JRMO Research Protocol for Interventional Studies

Full Title	**A controlled pilot study assessing the feasibility of using clitoral vibrators to aid vaginal dilator therapy in women presenting to psychosexual services with vaginismus.**
Short Title	**Feasibility of use of vibrators with vaginal dilators for vaginismus**
Sponsor	Barts Health NHS Trust Contact person: Dr Mays Jawad Research & Development Governance Operations Manager Research Services Dept W 69-89 Mile End Road London, E1 4UJ Phone: 020 7882 7275/6574 Email: research.governance@qmul.ac.uk
IRAS Number	**278027**
Edge Number **REC Reference**	136594
Chief Investigator	*Dr Jessica Gaddie* *Specialist Registrar HIV/GUM* *Barts Health NHS Trust, AKC, The Royal London Hospital, Whitechapel Rd, London, E1 1BB* *07779286544* *j.gaddie1@nhs.net*
List of sites	*AKC, Royal London Hospital* *AS ABOVE*
List of laboratories	*N/A*
List of technical departments	*N/a*
List of central facilities	*N/A*

1. Contents

2. Glossary

Dyspareunia – pain with penetrative sex.
FSD - Female Sexual Dysfunction
FSFI - Female Sexual Function Index
FSDS - Female Sexual Distress Scale
GPPD - genito-pelvic pain/penetration disorder. This diagnostic term recognises the frequent overlap between the conditions of vaginismus and vulvodynia
Vaginismus results from the involuntary spasm of the pelvic floor muscles which surround the vaginal wall.
Vulvodynia chronic vulvar pain of at least three months duration
Vestibulodynia – Often used to describe vulvar pain at the introitus, or entrance to the vagina

3. Signature page

Chief Investigator Agreement

The study as detailed within this research protocol will be conducted in accordance with the principles of Good Clinical Practice, the UK Policy Framework for Health and Social Care Research, and the Declaration of Helsinki and any other applicable regulations. I agree to take responsibility for the statistical analysis and oversight of this study.

Chief Investigator Name: **Jessica Gaddie**

Signature: 

Date: _____ **20/09/2022**

4. Summary and synopsis

Short title	**Feasibility of use of vibrators with vaginal dilators for vaginismus**
Methodology	*Feasibility study*
Research sites	*AKC, Barts Health NHS Trust, E11BB*
Objectives / aims	*Firstly, is vibration therapy (through the use of handheld vibrators on clitoral and vulval area) acceptable to women as part of medical management of vaginismus, alongside current medical management.* *Does the use of external genital (clitoral/ vulval) vibrators help women to progress more easily with the use of vaginal dilators compared to women not using these? Is there any self-reported difference in experiences of pleasure or enjoyment around sexual experiences in the two groups of women? Are there any differences noted in reported ability to have penetrative sexual intercourse?*
Number of participants	*30*
Inclusion and exclusion criteria	*Inclusion:* *Female* *>18 years old* *Clinical diagnosis of Vaginismus (self-reported difficulties with penetration and genital exam consistent with a degree of vaginismus)* *Willing to be enrolled in pilot study:*

	Exclusion: *Any vulval skin dermatoses excluding medical management of vaginismus* *Transgender male / on testosterone therapy* *Symptoms of genital herpes episode in preceding 3 months* *Unable to speak/ understand English or needing an interpreter* *Declines to be enrolled in research study* *Pregnancy*
Statistical methodology and analysis (if applicable)	*n/a*
Study duration	*Up to 48 months*

5. Introduction

VITA DIVA- Vibration Therapy And Dilators for Vaginismus

Vaginismus results from the involuntary spasm of the pelvic floor muscles which surround the vaginal wall. This can make sexual intercourse uncomfortable, painful, or impossible, with resultant impacts on a woman's sexual pleasure and ability to conceive. There is often overlap with vulvodynia (also termed vestibulodynia), chronic vulvar pain of at least three months duration. Various clinical definitions have been proposed for vulvodynia or vestibulitis.

