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Section 1 Study Documentation

UNIVERSITY COLLEGE LONDON HOSPITALS NHS FOUNDATION TRUST

SAFFRON Trial

Study Closedown Plan

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v1.5

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This document outlines the requirements to terminate this trial ahead of the previously contracted end date due to trial closure as requested by NIHR/HTA. It includes details about ongoing activities, completed activities, the cost analysis, information about deliverables, staffing and other resources, and a suggested time frame (including a Gantt chart).

Authors, investigators, experts and advisors involved in the trial

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Trial Sites

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PRIMENT Clinical Trials Unit
PRIMENT is a fully registered UK Clinical Research Collaboration (UKCRC) Clinical Trials Unit (CTU) (reg number 20) based in three centres in UCL: the Department Of Primary Care And Population Health; the Division of Psychiatry; and the Department of Statistical Science.

List of acronyms

CI	Chief Investigator
CTU	Clinical Trials Unit
DMEC	Data Management and Ethics Committee
IP	Intellectual Property
IPT- GO	Interpersonal Psychotherapy for Sexual Adjustment post Gynaecological Cancer
RA	Research Assistant/ Associate
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
TMG	Trial Management Group
TMT	Trial Management Team
TSC	Trial Steering Committee
UCLH	University College London Hospitals NHS Foundation Trust
UH Bristol	University Hospitals Bristol NHS Foundation Trust

Activities Completed for Closedown to Date

- A meeting of the TMG was held on 26/11/15 and all co-investigators were informed of the trial closure. An early draft of the closedown plan was discussed.
- A meeting of the TMT was held on 30/11/15 and activities required for the closedown plan were delegated to RAs. A second TMT meeting on the 07/12/2015 discussed the draft plan and made further recommendations which were circulated to the project team. A further TMT meeting on 14/12/2015 reviewed final changes for the document to be sent to members of the TSC for comments.
- RAs met with the trial co-ordinator from Priment CTU to discuss contractual agreements with the CTU and external bodies (e.g. Sealed Envelope database developers).
- Heads of Gynaecology-Oncology team at both UCLH and UH Bristol were informed about the trial closure.
- Members of the TSC were informed about the trial closure by email. This draft is for members of the TSC for their consideration, recommendations and ultimately endorsement when it meets their requirements.

Cost Analysis

(Spreadsheet to be attached subsequent to TSC approval of activities within the plan)

Ongoing Activities

Site Visit to Bristol

In Month One of study closure the CI and RAs will visit the site at University Hospital Bristol in order to discuss the closedown of the study and the implications for the team there. The two RAs had developed good working relationships with the clinical team at Bristol and it was suggested by the TMG that it would be appropriate for them to go (as well as the CI) and break the news in person, explain the reasons for the closedown, and explain the possibilities going forward.

The MDT co-ordinator will be contacted to find a suitable date for this visit and these discussions to take place. This visit will require the cost of train travel and overnight accommodation for three staff members.

Payment to Co-investigators

Co-investigators have been notified of the closure of the study. It must be clarified with the holders of the fund that all invoices for work previously carried out have been submitted before the final closure. The details of these payments are included in the financial reconciliation statement (see separate document *to be attached once this plan is agreed*) and the amount to be paid will be negotiated with the NIHR/HTA.

Training

The training for level 2 and 3 practitioners is now complete. However, following the early closure of the trial an additional training session for both level 2 and level 3 practitioners will be required to discuss how the study materials can be used in clinical practice and the restrictions on usage (see Intellectual property section). Detailed discussion is necessary on how best to use the new knowledge they have gained, and it is crucial to stress to them that the intervention cannot be delivered to future patients as an evidence based tool, and current best evidence-based practice should be adhered to. Train travel will need to be provided for the Level 2 and Level 3 practitioners from Bristol to come to

London to attend this training session. As Prof Lemma has severely restricted time available this is likely to require two separate days for psychologists and CNS/radiographer.

Approvals Process

The approvals process for the study is still underway and so the TMT will need to inform REC, and trial registration bodies.

Feedback to Organisations

A number of delays to the study occurred due to structural and systemic issues within clinical and research organisations. We intend to analyse and record in detail all of these, and feedback to these organisations in order for them to address these issues and avoid delays on future projects.

Informing DMEC and Ethics Committee

Data Monitoring Committee members will need to be informed individually about the closedown of the study. The Ethics committee will be formally notified once the closedown plan is agreed by HTA.

