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Development of a new penile clamp to prevent urine leakage in men who have urinary incontinence following treatment for prostate cancer

Submission date
27/01/2020

Recruitment status
No longer recruiting

Registration date
26/03/2020

Overall study status
Completed

Last Edited
01/04/2020

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Treatment for prostate cancer can damage the bladder and urethra (the tube that urine passes through on its way from the bladder and through the penis) causing urinary incontinence (UI). Between 2 and 3 of every 20 men who have had surgery for prostate cancer have life-long UI requiring the daily use of incontinence products. Incontinence has a big effect on quality of life. It can leave men depressed and isolated, affecting personal relationships and resulting in stigma and limited social and professional opportunities. When treatment fails or is not appropriate, it is essential to control urine leakage. Men have a range of products available to them and often choose to use a mix of two or more products to meet changing needs. Most men use a pad at least some of the time, and a sheath or body-worn urinal for containing leakage over longer periods. The penile clamp (clamp) is a device that fits over the penis and is meant to squeeze the urethra closed, so that no urine can leak out. Men often find these clamps useful for short-term and/or vigorous activities e.g. dancing, swimming and going for long walks.
Previous research has shown that the available clamps do not perform well in terms of preventing leakage, being acceptable to the user and avoiding negative effects on skin health and blood flow in the penis. Therefore the researchers have concluded that there is a need for a better clamp. The new clamp will be developed by a research team at the University of Southampton, including engineers and healthcare professionals, working closely with men with UI following treatment for prostate cancer. Some of these men are experienced clamp users who assisted with the previous research testing clamps already on the market. This study aims to develop and test a prototype which, if successful, will be manufactured and sold.

Who can participate?
Men aged over 18 years who have UI following treatment for prostate cancer, including those who are experienced in using penile clamps and those who are not.

What does the study involve?
In the first part of the study, men who are experienced clamp users will visit the hospital and will

wear each prototype clamp and an incontinence pad for 30 minutes and will be asked to do some exercises that can encourage urinary leakage. The pads will then be weighed to measure the amount of urine that has leaked out. The men will also fill in a questionnaire to assess their experience of using each clamp.
If one of the prototypes is effective at preventing urine leakage and is acceptable to the participants, it will be tested further to assess its effect on skin health, pressure and blood flow in the penis, inflammation, and damage to the urethra. The participants from the first part will be invited to come to a hospital laboratory for up to four 3-h sessions of testing. This will involve non-invasive tests using machines as well as taking urine samples.
If a prototype is acceptable in terms of skin health, blood flow inflammation and tissue damage, it will move into the user evaluation stage. Men who have not been previously involved in the study will be recruited and will test up to four clamps (including the prototype and a clamp that is on the market) by using them for up to 2 weeks. They will be told that they do not have to use the clamp if they find it uncomfortable and can take breaks from testing the clamp when they wish. They will fill in questionnaires on each clamp after each period of testing and will be asked which clamp they preferred once they have tested them all.

What are the possible benefits and risks of participating?
There is a small risk that circulation in the penis might be damaged if the clamp is fitted too tightly. The first time each is fitted, it will be done by a nurse with experience in fitting male devices. The clamp will be fitted at the loosest setting initially and tightened as necessary. The previous research conducted by the research team will inform the design of the prototype clamp and the design will seek to prevent problems caused by the clamp being too tight. In addition, the researchers will have applied the prototype clamp design to a computer model to estimate pressure applied on soft tissue before it is tried out on men.
Men who have reduced sensation in their penis, lack of awareness of bladder filling, urge incontinence as their main symptom or poor memory (which means they might forget to release the clamp regularly) will not be allowed to participate in the study. Many participants will have had experience of using clamps previously.
Skin reddening and grazing is possible from the mechanical action of the devices. The risk will be minimised by expert fitting of the devices by an experienced research nurse. Instructions will be given on how to identify potential skin problems and actions to take. Telephone support will be available for the men.
In the previous research study, one of the available clamps caused a small amount of bleeding from the urethra. The participant will be instructed to stop using a clamp if this occurs until bleeding has stopped. Once bleeding has stopped (and not sooner than 14 days later) he may restart testing the clamp or move onto the next one. He will be asked to inform the research nurse if this happens.
There is also a small risk of emotional distress when evaluating continence products, especially when associated with a diagnosis of cancer. The research nurses involved in the trial are all experienced in discussing incontinence with men and will ensure that all participants are aware of the risks and know how to identify and manage them. The participants will have telephone support from the research nurse who can make additional home visits if necessary.
As it is the research team's intention to develop an improved clamp, the prototype clamps may prove more effective and popular with the men than the clamps currently available. Participants may be disappointed that they are unable to keep the prototypes. The research team will minimise this risk by explaining carefully at the outset that the prototypes will have to be returned.
In everyday life, men purchase and use clamps with very little informed guidance. The men in this study will have regular contact with the research team and will have a much higher level of supervision than would be usual in clinical practice.