Successful treatment for both vulvodynia and vaginismus relies often on both medical and psychosocial interventions alongside self-help and practice. Current medical therapy for vaginismus often consists of the use of topical local anaesthetic gel, sometimes in addition to oral medications such as low dose Tricyclic Antidepressants together with recommendation of progressive vaginal dilator therapy (often termed systemic desensitisation) and physiotherapy. The fact there is not a clearly culpable etiology (and indeed causes are likely to be multifactorial) means that there is no 'gold standard' treatment for vaginismus and vulvodynia (Zolnoun, 2008). A multi-modal approach is recommended.

Anecdotally, some women find that clitoral stimulation can sometimes have a positive impact on the ability to progress with vaginal dilator treatment and general enjoyment of sexual intimacy, but this has not yet been evaluated in a research setting.

Background

Various clinical definitions exist for vaginismus and vulvodynia, which have been recognised as a syndrome by the American Medical Association in the DSM-5 as genito-pelvic pain/penetration disorder (GPPD). This diagnostic term recognises the frequent overlap between the conditions of vaginismus and vulvodynia (AMA, 2013). Diagnosis per the DSM-5 criteria requires the presence of one of the following: persistent or recurrent difficulties with vaginal penetration during intercourse; marked vulvovaginal or pelvic pain during penetrative intercourse or attempts; fear or anxiety about vulvovaginal or pelvic pain in anticipation of, during, or as a result of vaginal penetration; or marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration. Additional criteria are presence of symptoms for at least six months, significant distress, and not explained by a diagnosis of non-sexual disturbance, causing relationship problems and not attributed to the effects of any substance or any other medical condition.

In review of literature, searched for the terms vulvodynia, vestibulodynia, female genital pain, sexual disorders, and vibration, vibrator or clitoral or genital stimulation. Of the 85 results, 9 were relevant and in English. Of these, one related to the use of vaginal dilators, 5 related to genital vibratory stimulation devices, 3 related to genital stimulation and perception of pain. No studies assessing the acceptability of clitoral vibrators specifically in self-treatment of patients with vaginismus were found.

Genital stimulation/ sensation and pain perceptions

Calens et al carried out a web-based questionnaire of sexually active women n=256, median age 22 range 18-49. Questions included the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS). Women reported the clitoris to be more sensitive than the vagina in terms of pleasurable responses, but not painful response. Women with Female Sexual Dysfunction reported impaired self-perceived genital sensation, less sexual pleasure and orgasm, and more association of orgasm with discomfort in the genital area than women without FSD. They conclude that "enhancing the pleasurableness of genital sensations, especially during partnered sex, could decrease the likelihood of experiencing pain and concomitant FSD" (Calens, 2016).

Paterson et al found that women who masturbated to orgasm in private found that this appeared to maintain pleasurable genital sensitivity, but increase in pain sensitivity with higher vulvar pain sensitivity when orgasm occurs. Enhancing stimulation pleasurableness, psychological sexual arousal can mitigate normative increases in pain sensitivity during sex(Paterson, 2013).

Whipple et al investigated the effectiveness of genital self-stimulation in elevating pain thresholds. This was a study of only 10 women who applied pleasurable sensations to the anterior vaginal wall, the posterior vaginal wall, and the clitoris. Increases in pain thresholds but not tactile thresholds were noted in this group compared to distraction control (Whipple, 1988).

Use of devices in self-directed therapy for vaginismus and vulvodynia:

One study assessed the acceptability of vulvar vibration therapy as a treatment for vulvodynia. 69 patients enrolled of whom 49 were eligible for analysis. Vulvular pain and dyspareunia were the primary complaints, and median duration of these was two years and three years respectively (Zolnoun, 2008). Although this may be a somewhat different population; (the primary presenting complaint was vulvodynia or dyspareunia, as opposed to vaginismus, and only two of the 49 had ever used vaginal dilators). Furthermore, it was acknowledged in the study that the generalisability of results was limited as the study population was primarily white, married, well-educated and from a single geographical location. 83% of those surveyed who had used vulvar vibration therapy for at least two weeks had found it an acceptable and 73% found it a convenient treatment. In this study, Zolnoun et al. proposed that VVT therapeutic rationale was based on the anti-nociceptive properties of vibration and on the favourable response of vulvodynia to physical therapy.