Archiving

Study materials will need to be archived in accordance with ethical guidelines. This includes Trial Master File and Investigator Site File.

Deliverables

Final Report

SAFFRON RAs, in collaboration with co-investigators, will work on putting together a final report to the HTA including lessons learnt about conducting a psychosocial study in a medical setting.

Analysis Plan

Although no patients were recruited to the study, the development phase of the SAFFRON trial faced many barriers and challenges leading to preliminary feasibility findings in regards to setup of a psycho-sexual multi-centre RCT in an NHS setting. We believe it is important that these findings are properly considered and analysed for inclusion in the report so lessons learnt can be disseminated.

Dissemination

A report to HTA describing set up of the study with lessons learnt as part of the feasibility report on factors affecting the effective introduction of psychological intervention studies into existing medical clinics.

Feedback to organisations and governance bodies will be given to ensure that issues encountered by the research team can be addressed. Although not associated with the delays that led to closure feedback thus far has led to the development of a new SOP in PRIMENT CTU in regards to the role of health economists in trials.

Publication

If there is sufficient material, and in order to optimise the returns on the time spent on the study so far, we consider that there may be two publishable papers following from the final report.

1. A paper addressing feasibility issues in setting up a psychological intervention study within existing clinical teams within the NHS. The qualitative and narrative experience of the trial team can be used for this.

2. An organisational change paper detailing changes needed in a range of organisations to respond to psychosocial research in cancer settings. We have learned recently that SAFFRON is not the first study to face major delays in our settings for procedural and bureaucratic reasons. Making these explicit, together with a summary of costs in time and money lost would be valuable for the planning of future trials in the current environment, where there is a great desire to increase psychological intervention studies in the field of cancer. Such a paper should be useful to both the settings of UCL/UCLH and to NIHR.

Intellectual Property

UCL's Intellectual Property (IP) Rights office have been contacted about putting the materials developed for the three levels of intervention into the public domain as mentioned by Prof Whalley in his letter. These comprise: Level 1 – psycho-education self help booklet; Level 2 - adaptation of psychological intervention originally devised by Brotto and Heiman; Level 3 – a newly written adaptation of Interpersonal Therapy (IPT) for gynaecological cancer patients after treatment (IPT-GO).UCL has advised the research team to approach all involved parties and get their formal agreement to put this information into the public domain. We foresee difficulties with this process, however, as the original contract vests the copyright of any output with UCL, and copyright holders may not allow the release of these materials. Further, there are ethical constraints on the release of materials that have not been validated or tested empirically. Therefore although the study team have worked on, and adapted, the original materials, there are serious constraints on these entering the public domain. Materials are as follows:

1. The original copyright owners for level 1 only gave permission to the CI for their use in the SAFFRON study. UCL has advised that their prior art (drawings and figures that appeared in the original versions of the materials) and the restrictions on third party access rights will prevent any publication of the content unless express permission has been granted. Thus, this will need to be done during close down (from the authors Dara Brandenburg, Lorraine Grover, Barry Quinn, Leslie Schover & Michael Randers-Pehrson, plus the American Cancer Society who currently hold the copyright and some of the IP for some sections).

2. Similarly the nurse-led psychoeducation intervention (treatment manual and worksheets), that was used as the level 2 intervention, also has publication restrictions. The authors Brotto & Heiman only gave permission for use within the SAFFRON study. These two authors would need to be approached individually and permissions gained to release these documents into the public domain.

3. The IPT-GO manual is an adaptation of a therapy (Interpersonal Therapy) which requires a structured and formal training process to certify practitioners. This certification includes participation in an accredited course that lasts two days or more, professional clinical training in a mental health setting and supervision by a certified IPT supervisor for two complete cases, as well as a judgment of clinical competence by the IPT supervisor. Such supervision must be based on audio-recordings of sessions and must be a minimum of one hour per two hours of therapy.

The full criteria for IPT Research Certification can be found at: https://iptinstitute.com/ipt-research-certification/.The trainer must be satisfied that the trainee can work within the model clinically before approving them as therapists within this model. For this reason it would be unethical for the manual to be released alone, whereby uncertified practitioners may attempt to use the manual. This could lead to liability issues if the publicly available therapeutic manual is misused. Furthermore, IPT is a restricted title and therapy and the original owners must approve the adaptation which has not yet happened. For

any output this is an action that must occur under IP. IPT is a trademark and there are therefore legal constraints in using this title without the express permission of Myrna Weissmann.