As for benefits, participants will receive reimbursement for travel expenses when attending Southampton General Hospital or other venues. They will be provided with refreshments as appropriate. Participants will have the opportunity to try out clamps that they might not otherwise come across. They will be able to contribute to the development of a new medical device.

Where is the study run from?
University of Southampton (UK)

When is the study starting and how long is it expected to run for?
December 2016 to March 2020

Who is funding the study?
Prostate Cancer UK

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
215740

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 32987, IRAS 215740

Study information

Scientific Title
Prostate Cancer UK Continence Management Module 3: Development of an effective and comfortable penile compression device (clamp) Phase 2: Development of a new clamp

Study objectives
Long-term urinary incontinence (UI) is a common consequence of treatment for prostate cancer, and between 10-15% of men who have had surgery for prostate cancer will suffer life-long UI requiring the daily use of incontinence products. Incontinence has a major effect on quality of life, leaving men depressed and isolated, affecting personal relationships and resulting in stigma and limited social and professional opportunities. The effective containment of incontinence when treatment fails or is not appropriate is essential. Men have a range of products available to them and often elect to use a mix of two or more products to meet changing needs. Most men use a pad at least some of the time, and a sheath or body-worn urinal for containing leakage over longer periods. The penile clamp (clamp) is a device which men often find useful for short-term and/or vigorous activities e.g. dancing swimming and going for long walks.

In Phase 1 of this study, we established that, although there are many clamps available, when tested by men in the laboratory and in use at home none of them performed well for key criteria of efficacy, user acceptability and physiological impact. We therefore concluded that there is a need for a better clamp which we aim to deliver in Phase 2. A new, improved clamp has the potential to benefit men with UI (usually stress urinary incontinence).

The new clamp will be developed by a research team at the University of Southampton (engineers and clinical specialists) working closely with groups of men some of whom are experienced clamp users who assisted with Phase 1. We plan to use an iterative process to develop a refined prototype which if successful following laboratory and home-based user evaluation, is intended for commercialisation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/02/2017, South Central – Hampshire B research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT; +44 (0)207 104 8054; nrescommittee.southcentral-hampshireb@nhs.net), ref: 17/SC/0008

Study design
Non-randomised; Interventional; Design type: Process of Care, Device

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
See additional file

Health condition(s) or problem(s) studied
Prevention of urine leakage in men who have urinary incontinence following treatment for prostate cancer

Interventions
This study includes three components: brief testing of early prototypes through an iterative process of user feedback and prototype refinement, laboratory testing of a refined prototype, and user evaluation of the refined prototype. Two groups of men will be recruited as follows:

Brief testing and laboratory testing: 6 men who are experienced clamp users and have assisted with Phase 1 (Group 1 men)
User evaluation: 12 naïve men with no previous involvement in the study (Group 2 men).

The components comprise the following:

Brief testing of early prototypes
The researchers plan to recruit up to 12 men, ideally those who participated in the previous study in this project, to ensure data from 6 men in total. If we are unable to recruit these men from Phase 1 participants, the researchers will recruit new men with experience of penile clamp use. The participants will have an opportunity to attend a number of focus groups (six maximum) to help refine the prototype design. They will handle the prototype clamp and if happy with the design, will wear the prototype clamp for up to 30 min with a pre-weighed absorbent pad in situ (to evaluate leakage). During this wear time the men will undergo a standard set of exercises and following this, the pad will be re-weighed and the difference in weight recorded. This will allow us to evaluate the effectiveness of the prototype clamp at preventing urinary leakage. The men will also be asked to complete a short questionnaire for each prototype clamp tested. This will allow inter-clamp comparison of important characteristics such as ease of application, comfort and discreetness under clothing. This method was used in Phase 1 of the study when evaluating existing clamps and by using the same method the researchers will also be able to compare prototype and existing clamps.
A maximum of four prototypes will undergo brief testing during the iterative process. It is anticipated that each testing period (per clamp), including wear time and questionnaire completing, will take approximately 45 min. With break periods, the men will be required for a maximum of 6 h at Southampton General Hospital. Appropriate refreshments will be provided.