Genital vibration devices were found to result in improvements in sexual function, satisfaction, sexually related distress and genital sensation in women with arousal and orgasm disorders in one study enrolling 70 women, 37 of whom were followed up after a period of 3 months (Guess, 2017). This was a single-arm study enrolling women with arousal and/or orgasm disorders, so again a slightly different study population to the proposed study. Mean age was 35.5, and 66% had never or seldom used genital vibratory device. The Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS) were carried out at baseline and follow up which was at 3 months.

Herbenick et al acknowledged that vibrators are frequently recommended by clinicians for female sexual dysfunction, although there is little awareness of the correlation of this to sexual function. 2, 056 women participated in the internet based

survey (54% of the 3, 800 nationally representative sample who were invited). This assessed the prevalence of vibrator use, and the relationship between vibrator use and psychological well-being. Tbe Female Sexual Function Index was used. Prevalence of vibrator use was 52.5%, and use was significantly correlated (P<0.001) with having performed genital self-examination in the past month. Vibrator use was associated with more positive sexual function (including higher levels of desire and arousal and lower levels of pain). It was rarely associated with side effects(Herbenick, 2009).

Rubin et al and Billips et al published clinical guides for role of mechanical devices in treating female sexual dysfunction. These acknowledge the paucity of clinical evidence of effectiveness but also highlight the fact that these are generally safe and without significant adverse effect. (Rubin 2019; Billips 2002)

Proposed study

The acceptability of vulvar vibration therapy has been evaluated in women with vulvodynia, and found to be acceptable, however has not been assessed in women with a primary complaint of vaginismus.

This proposed study looks at the feasibility and acceptability of using clitoral vibration therapy, alongside current therapy, for women with vaginismus. It is likely that many, if not most, of these women will also have an element of vulvodynia. We propose that the use of external clitoral or vulval vibration therapy is likely to be acceptable in most women with vaginismus, based on acceptability of vulvar vibration therapy in women with vulvodynia. We propose based on the evidence above that vibrator therapy may help women with female sexual dysfunction to use vaginal dilators, based on study showing improvements with sexual distress and satisfaction.

Enrollment

This is a nonrandomized controlled trial, with the initial cluster of patients receiving standard therapy, and the second cluster receiving standard therapy plus vibrator. We aim to recruit an initial 15 participants who will receive standard therapy, and another 15 who will receive an external vibrator.

We expect this to take place over approximately 24-48 months. Enrollment of patients will be from a joint psychosexual clinic led by a medical doctor and a clinical psychologist. Female patients are referred to this clinic by General Practitioners, from within the Sexual Health service, or via Gynaecologists, frequently with complaint of difficulty or pain with penetrative sex. Inclusion and exclusion criteria have already been outlined.

Trial information will be given at the initial appointment. If the patient wishes to enrol, than an initial baseline questionnaire will be given, and a follow up questionnaire will be filled out by phone contact at 6-24months afterward the initial consultation at the patients consent.

5.1 Preclinical data

Preclinical trials are not applicable in this study.

Vibrators we propose to use in this study are not medical devices and are made from FDA-approved medical grade silicone.

5.2 Clinical data

A full description of available and relevant clinical data is documented in the review of literature in section 5.0.

Clinical data which will be gathered at baseline in order to compare two groups: Age, Parity, previous vaginal delivery, postmenopausal/premenopausal, gynaecological surgery, sexual orientation, patient self-described ethnicity, gender

5.3 Rationale

Vaginismus is the involuntary spasm of the pelvic floor muscles which surround the vaginal wall. It affects roughly 13 to 34% of premenopausal women and 6 to 45% of postmenopausal women (Meana, 2017). Vulvodynia, which has significant overlap with vaginismus, was estimated to affect 16% of women based on a National Institutes of Health (NIH) population-based study (Harlow & Stewart, 2003). Vaginismus can make sexual intercourse uncomfortable, painful, or impossible, and can have resultant impacts on a woman's sexual pleasure and ability to conceive and is associated with depression and anxiety. It can lead to secondary vulvodynia, or vulvodynia can co-exist.

