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Trial to test the feasibility of an exercise and metformin intervention for men with prostate cancer

Submission date
18/07/2018

Recruitment status
No longer recruiting

Registration date
02/08/2018

Overall study status
Completed

Last Edited
27/05/2025

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Prostate cancer is the second most common cancer in men worldwide. Although survival rates are high, one third of men undergoing treatment for early stage prostate cancer will experience recurrence of the disease. There has been some scientific evidence that suggests an active lifestyle may help with the side-effects of treatment for some cancers, and that it may help prevent or slow recurrence of the disease. However, not enough is known to be sure it will be helpful for men with prostate cancer, or if they would find it difficult to include in their lives due to the side-effects of treatment or the commitments of everyday life.
Metformin is a drug that is commonly given to people with type 2 diabetes. Some evidence suggests that it may help prevent recurrence of cancer, but again, not enough research has been done to be sure if it will be helpful to men with prostate cancer or how it might work. metformin can give some people side-effects, and it is not known whether the potential benefits might outweigh any potential benefits for men with prostate cancer.
We would like to run a large trial to test if men with prostate cancer might benefit from physical activity or metformin but before we can do this, we need to refine our methods and check that men with prostate cancer will be willing and able to do extra physical activity or take metformin regularly. This is an important step in the process of developing good quality trials and is called a feasibility study.

Who can participate?
Men with localised or locally-advanced prostate cancer who are due to undergo active monitoring, radical prostatectomy or radiotherapy under the care of clinicians at Southmead Hospital, Bristol.

What does the study involve?
Participants will be randomly allocated to one of 4 groups. They will either receive exercise instructions, or metformin, or both, or continue as usual (no exercise or metformin) for 6 months. Before the trial period starts we will take blood samples and collect prostate tissue samples from participants' routine diagnosis biopsies. We will also ask participants to complete a questionnaire about their lifestyle, feelings and symptoms and ask them to count their steps for

a week, using a pedometer, to measure their usual activity.
All participants will then return to see the research nurse 3 and 6 months later to complete further questionnaires, count steps, and at the 6-months visit, have more blood samples taken. We will be collecting samples of prostate tissue from prostates that were removed routinely as part of the prostate cancer treatment for some men, and from the routine follow-up biopsies of men undergoing Active Surveillance. Some participants will be invited to an interview with a researcher to find out their experiences with the physical activity or metformin.
Six months after the trial period has ended, participants will receive a follow-up questionnaire and be asked to count steps again to look for any changes.

What are the possible benefits and risks of taking part?
The possible benefits for participants in the groups taking part in exercise include the positive influence of physical activity on health and wellbeing. However, a possible risk is that participants may find the commitment of taking part in regular exercise for a 6 month period difficult, along with the minor risks of exercise-related injuries.
For participants in the groups taking metformin, there are no known benefits. Metformin is a widely-used drug; however, there is a small risk of some side-effects, including nausea, diarrhoea or lactic acidosis.

Where is the study run from?
Southmead Hospital, North Bristol Trust, Bristol, UK

When is the study starting and how long is it expected to run for?
June 2017 to March 2021

Who is funding the study?
NIHR Bristol Biomedical Research Centre (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
2840

Study information

Scientific Title
Pre-EMpT: Prostate cancer – Exercise and Metformin Trial: a feasibility study

Acronym
Pre-EMpT

Study objectives
The aim of the study is to explore the feasibility of randomising men with prostate cancer to performing regular exercise or to taking metformin and adherence to these interventions at 6 months. These, and other outcomes will be used to inform development of a main trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 1, favourable opinion given on 17/04/2018, 18/WA/0067

Study design
Interventional single-center open-label 2x2 feasibility randomised controlled trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
Participants are randomised into two groups, the intervention or the control. The intervention will be either physical activity or to take metformin. Each participant will be randomised within the treatment group to either physical activity or control, and then to either metformin or control, resulting in 4 groups:
1. Physical activity and metformin
2. Physical activity only
3. Metformin only
4. No intervention (control)
Participants in the physical activity only group will be asked to undertake brisk walking for 30-

minutes per day, 5-days per week, on top of their usual activity, with the additional aim to walk 10,000 steps per day. Some participants in this group will be provided a Garmin wrist-worn activity monitor which will provide real-time feedback and motivational reminders - these will be provided to participants who are willing to wear them. Offers to wear a Garmin will be managed to a certain extent, to ensure an even spread across the treatment groups (active surveillance, radical prostatectomy, radiotherapy), but there will be no formal randomisation for these.
Participants in the metformin only group will take one 500mg of modified release Metformin, once a day with food.
Participants in the physical activity and metformin group will be asked to undertake the same activities as both the physical activity only and metformin only groups.
Participants in the control group will not receive intervention instructions or training.
The intervention period is 6 months, beginning close to start of cancer treatment for participants waiting to receive prostatectomy or radiotherapy. For participants receiving active surveillance treatment, the intervention period will be 6 months after the start of active surveillance, to align end of intervention with the routine biopsy that takes place at 12 months post-diagnosis for these patients.