Laboratory testing of the refined prototype:
If a prototype is developed that is found to be acceptable to the Group 1 men and effective at preventing urine loss in the brief testing, it will be put forward for laboratory testing. The laboratory tests are modifications of those used in Phase 1 for which ethics committee approval was received. Each participant from Group 1 will attend SGH Wellcome Trust for up to four 3-h sessions.

Following collection of baseline measurements, the men will undergo tests while supine on a hospital-style bed. Present will be the research nurse, technician and engineer. Laboratory testing will involve the following:
1. Baseline data: Height and weight of the participant will be recorded for complete demographic data. Current medication will be recorded as some medications affect inflammatory response. The researchers will ask participants if they experience penile retraction

and have penile shortening (a common consequence of prostate surgery) and if they have been circumcised. Fitting of the device to a retracted penis may leave too little room to get a proximal blood flow measurement. Ideally the clamp is fitted behind the glans on the shaft of the penis.
2. Penile laser Doppler Flowmetry (MoorLDI2-IR laser Doppler blood flow imager, Moor Instruments UK). Circulatory impedance will be assessed with the clamp in position and after removal.
2.1. For the intermittent testing; measurements will be taken at baseline with no clamp, at 10 min and 60 min with the clamp in situ, after which the clamp will be removed and two further measurements will be made at 10 min after removal to assess initial recovery of blood flow and finally 30 min post removal to allow a significant rest period (100 min total testing).
2.2. For the continuous testing; measurements will be taken at baseline with no clamp and 120 min with the clamp in situ, after which the clamp will be removed and four further measurements will be made at 10 min after removal, to assess initial recovery of blood flow, again at 30, 60 and 120 min post removal to allow a more significant rest period (240 min total testing). Then the clamp will be reapplied for 120 min and at the end of this period a Doppler measure will be taken with the clamp in situ, and finally 10 min after removal.
Blood flow assessment will be made proximal, central and distal to the device where possible. This test will assess the impact of the clamp on blood flow over time.
3. Skin and Interface pressure testing: Although there are no published reports on skin injury from clamp use, penile clamps could potentially lead to mechanical-induced soft tissue injury and the formation of pressure ulcers. Accordingly it is important to monitor the interface pressures between the clamp and the soft tissues of the penis. One cell, 20 mm in diameter, will be positioned on the ventral surface of the penis under the arms of the clamp. It will be attached to a commercial pressure monitoring system (Talley Mk3 Pressure Monitor, Talley Medical, Romsey, UK). The clamp will then be applied using the loosest setting and then tightened as necessary to a level which is comfortable for the participant and prevents leakage. Participants will have recent experience of trying out the clamp at home and will be able to advise on the best fit. Interface pressure measurements will then be recorded for a period of 30 s and a mean value of interface pressure calculated from three repeats.
3.1. For the intermittent testing. These measurements will then be repeated after 10 min and at the end of the 60 min test period.
3.2. For continuous testing. These measurements will then be at baseline and after 120 min wear time.
4. Inflammatory response: As with skin and interface pressure assessment, it is important that the potential skin irritation risk is assessed. It is known that the presence of medical devices can lead to mechanical-induced irritation to soft tissue resulting in the release of pro-inflammatory mediators, in the form of cytokines and chemokines (proteins which are intercellular mediators in the modulation of immune response). These mediators can be collected using Sebutape. One strip of Sebutape (area 4 cm2, CuDerm Corp., Dallas, TX, US) will be gently applied to the dorsal side of the penile tissues and a baseline sample will be collected. The tape will be gently removed after 2 min. The clamp will then be positioned and closed using the loosest setting and tightened as necessary to a level which is comfortable and prevents leakage.
4.1. For the intermittent testing, collections using fresh Sebutape will be repeated at 10 and 60 min with the clamp in situ and 30 min after clamp removal.
4.2. For continuous testing, at baseline, after 120 min wear time and 30, 60 and 120 min after clamp removal. The clamp is reapplied for 120 min and a final measure taken at 370 min total.
The four tapes per clamp from intermittent testing, and six tapes per clamp from continuous testing will subsequently be processed and analysed for levels of a range of mediators, including IL-1α, IFN-γ, IL-1RA and IL-8. If the participant desires the clamp to be removed at an earlier period than the 10, 50 or 120 minutes wear for any reason, an endpoint Sebutape test will be made.
5. Urinalysis: urine will be collected for two tests as follows:

5.1. Intermittent
5.1.1. Cytokines: A urine sample will be collected at baseline and after 60 min to identify cytokines which could indicate an inflammatory response within the bladder/urethra.
5.1.2. Red blood cells: A dip stick urine test will be done at baseline and after 60 min to detect any red blood cells present which may infer urinary tract damage.
5.2. Continuous
5.2.1. Cytokines: A urine sample will be collected at baseline, after 120 min wear, and after the second 120 min wear period to identify cytokines which could indicate an inflammatory response within the bladder / urethra.
5.2.2. Red blood cells: A dip stick urine test will be done at baseline, after 120 min wear, and after the second 120 min wear period to detect any red blood cells present which may infer urinary tract damage.
NB: The presence of cytokines and/or red blood cells in the urine could be indicative of bladder cancer. The study urologist will review the participants' notes and will write to the participants' GP if he is concerned that this may be indicative of cancer. Volunteers are made aware of the implications of this test in the Participant Information Sheet before informed consent is taken.