Successful treatment relies often on both medical and psychosocial interventions alongside self-help and practice, although no standardised treatment exists. Current medical therapy for vaginismus often consists of the use of topical local anaesthetic gel, often in addition to oral medications such as low dose Tricyclic Antidepressants together with recommendation of progressive vaginal dilator therapy and physiotherapy. Whilst no one treatment or approach has a high degree of success, a combined approach has been shown to offer the most significant improvements.

Whilst anecdotally, some women find that clitoral stimulation can sometimes have a positive impact on the ability to progress with vaginal dilator treatment and enjoyment of sexual intimacy, this has not yet been evaluated in a research setting. This study looks at the feasibility and acceptability of using clitoral vibration therapy, alongside current therapy, for women with Vaginismus. This has the potential to guide clinicans' recommendations, which are currently not based in evidence, and if found to be acceptable, to pave the way for studies into efficiacy.

5.4 Risks / benefits

Of 49 eligible patients with vulvodynia, 83% of those surveyed who had used vulvar vibration therapy for at least two weeks had found it an acceptable treatment (Zolnoun, 2008)

Rubin et al published a clinical reference guide on sexual devices for clinicians in 2019 which stated that risks associated with sexual devices (such as vibrators) were traumatic injury or infection. Since we are recommending use of the vibrator for external use only, barrier use over sexual devices if shared, and proper disinfection to reduce risk of infection (Rubin, 2019).

The treatment period duration is 6-12 months.other studies looking at vulvar vibration therapy as an intervention have study periods of approximately 3-6 months.. We find that this allows patients to have completed any recommended intervention.

6. Study objectives

6.1 Primary objective

Is vibration therapy (through the use of handheld vibrators on clitoral and vulval area) acceptable to women as part of medical management of vaginismus and vaginismus/vulvodynia, alongside current medical management.

6.2 Secondary objective

Does the use of clitoral/ vulval vibrators help women to progress more easily with the use of vaginal dilators compared to women not using these? Is there any self-reported difference in experiences of pleasure or enjoyment around sexual experiences in the two groups of women as reported by FSDS and FISI Scores? Do more women report enjoyable sex? Are there any differences noted in reported ability to have or enjoyment of penetrative sexual intercourse?

6.3 Primary endpoint

Baseline and follow up questionnaires will be used – to assess acceptability and perceived acceptability of control therapy and intervention.

6.4 Secondary endpoint

Baseline and follow up questionnaires will be used specific to study and also FSDS and FISI.

7. Study population

Potential participants will be identified from the patients presenting to the Female Sexual Wellbeing Clinic. Identification of participants beyond this will not be needed. The identification of suitable participants will be done by the clinicians, using the inclusion and exclusion criteria taken into account. The clinic is a joint clinic run by a clinical psychologist and medical doctor, who will be providing the initial

questionnaire and the follow up phone interview. Medical students (with honary contract obtained) may also carry out interviews but not consent for the study.

Potential participants will be advised of the study verbally and given a written leaflet during their clinic appointment. Enrolment will be offered on the day on the understanding that the patient can decide to leave the study at any point.

Informed consent will be obtained. Consent will be taken by either the medical doctor or clinical psychologist in clinic. Verbal explanation of the study, together with a leaflet explaining the study will be provided.

If the study participants wish to enrol on the day, they will be able to. This may be preferable for convenience to avoid having to return to the clinic. Otherwise they will have 24hrs - 1 week to enrol. Enrolling on the day may be a preferred option for the patient so they do not have to return to clinic again. If they wish, they can take the written information away with them and return on another day.

Participants will enrol for approximately 6-24 months; this will be from the initial consultation until the follow up questionnaire, although no contact in the interim will be required as part of the research project there may be contact as part of any medical or psychological intervention separate to the project.

