the colour, aroma and taste). Many are available over the counter supplement and already taken by men with a diagnosis of prostate cancer. Because of this, you will be asked be to stop any other over-the-counter supplements during the trial, and instead will be given a specific phytochemical supplement to take. This ensures that all participants are on the same phytochemical supplement, so that if the trial shows a difference between the two groups, it would more certain that this relates to probiotic or placebo.

As a secondary end point, we also are interested to find out if grip strength, an indicator of overall physical fitness, is linked to PSA progression. We are aiming to recruit 180 men into this trial in total.

**Why is this trial important?** In most men with your type of prostate cancer, progress is usually slow, although about 20%-30% of men would experience a PSA rise, which could trigger treatment interventions such as hormones, surgery or radiotherapy. There is some evidence that gut health can influence prostate cancer, but no trial has yet shown whether probiotic supplements influence a PSA rise or alter symptoms.

**What if I do not agree to take part?** Participation in this trial is entirely voluntary. Agreeing, or not agreeing, to enter this trial does not change in any way the other treatments that you may receive connected to your disease. If you do agree to participate, but later decide to withdraw from the trial at any stage, this would also not affect any future treatment decisions.

**Giving consent to take part in this clinical trial.** Attached to this participant Information leaflet is a Consent Form. Once you completely understand this trial and wish to participate, we will ask you to sign and date the Consent Form. If you do consent to enter this trial, we will ask for your permission to inform your GP as this is optional, and for a member of the trial team to access your hospital medical notes for the duration of your participation.

**What will you have to do if you enter the trial** If you agree to take part in the trial, you will be asked to complete two questionnaires about your current, during your appointments at the beginning and at the end of the trial symptoms (attached to the back of this information sheet). At these appointments we would also like to measure your grip strength with a hand grip strength meter. This involves squeezing a handle, as hard as you can on a hand-held device, for 5 seconds. Blood tests are a part of your routine surveillance management, so whilst you will have blood tests at the beginning and at the end of this trial, these are not in addition to your standard treatment.

Every participant will be given a 4 months' supply of a phytochemical-rich food supplement (one capsule to be taken twice a day) and you may be asked to stop the over-the-counter supplements that you usually take (if any). You will also be randomly assigned to receive 4 months' supply of a second supplement, and we will also ask you to take one capsule, two times a day. This supplement will be labelled as Arm A or Arm B, and neither you nor the medical team will know if you are taking a probiotic or a placebo.

After 4 months, before your routine consultation, you will have a second routine blood test. During the consultation we will also repeat the grip strength measurement and ask you to complete the two questionnaires again asking which record prostate related symptoms (form attached)

**What is randomisation?** This means that it is down to chance whether you receive the probiotic or placebo, and you will be randomly allocated to supplement A or B, to ensure that there is no bias. A computer will randomly generate the treatment arms for each participant, which will be labelled 'Arm A' or 'Arm B'. As the trial supplements will be labelled in this way, neither you nor the research team, will know whether you have been given the probiotic or placebo. As mentioned earlier, all participants will receive the phytochemical-rich plant-based supplement. In summary, you will:

- all receive the phytochemical-rich, plant-based supplement
- have a 50% chance of receiving both the phytochemical-rich, plant-based supplement plus the probiotic supplement
- have a 50% chance of receiving the phytochemical-rich, plant-based supplement plus a placebo (dummy) supplement.

**About the trial capsules?** The wholefood capsule is a cylindrical, vegan capsule measuring 22.4mm long, and is best taken with a drink, with or without food. The probiotic and placebo capsules both look identical and measure 21.4mm long. Both should be taken with a drink, and with or without food. If you find it difficult to swallow the capsule whole, it can be opened up and added to food. These capsules contain no animal products and have been designed by the trial scientific committee. They have been manufactured by a fully-licensed UK manufacturer, who has met all the necessary EU and UK regulations for nutritional and food products. The wholefood capsule contains the dried wholefood and extracts of broccoli, turmeric, pomegranate, green tea, cranberry and ginger. The probiotic capsule has 5 strains of non-diary, lactobacillus bacteria with some prebiotics made from chicory and a small amount of vitamin D (which help these bacteria to grow). The placebo contains safe, inert fillers which are used regularly to support ingredients in food supplements.

**How long will the trial last?** If you agree to take part in the trial, you will be asked to take the trial supplements for 4 months, from the date that you receive them.