Participants will be accompanied by the research nurse for each of the laboratory visits. They will be offered refreshments and will have a break between clamp testing. It is anticipated that measurements can be completed for two devices in one day, with each set of measurements taking up to a maximum of 3 h for the intermittent testing and one day for each clamp for the continuous testing.

User evaluation of the refined prototype:
If a prototype is found to be acceptable for physiological impact (blood flow and skin health) in the laboratory testing, it will be entered into a small crossover design user evaluation. Men will try out up to four clamps (including at least one prototype and the reference clamp) in their own home. 16 new men who have not previously been involved in the study (Group 2) will be recruited to allow for a 25% attrition and ensure 12 full datasets. They will test the clamps in a randomised order to avoid order bias. Randomisation will be carried out using Latin squares. Testers will be asked to discontinue using any product which they find unsuitable and they will take a break from testing for social or other reasons if they wish. Each clamp will be tested for up to 2 weeks giving a maximum testing period of 10 weeks.

Recruitment strategies:
1. Men who have participated in previous clamp research (including Phase 1 of this study) and who consented to be contacted regarding further similar research will be contacted by phone or in writing. They will be invited to contact researchers if they wish to find out more about the study.
2. Participant Identification Centres (PIC), including urology outpatients at SGH and North Bristol Trust, and local Continence Advisory Services, will be used. The centres will invite patients who fit the inclusion criteria to contact the research team. This will be done by letter distributed by the clinical team with an 'Expression of Interest' form to contact the research team.
3. The study will be advertised via prostate cancer support groups and national prostate cancer and incontinence organisations using a poster suitable for hard copy or a website.
4. If the above does not deliver sufficient recruits, the researchers will also engage local GP surgeries to act as PICs. This will involve asking selected local practice teams to check their databases for patients who fulfil the inclusion criteria and sending a letter to eligible patients inviting them to contact the research team if they wish to receive further information.

Interested men who return an 'Expression of Interest' form will be sent the appropriate Participant Information Sheet (PIS). They will have a chance to have questions answered and, if

they are still interested in taking part, will be asked to sign the appropriate consent form. As part of the screening procedure, they will complete a number of questionnaires to establish eligibility for the study. They will do the Mini Mental State exam to establish cognitive ability and the Barthel Index to establish level of dexterity. Baseline assessment will require them to complete the EQ-5D-5L and the EPIC questionnaire to assess quality of life.

The research nurse will visit the men at home or if they prefer at SGH and explain the process.

Data collection:
1. Pad test: The men will complete up to three pad weight tests for each clamp. The pad will be weighed in a sealed plastic bag before and after the test; the pre-use weight is subtracted from the post-use weight and the difference indicates the extent of urine leaked while the clamp is in situ. They will also record details of any leakage that occurs whilst wearing the clamp beyond the pad onto clothing as 'none' 'a little' or 'a lot'. On one day they will do a pad weight test without a clamp in situ as a control. This will provide data on the usual amount of urine leakage experienced by the men in a 2-h period. From this the researchers will be able to assess the effectiveness of the clamp.
2. Product performance: At the end of each clamp testing period participants will record their views on the performance of the clamp by completing the Clamp Product Performance Questionnaire.
3. Product preference: At the end of the 2-week period a Clamp Preference Questionnaire will be completed.
4. Overall opinion: When all clamps have been tested participants will complete a final Overall Opinion questionnaire.
5. EQ-5D-5L and Expanded Prostate Cancer Index Composite-26 questionnaires will be completed before and after testing to assess changes in quality of life.

User interviews:
The researchers would like to make a series of interview recordings of men describing their experience of clamp use. We have found that this type of video clip is very useful for men when thinking about how to select products. The interviews would be used on the Continence Product Advisor website. There will be a separate consenting process for this. There are specific questions on the consent form regarding audio and video recording and this will be optional for the participants. They may decline to be interviewed but still participate in the study.