7.1 Inclusion criteria

- Able and willing to give informed consent (additional measures have to be in place if children, vulnerable adults or adults unable to give consent are included)
- Female
- Over the age of 18
- With symptoms and clinical signs consistent with vaginismus/ vaginismus and vulvodynia.

7.2 Exclusion criteria

- Unwilling or unable to give consent
- Transgender male / on testosterone therapy
- Inability to understand written and / or verbal English
- Current dermatological skin conditions requiring active treatment
- Genital herpes simplex virus symptoms within preceding 3 months
- Not reporting symptoms of vaginismus, and no evidence of vaginismus on clinical examination.

Pregnancy – via history from patient.

8. Study design

This study is a feasibility and acceptability study. The collection of qualitative data collection will be questionnaires, and interviews as described below. The data obtained will be analysed using thematic analysis to identify topics and patterns. In addition two formal, validated questionnaires will be used that can be scored to assess any change in sexual function and/or sexual distress.

Group 1 (Standard treatment)
We aim to recruit an initial 10-15 participants who will receive standard therapy with vaginal dilators and current medical management which usually consists of some or all of lidocaine gel (topical local anaesthetic applied to the vulva), tricyclic antidepressants (used in co-existing vulvodynia or vulval pain syndromes) and physiotherapy. Standard treatment also includes Group or individual psychotherapy.

Group 2 (Intervention)
In addition the standard treatment outlined above, the next 10-15 recruited will receive dilators and an external vibrator. This will take place over 6-24 months in a joint psychosexual clinic which is led by a medical doctor and a clinical psychologist.

Both groups:
Trial information will be given at the initial appointment. If the patient wishes to enrol, than an initial baseline questionnaire will be given for a patient to fill out after the clinic. A private space will be provided for the patient to do this, and there will be an offer for the patient to return to do this if preferred. Two formal, validated questionnaires will be carried out at baseline and follow up. These are the Female Sexual Distress Scale - R (FSDS) and the Female Sexual Function Index.

The follow up questionnaires will be filled out by phone contact 6-24 months after the initial consultation at the patients consent if they agree to remain enrolled in the trial for both group 1 and group 2. This will take approximately 30 mins and will be arranged at a time convenient for the patient. This interview will be carried out by a doctor. Answers will be recorded directly onto the follow up questionnaire proforma.

4 point Likert scale 1 (Strongly disagree) to 4 (Strongly agree)

9. Study procedures

- Informed consent – verbal and written will be given, patients will be offered opportunity to enrol on the day (for convenience) or to return at another point to enrol.
- Screening and recruitment – as outlined previously recruitment will be directly from clinic
- Randomization – this is a non-randomized controlled trial, as trial participants need to be identified as time goes on, and a certain number of control and intervention participants are needed. The initial 10-15 recruited will receive standard treatment, and then the next 15 will receive intervention.

Study interventions

Study intervention	***Contact (Visit) 1***	***Contact 2***		
Medical history	*X*			
Consent	*X*			
Baseline Questionnaires (FSDS, FSFI, custom questionnaire)	*X*			
Phone Interview (FSDS, FSFI, custom questionnaire)		*X*		

Vaginal dilators will be provided to both groups (if available) and external genital vibrators to the second (intervention) group.

- Concomitant medications – per standard treatment, patients with vulvodynia may be prescribed topical lidocaine gel and may also receive nortriptyline if there is unprovoked vulvodynia present.

- Criteria for discontinuation – if patients withdraw consent for being enrolled in the study then follow up will discontinue.

- Procedure for collecting data, including Case Report Forms (CRFs) and storage: CRFs will be filled out electronically, and stored in a password protected file. The research data will be archived for 25 years according to Queen Mary University of London/ Barts Health NHS Trust policy, JRMP SOP 20.

- Follow up will be via phone interview. Patients enrolled will receive a contact email address in case of queries in the meantime during research period.