**Possible side effects.** Based on information from previous trials of these ingredients, the chance of side effects is small. About 6% of participants experienced some mild flatulence (wind) or loose stools, which usually wore off within a few days. Any side effects will be recorded in trial-specific forms during your consultation, but if in between your two appointments you experience a symptom which began ***after*** you started taking the supplements, please contact the research team on 01234 795 787.

**Will you have to change your diet?** No, you will not have to change your diet and you are completely free to eat and drink as you wish. As explained earlier, your consultant may ask you not to take similar other over-the-counter supplements whilst you are on the trial.

**Possible interaction with other drugs.** No person in a trial involving a similar supplement had any adverse effect on the blood pressure (if on anti-blood pressure medication), or INR (if on warfarin). However, as there is a potential for a rare interaction with warfarin, if you are taking warfarin, it would be sensible to check and record your INR weekly for the first month, and report any abnormal levels to the research team immediately: 01234 795 787.

**All the information collected during the trial be confidential?** All the information that you provide during the trial is confidential and will be known only to the research team. After consent, you will be allocated a unique trial number which is the only identifier on all data recorded thereafter. Any trial results which are published in medical journals or at conference, will not identify you or any other participants. We will ensure that no-one can identify you are from the reports which we write. When the trial results are published, unless you request otherwise, we will write to you with a lay summary of the results. If you consent to take part in this trial, your records will be securely stored by the Hospital for up to 5 years. All data collected during the trial will be processed and stored in accordance with the guidelines set out in the Data Protection Act 2018 and the Good Clinical Practice (CGP) guidelines. Your GP will be informed of your participation in the trial, unless you request otherwise on the Consent Form.

**What are your choices about how your information is used?**
You can stop being part of the trial at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- via our leaflet available from The Hospital's information governance officer (Llinos Bradley 01234 730396, email: Llinos.Bradley@bedfordhospital.nhs.uk)
- by contacting Madeleine Williams, Research Manager, on 01234 795 787 or emailing madeleine.williams@bedfordhospital.nhs.uk.

**Who is funding this trial?** This trial is funded by the Primrose Unit Fund (folio account: BH7A), which is part of 'Bedfordshire Hospitals NHS Foundation Trust Charitable Fund', registered charity number 1058704. The research team involved in the trial are not being paid to recruit you into the trial. There are no copyright or patents issued on any of the investigational products and the anonymised results of the trial will be published the public domain.

**Regulation and design:** This trial has been approved by the Bedfordshire Hospitals NHS Foundation Trust Research and Development Department, and the National Research Ethics Committee (number 321309). It has been registered on the international register (Eudract number XXXXXXX). The trial will be independently audited by an external agency to ensure accuracy and probity.

**What if you have any further queries about this trial?** Please contact Madeleine Williams, Professor Thomas' Research Manager, on 01234 795 787.

**Additional concerns.** If you have any additional comments or concerns about this trial, you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way in which you have been approached or treated during the trial, you should contact the Bedford Hospital Patient Advice and Liaison Service Lead, Jessica Toraman, on 01234 355122 ext. 4624. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence you may have grounds for legal action for compensation against Bedfordshire Hospitals NHS Foundation Trust, but you may have to pay for legal costs. The National Health Service complaints mechanisms will still be available to you.

**The research team thank you for taking the time to read this information sheet and for considering participating in this research trial.**

**Professor Robert Thomas MRCP MD FRCR**
**Principal Investigator**
**Consultant Oncologist**
**Bedford and Addenbrookes Hospitals**
**Visiting Professor University of Bedfordshire**

NHS
Bedfordshire Hospitals
NHS Foundation Trust

# International prostate symptom score (IPSS)

Initials ..... Trial number ..... Date:.....