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
1. Overall opinion of clamp assessed using Overall Opinion questionnaire after all the clamps have been tested in the user evaluation stage
2. User evaluation assessed using a visual analogue scale (VAS) after all the clamps have been tested in the user evaluation stage
3. Penile blood flow in the intermittent test assessed using circulatory impedance measured using penile laser Doppler Flowmetry (MoorLDI2-IR laser Doppler blood flow imager, Moor Instruments, UK) at baseline, at 10 and 60 min wear-time and at 10 and 30 min after removal of the clamp in the laboratory testing stage
4. Penile blood flow in the continuous test assessed using circulatory impedance measured using

penile laser Doppler Flowmetry (MoorLDI2-IR laser Doppler blood flow imager, Moor Instruments, UK) at baseline and 120 min wear-time,at 10, 30, 60 and 120 min after removal of the clamp after the initial wear, and at 120 min after a second application of the clamp and 10 min after the second removal in the laboratory testing stage
5. Interface pressure in the intermittent test assessed using a Talley Mk3 Pressure Monitor (Talley Medical, Romsey, UK) at baseline and after 10 and 60 min wear time
6. Interface pressure in the continuous test assessed using a Talley Mk3 Pressure Monitor (Talley Medical, Romsey, UK) at baseline and after 120 min wear time
7. Inflammatory reaction in penis skin next to the clamp in the intermittent test assessed using analysis of Sebutape (CuDerm Corp., Dallas, TX, US) at 10 and 30 min wear time and 30 min after clamp removal
8. Inflammatory reaction in penis skin next to the clamp in the continuous test assessed using analysis of Sebutape (CuDerm Corp., Dallas, TX, US) at baseline, after 120 minutes wear time, 30, 60 and 120 minutes after initial clamp removal, and 10 min after a second 120-min period of clamp wear
9. Inflammatory response in the bladder and urethra in the intermittent test assessed by analysis of cytokine levels in urine collected at baseline and after 60 min of clamp wear
10. Inflammatory response in the bladder and urethra in the continuous test assessed by analysis of cytokine levels in urine collected at baseline, after 120 min wear and after a second 120-min wear period
11. Urinary tract damage in the intermittent test assessed using presence of red blood cells in urine detected using a dip stick test at baseline and after 60 min of clamp wear
12. Urinary tract damage in the continuous test assessed using presence of red blood cells in urine detected using a dip stick test at baseline and after 60 min of clamp wear at baseline, after 120 min wear and after a second 120-min wear period

Secondary outcome measures
1. Leakage performance assessed using the Pad Leakage Diary prior to wearing the clamp for 2 hours and whilst wearing the pad for 2 hours on three occasions during the 2-week user evaluation of each clamp
2. Comfort assessed using the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
3. Reliability assessed using the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
4. Pain assessed using a visual analogue score (VAS) in the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
5. Ease of use assessed using the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
6. Discreetness assessed using the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
7. Ease of cleaning the clamp assessed using the Clamp Product Performance Questionnaire after the 2-week user evaluation of each clamp
8. Product preference as a measure of performance against the reference clamp using the Clamp Product Preference Questionnaire after all clamps have been tested in the user evaluation

Overall study start date
08/12/2016

Completion date
31/03/2020

Eligibility

Key inclusion criteria
1. Urinary incontinence
2. Previous prostate cancer diagnosis
3. Aged 18 years or over
4. Sufficient manual dexterity to apply and release the reference clamp
5. For Group 1, experience of using a penile clamp

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 18; UK Sample Size: 18

Key exclusion criteria
1. Absence of sensation to the penis (self-report)
2. Absence of bladder sensation due to neurological impairment (self-report)
3. Urge incontinence (a strong uncontrollable urge to pass urine and leakage before reaching the toilet) as the predominant urinary symptom (self-report)
4. In the terminal stage of an illness
5. Cognitive impairment (score of <27 on Mini Mental State Exam [MMSE] - to be carried out face-to-face by the research nurse)

Date of first enrolment
24/07/2018

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Southampton General Hospital
Southampton University Hospitals NHS Trust
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ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Charity

Funder Name
Prostate Cancer UK

Alternative Name(s)
Prostate Cancer, Prostate Action, ProstateUK, prostatecanceruk

Funding Body Type

Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
It is the researchers' intention to develop a functioning prototype. At this point, the results of this study will be published in a high-impact peer-reviewed journal.

Intention to publish date

Individual participant data (IPD) sharing plan
Researchers interested in using the study data should contact the principal investigator to request access.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.9	04/07/2017	01/04/2020	No	Yes
HRA research summary			28/06/2023	No	No