- End of study duration will be at follow up questionnaire (at 6-24 months post initial appointment and questionnaire)

10. Assessment and management of risk

Patients the Female Sexual Wellbeing clinic sometimes find discussions embarrassing as we discuss sexual difficulties. This is not confined to patients in the study. We aim to minimise embarrassment and difficulties discussing sensitive topics by providing a questionnaire at baseline, and a follow up phone call rather than face to face interview is also likely to help reduce embarrassment. If the pilot study suggests that patients would prefer a different form of communication then this will feed into any further research. Financial loss for participants is not expected.

The clitoral vibrators supplied to the patients in the intervention group are already available for sale to people in the UK. No published long term side effects from the use of these are known or foreseen.

Rubin et al published a clinical reference guide on sexual devices for clinicians in 2019 which stated that risks associated with sexual devices (such as vibrators) were traumatic injury or infection. Since we are recommending use of the vibrator for external use only, barrier use over sexual devices if shared, and proper disinfection to reduce risk of infection (Rubin, 2019).

In the unexpected case of an SAE this will be reported via the appropriate routes and the study management group will decide on whether the study should proceed or not. Participants will have an email address to contact the CI in case of AE or SAE.

No risks to researchers foreseen.

11. Statistical considerations

Qualitative study N/a

11.1 Sample size

Pilot / Feasibility study
30
This is a realistic number we can expect to recruit (15-20 in each study arm) over the course of 24-48months as a feasibility study.

11.2 Method of analysis

Qualitative analysis with thematic analysis. Some numerical analysis of formalised questionnaires, although statistical analysis will not be relevant will small numbers proposed.

12. Ethics

We do not anticipate any complex ethical, legal or management issues arising from the study at present. We are not proposing a deviation away from our current standard of care, but an additional therapy to be offered to patients enrolled in the intervention arm of the study.
Informed consent: patients will be given the opportunity to enrol in the study at the initial appointment but will be given the option to return 24hrs to one week later if they wish to enrol later.

Recruitment:

- We have necessary and exclusion criteria, one of which being requirement of use of a translator. The initial appointment and consenting for the study will involve a lot of information verbally, and translating questionnaires and patient information leaflets will not be an option for us.

Burdens foreseen:

- It is likely that explanation of the research, and how to use a clitoral vibrator, will require some additional time investment during the clinic although again we do not predict that this will have a negative impact on the quality of service offered in the clinic.
- The burden to the patient we feel will be minimal, with the offer of enrolment into the study on the day of clinic this will potentially avoid unnecessary visits. The follow up questionnaire will be via phone interview so further vists will be avoided.

Benefits foreseen:

- Patients will not receive monetary compensation but if in intervention group will receive a clitoral vibrator as part of the study which they will be able to keep

Other impacts:

Patients in our clinic sometimes find discussions embarrassing as we discuss sexual difficulties. This is not confined to patients in the study. We aim to minimise embarrassment and difficulties discussing sensitive topics by providing a questionnaire at baseline, and a follow up phone call rather than face to face interview is also likely to help reduce embarrassment. If the pilot study suggests that patients would prefer a different form of communication then this will feed into any further research.

Conflict of interest:

- None foreseen. None of the investigators are receiving any personal monetary grant or fund from study funders.

12.1 Annual Safety Reporting

The CI will send an Annual Progress Report to the REC and the sponsor using the HRA template on the anniversary of the REC "favourable opinion".

13. Public Involvement

This is a pilot study and is aiming only to look at feasibility and acceptability. Results and feedback from this study can therefore be used to guide any further research. Findings will be disseminated via the wordpress site we currently use to provide information to patients and staff, and we will seek advice from patients in how they wish us to disseminate findings and who they feel we should reach out to with results.

14. Data handling and record keeping

14.1 Data management

Methods of data capture:

- Patient medical records
- Baseline and follow up questionnaire
- Design of data capture forms – transcription of questionnaire results onto spreadsheet for further analysis
- Transfer and storage of data in central study database on shared drive password protected.