Due to the complexity of these negotiations this is expected to span at least two months.

Staffing Resources

All activities outlined above will be led by the CI and carried out by the RAs in dialogue with the co-applicants and PRIMENT CTU. These activities, as summarised in the table below, will require 3 months from the agreement of the closedown plan. In addition, we are under a moral obligation to the RAs to provide a sufficient notice period so as not to negatively affect their career progression and alternative employment prospects. The 3 month notice period would also allow for redeployment within UCL.

If the RAs find alternative employment before the end of the 3 month closedown period the achievement of the contents of this plan will require temporary staff to complete the specified work and documents in accord with the Gantt chart timings. The CI is fully clinically committed outside the SAFFRON hours and cannot increase this time commitment.

CI time also needs to continue over this period for management of the close-down and of the RAs' activity.

Other Resources

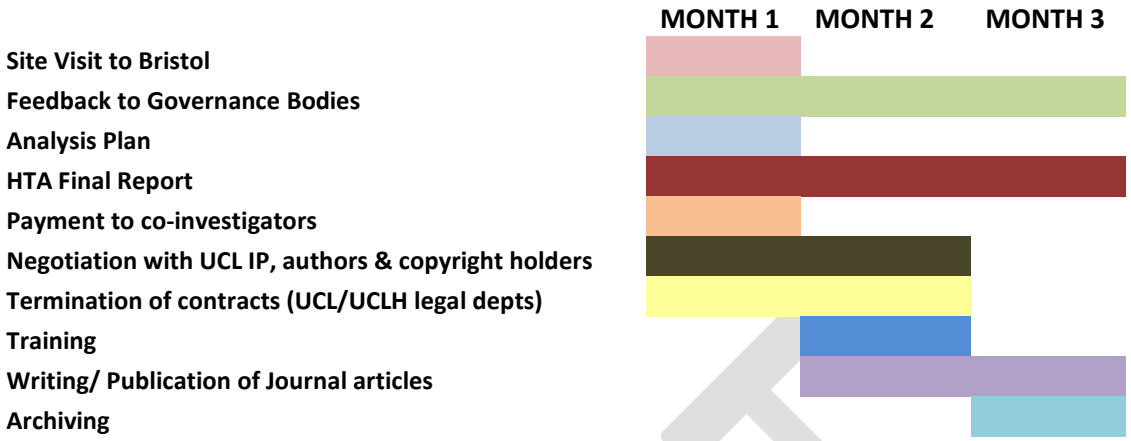
- Toner and paper to cover 3 month closedown period
- Postage costs
- Travel to and from Bristol for CI, RAs and level 2 and 3 practitioners

Timeframe

We suggest a 3 month timeframe starting from the point of closedown agreement between the research team and the funder. The breakdown of this time use is displayed in the Gantt chart below.

It is predicted that at least one month will be needed to produce the final report for HTA. Organisation of training for collaborators and intervention deliverers (finding agreed dates) will take time, and likely require separate days for level 2 and level 3. Feedback to governance and organising bodies will be an ongoing process over a number of weeks, dependent on availability of key staff.

Gantt Chart



Recommendations from TSC

TSC were sent a copy of the Closedown Plan on the 16/12/2015 in place of the pre-arranged TSC meeting. Members were given the opportunity to comment on the closedown plan.

The Chair of the TSC consulted with the other members and reported to NIHR and the CI on 03/01/2015. Their recommendations are listed below:

1. TSC members were unanimously agreed that the intervention materials have not been tested in a trial, and that it is premature to make these available to the general public. The intellectual property of the original authors needs to be respected and these authors need to be reassured formally by the team that their work will not be used or made available to others unless a new contract is instigated. We realise a huge amount of time has gone into developing these materials and commend the team for their work in this area. We hope that versions of the treatment and training materials can be used in a future RCT so that the work is not wasted.

2. We agree that staff already trained in the intervention need to be debriefed including engaging in a detailed discussion on how best to use the new knowledge they have gained. It is important to stress that the intervention cannot be presented to future patients as an evidenced based tool and where possible, current best evidence should be adhered to.

3. We agree that lessons learned from this trial experience should be shared for the benefit of other teams involved in or considering running complex intervention trials. HTA reports are open access and we wondered if it might be best to have a single source to deal with all the issues raised. For this reason, we feel the report should be the key focus of the outputs for the closedown plan. This can then be followed by a published article or possibly two if there is sufficient material.