| | Not at all | Less than 1 time in 5 | Less than half the | About half the time | More than half the | Almost always | **Your score** |
|---|---|---|---|---|---|---|---|
| Incomplete emptying<br>Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating? | 0 | 1 | 2 | 3 | 4 | 5 | |
| Frequency<br>Over the past month, how often have you had to urinate again less than two hours after you finished urinating? | 0 | 1 | 2 | 3 | 4 | 5 | |
| Intermittency<br>Over the past month, how often have you found you stopped and started again several times when you urinated? | 0 | 1 | 2 | 3 | 4 | 5 | |
| Urgency<br>Over the last month, how difficult have you found it to postpone urination? | 0 | 1 | 2 | 3 | 4 | 5 | |
| Weak stream<br>Over the past month, how often have you had a weak urinary stream? | 0 | 1 | 2 | 3 | 4 | 5 | |
| Straining<br>Over the past month, how often have you had to push or strain to begin urination? | 0 | 1 | 2 | 3 | 4 | 5 | |

| Nocturia (getting up at night) | None | 1 time | 2 times | 3 times | 4 times | 5 times or more | **Your score** |
|---|---|---|---|---|---|---|---|
| Over the past month, many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning? | 0 | 1 | 2 | 3 | 4 | 5 | |

| Total IPSS score | |
|---|---|

| Quality of life due to urinary symptoms | Delighted | Pleased | Mostly satisfied | Mixed – about equally satisfied and dissatisfied | Mostly dissatisfied | Unhappy | Terrible |
|---|---|---|---|---|---|---|---|
| If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that? | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

**Total score:** 0-7 Mildly symptomatic; 8-19 moderately symptomatic; 20-35 severely symptomatic.

NHS
Bedfordshire Hospitals
NHS Foundation Trust

# International Index of Erectile Function

These questions ask about the effects that your erection problems have had on your sex life over the last four weeks. Please try to answer the questions as honestly and as clearly as you are able. Your answers will help your doctor to choose the most effective treatment suited to your condition. In answering the questions, the following definitions apply:

- **sexual activity** includes intercourse, caressing, foreplay & masturbation
- **sexual intercourse** is defined as sexual penetration of your partner
- **sexual stimulation** includes situation such as foreplay, erotic pictures etc.
- **ejaculation** is the ejection of semen from the penis (or the feeling of this)
- **orgasm** is the fulfilment or climax following sexual stimulation or intercourse

| | | |
|---|---|---|
| ☐ Q1 | **How often were you able to get an erection during sexual activity?** | 0 No sexual activity<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q2 | **When you had erections with sexual stimulation, how often were your erections hard enough for penetration?** | 0 No sexual activity<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q3 | **When you attempted intercourse, how often were you able to penetrate (enter) your partner?** | 0 Did not attempt intercourse<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q4 | **During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?** | 0 Did not attempt intercourse<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q5 | **During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?** | 0 Did not attempt intercourse<br>1 Extremely difficult<br>2 Very difficult<br>3 Difficult<br>4 Slightly difficult<br>5 Not difficult |
| ☐ Q6 | **How many times have you attempted sexual intercourse?** | 0 No attempts<br>1 One to two attempts<br>2 Three to four attempts<br>3 Five to six attempts<br>4 Seven to ten attempts<br>5 Eleven or more attempts |
| ☐ Q7 | **When you attempted sexual intercourse, how often was it satisfactory for you?** | 0 Did not attempt intercourse<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q8 | **How much have you enjoyed sexual intercourse?** | 0 No intercourse<br>1 No enjoyment at all<br>2 Not very enjoyable<br>3 Fairly enjoyable<br>4 Highly enjoyable<br>5 Very highly enjoyable |
| ☐ Q9 | **When you had sexual stimulation or intercourse, how often did you ejaculate?** | 0 No sexual stimulation or intercourse<br>1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |

| | | |
|---|---|---|
| ☐ Q10 | **When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?** | 1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q11 | **How often have you felt sexual desire?** | 1 Almost never or never<br>2 A few times (less than half the time)<br>3 Sometimes (about half the time)<br>4 Most times (more than half the time)<br>5 Almost always or always |
| ☐ Q12 | **How would you rate your level of sexual desire?** | 1 Very low or none at all<br>2 Low<br>3 Moderate<br>4 High<br>5 Very high |
| ☐ Q13 | **How satisfied have you been with your overall sex life?** | 1 Very dissatisfied<br>2 Moderately dissatisfied<br>3 Equally satisfied & dissatisfied<br>4 Moderately satisfied<br>5 Very satisfied |
| ☐ Q14 | **How satisfied have you been with your sexual relationship with your partner?** | 1 Very dissatisfied<br>2 Moderately dissatisfied<br>3 Equally satisfied & dissatisfied<br>4 Moderately satisfied<br>5 Very satisfied |
| ☐ Q15 | **How do you rate your confidence that you could get and keep an erection?** | 1 Very low<br>2 Low<br>3 Moderate<br>4 High<br>5 Very high |