14.2 Source data

Source Data (baseline questionnaire, follow up questionnaire) generated by study. Source documents – medical history, patient demographics (age) will be accessed only to obtain the medical history necessary for the study (diagnosis, treatments provided, patient age).

14.3 Confidentiality

Potential participants will be identified from the patients presenting to the Female Sexual Wellbeing Clinic. Identification of participants beyond this will not be needed. Information related to study participants will be kept confidential and managed in accordance with the Data Protection Act, the General Data Protection Regulation (GDPR) 2018, NHS Caldecott Principles, the UK Policy Framework for Health and Social Care Research, and the conditions of Research Ethics Committee favourable opinion.
Access to participant healthcare records and source documents will only be by treating medical team which includes CI and PI.
Anonymisation of research data will take place upon data collection.

14.4 Record Retention and Archiving

The research data will be archived for 25 years according to Barts Health NHS Trust policy. The data will be archived in the Modern Records Facility, 9 Prescot Street, Aldgate, London, E1 8PR, in physical form. After this point, the records will be destroyed.

15. Laboratories

N/a

16. Interventions and tools

16.1 Devices

Vibrator for external use. Not a medical device. Carries the CE MARK and complies with Directive 2011/65/EC Restriction on Hazardous Substances.

16.2 Techniques and interventions

Patient information leaflet will be supplied, which will detail explanations of vaginismus and vulvodynia, female sexual arousal, and massage techniques useful in these conditions.
The intervention group will receive an external clitoral vibrator for home use.

16.3 Tools

Two formal, validated questionnaires will be used at baseline and at follow up in the study participants to assess response to treatment and intervention; the Female Sexual Distress Scale and the Female Sexual Function Index.

The Female Sexual Distress Scale (FSDS) (Derogatis, 2002) measures sexually related personal distress in women. The reliability and validity of the scale was assessed in sexually functional and dysfunctional women in three studies of approximately 500 women. The revised version contains 13 questions. It has been used to assess treatment response.

The FSDS-R measures patient-reported outcomes covering different aspects of sexual activity-related distress in women. Responses are scored from never (0) to always (4) and results in a total score of 0 to 52. Higher scores therefore equate to a higher reported level of sexual distress.
The FSDS-R had considerable scale reliability – Cronback's alpha values ranged from a=0.87 to a=0.93 and good test-retest reliability (intraclass correlation coefficient from r=0.74 to r=0.86. A cutoff score >11 was shown to be effective in differentiating women with and without Female Sexual Dysfunction.

The Female Sexual Function Index is another questionnaire which is widely used in the evaluation of female sexual dusfunction, assessing six main areas: desire, subjective arousal, lubrication, orgasm, satisfaction, and pain (Rosen, 2006). Higher scores equate to better sexual function. A score under 26.55 relates to low sexual function, with an individual score under 3.6 signifies low function in that area (Wiegel, 2005).

16.4 Medicinal product

N/a

16.5 Other biological or chemical products

N/a

17. Safety reporting

Adverse Events (AEs) and Adverse Reactions (ARs) will be recorded.
Serious Adverse Events (SAEs) and Serious Adverse Reactions (SARs) will be reported to the CI as medical assessor for the sponsor and coordinating team.
All unexpected SARs (SUSARs) will be reported to the JRMO and REC.

DEVICE DEFECTS, RECALLS and ALERTS

The intervention is an external vibrator which is available for sale in the UK. It is not a medical device.

17.1 Adverse Events (AEs)

An AE is any untoward medical occurrence in a participant to whom an intervention has been administered, including occurrences which are not necessarily caused by or related to that intervention. An AE can therefore be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with study activities.

In a study of the effects of genital vibration therapy in women with arousal and orgasm disorders, light-headedness, agitation, headache, facial flushing, were each reported by 4-8% of participants, with 2% reporting some genital numbness, dizziness or cramping (Guess, 2008).

17.2 Adverse Reaction (ARs)

An AR is any untoward and unintended response in a participant to an intervention. All adverse events judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to the intervention qualify as adverse

reactions. The expression 'reasonable causal relationship' means in general that there is evidence or an argument to suggest a causal relationship.