Intervention Type
Mixed

Primary outcome(s)
1. Proportion of eligible men who agree to be randomized
2. Adherence to intervention, calculated separately for physical activity and metformin, assessed at 3 and 6 months after start of intervention.
2.1. For physical activity, adherence will be assessed by step count, recorded by pedometer and reported by the participant.
2.2. Metformin will be assessed by a count of the pills returned by the participant to the research clinics. In addition, blood samples will be taken which may be examined for metformin.
2.3. Both of these will be assessed for participants in the physical activity and metformin group

Key secondary outcome(s))
1. Intervention tolerability, assessed using qualitatively collected data and reporting of adverse events from qualitative interviews for selected participants after the end of the 6 month intervention period
2. Trial retention, assessed by number of participants successfully followed-up at the end of the 6 month trial, as a proportion of those who we recruited to the trial and randomised into a study arm at the start of the trial)
3. Feasibility of measuring prostate specific antigen (PSA) level, assessed using a blood sample at the baseline and 6 month follow up
4. Feasibility of measuring insulin-like growth factor I (IGF-I), assessed using a blood sample at the baseline and 6 month follow up
5. Feasibility of demonstrating methylation and gene expression profiles in prostate tissue and blood, assessed using blood and tissue samples (prostate tissue removed during surgery and tissue removed during biopsy as part of standard care) at the baseline and 6 months
6. Feasibility of assessing physical activity levels, self-reported using the Godin Exercise Leisure-time Questionnaire at the baseline, 3, 6 and 12 months
7. Urinary symptoms, assessed using the International Continence Society male - Short Form (ICSmale-SF) at the baseline and 3, 6 and 12 month follow up, along with 7 weeks following main consent for the surgical patients
8. Psychological factors, assessed at the baseline and 3, 6 and 12 month following using:
8.1. Profile of Mood States – Short Form (POMS-SF)

8.2. Benefit Finding Scale
9. Patient function and bother after prostate cancer treatment, assessed using he Expanded Prostate Cancer Index Composite (EPIC-26) at the baseline and 3, 6 and 12 months follow up
10. Health beliefs, assessed at the baseline and 3, 6 and 12 month follow up using:
10.1. Items from the Theory of Planned Behaviour (Ajzen, 1991) - there is no standard TPB questionnaire but Ajzen provided advice on questionnaire construction and gave examples and the questionnaire was designed to be applicable to this study
10.2. Items based on work from Prochaska and Di Clemente's Transtheoretical Model of Stages and Processes of Change
11. Quality of life measures, assessed using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) at the baseline and 3, 6 and 12 month follow up
12. Cancer related fatigue, assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) and EuroQol five dimensions questionnaire (EQ-5D) at the baseline and 3, 6 and 12 month follow up. This is additionally collected at 6 weeks following completion of radiotherapy for the radiotherapy patients, which is approximately 4.5 months after main consent
13. General lifestyle factors, assessed using self-reported levels of smoking and drinking at the baseline, 3, 6 and 12 months
14. Feasibility of men with localised prostate cancer wearing wrist worn activity trackers, assessed by qualitative interview and monitoring form at the end of the 6 month intervention period
15. Impact of wrist worn activity trackers on adherence to the physical activity intervention, assessed using 7 day step count on monitoring form and data recorded by wrist worn activity trackers at the baseline, 3, 6 and 12 months
16. Weight and body mass index, measured by a nurse at the baseline
17. Attitudes and views of men about physical activity and metformin interventions and participation within the trial,. assessed using qualitatively collected data

Completion date
31/03/2021

Eligibility

Key inclusion criteria
1. Localised or locally advanced prostate cancer
2. Due to undergo radiotherapy or radical prostatectomy, or due to begin the active surveillance pathway
3. Due to receive treatment at Southmead Hospital, North Bristol NHS Trust or Bristol Haematology & Oncology Centre (University Hospitals Bristol NHS Trust)
4. Capacity to consent for themselves as judged by a member of the research team with appropriate training and experience
5. Aged 18 or over
6. Have sufficient understanding of the English language, including being able to read and speak English at a basic level

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. Inability to give informed consent or unavailability for follow-up
2. Being identified as unsuitable to participate following guidance of their clinician
3. Currently taking metformin or insulin
4. Co-morbidities which could prevent participation in the metformin arm of the intervention, including:
4.1. Diabetes
4.2. Hypersensitivity to metformin hydrochloride or to any of the excipients
4.3. Diabetic ketoacidosis, diabetic pre-coma, renal failure or renal dysfunction (eGFR <30mL /minute/1.732)
4.4. Acute conditions with the potential to alter renal function such as:
4.4.1. Dehydration
4.4.2. Severe infection
4.4.3. Shock
4.4.4. Intravascular administration of iodinated contrast agents
4.4.5. Acute or chronic disease which may cause tissue hypoxia such as cardiac or respiratory failure or recent myocardial infarction
4.5. Hepatic insufficiency
4.6. Acute alcohol intoxication
4.7. Alcoholism
4.8. Stoma
5. Use of a mobility aid other than a walking stick, which would prevent them from carrying out the brisk walking intervention

Date of first enrolment
23/07/2018

Date of final enrolment
23/01/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Southmead Hospital
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Westbury-on-Trym
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Sponsor information

Organisation
University of Bristol

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Not defined

Funder Name
NIHR Bristol Biomedical Research Centre (Nutrition Theme)

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/05/2025	27/05/2025	Yes	No
Protocol article		12/08/2022	15/08/2022	Yes	No
HRA research summary			28/06/2023	No	No