17.3 Notification and reporting of Adverse Events and Reactions

If the AE is not defined as serious, the AE will be recorded in the study documents and the participant followed up by the research team. The AE will be documented in the participants' source documents, the Case Report Form (CRF), and, where appropriate, medical records.

17.4 Serious Adverse Events (SAEs) or reactions

A serious adverse event (SAE) is defined as an untoward occurrence that:

- Results in death,
- Is life-threatening,
- Requires hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability or incapacity,
- Consists of a congenital anomaly or birth defect, or
- Is otherwise considered medically significant by the investigator.

SARs will be reported to the REC where in the opinion of the Chief Investigator the event was serious and:

- Related (it may have resulted from administration of any of the research interventions), and
- Unexpected (the type of event is not listed in the protocol or other Reference Safety Information as an expected occurrence).

17.5 Notification and reporting of Serious Adverse Events

Serious Adverse Events (SAEs) that are considered to be 'related' and 'unexpected' will be reported to the sponsor within 24 hours of learning of the event, and to the REC within 15 days in line with the required timeframe.

17.6 Urgent Safety Measures

The CI will take urgent safety measures if necessary to ensure the safety and protection of the clinical study participant from immediate hazards to their health and safety. The measures will be taken immediately. The approval of the REC prior to implementing urgent safety measures is not required. However the CI will inform the sponsor and Research Ethics Committee (via telephone) of this event immediately.

The CI will inform the REC in writing within 3 days, in the form of a substantial amendment. The sponsor (Joint Research Management Office (JRMO)) will be sent a copy of the correspondence with regards to this matter.

17.7 Annual Safety Reporting

The CI will send the Annual Progress Report to the REC using the HRA template (the anniversary date is the date on the REC "favourable opinion" letter) and to the sponsor.

17.8 Overview of the Safety Reporting responsibilities

The CI is the medical assessor on behalf on the sponsor and will review all events reported. The CI will ensure that safety monitoring and reporting is conducted in accordance with the sponsor's requirements.
The CI and PIs will ensure all SAE reporting is conducted in accordance with the sponsors timelines. Any SAE will be acted upon within a week of receipt of and where necessary, any relevant patients contacted and the intervention will be recalled.

18. Monitoring and auditing

The sponsor or delegate retains the right to audit any study, study site, or central facility. Any part of the study may be audited by the funders, where applicable.

This is an initial, small feasibility study. Proposals will go through an internal peer review process with our research lead. Due to the low risk of safety issues associated with this intervention, no monitoring will occur routinely for the pilot study. Contact details are available for the patients if any issues occur.

19. Trial committees

A study management group consisting of the CI, PIs, collaborators, and any grant holders, will ensure appropriate oversight of the study data and participant safety. A meeting will be held in the case of any AE or issues raised by participants or investigators in the study. This is a small, single-centre study. A trial steering committee will not be necessary.

20. Finance and funding

Subsidised (cost-price vibrators) from 'Mysteryvibe'.
Organisation:
Mysteryvibe
Soumayadip Rakshit (CEO)
Mysteryvibe, 10 York Road
London
SE1 7ND

21. Indemnity

NHS indemnity scheme will apply. It provides cover for the design, management, and conduct of the study.

22. Dissemination of research findings

Will aim for peer reviewed publication, but if this does not happen then minimum would be dissemination on website and to the regional sexual health network.
If participants wish they will be emailed a summary of the results.

- Aiming for publication in a peer reviewed journal
- The sponsor will be acknowledged in any write up
- If published, the results will be accessible on a publically accessible database
- Presentation at academic conferences if accepted – will apply for this
- Communicating results to former study participants and the public – via email if participants agree to this
- Involving research participants in the dissemination process – we will take input from participants in how they want the research disseminated if not covered by the above
- Internal dissemination at Barts Health NHS Trust and Queen Mary University of London
- Use of the results to change practice or to develop new research or innovation – will provide support for recommendation of vibration therapy for vaginismus/vulvodynia.

23. References

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